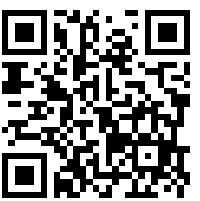

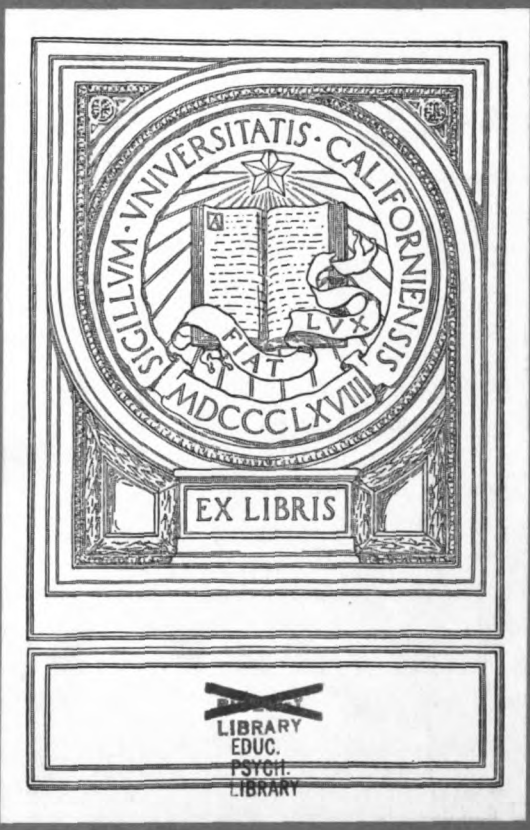

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MENTAL SCIENCE

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VOL. LXXXVI

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MCMXL

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- (vi) Municipal Hospitals: Erdington House (Birmingham), Smithdown Road (Liverpool).

(2) SCOTLAND.
- (i) Royal Asylums and Hospitals: Aberdeen, Crichton (Dumfries), Dundee, Edinburgh, Glasgow (Gartnavel), Montrose, James Murray's (Perth).
- (ii) All City and District Asylums and Mental Hospitals.
- (iii) Poor Law Asylum: Greenock.
- (iv) Poor Law Hospital: Stobhill Hospital (Glasgow).
- (v) Private Mental Hospital: New Saughton Hall (Polton).

(3) IRELAND.
- (i) All County, City and District Asylums and Mental Hospitals.
- (ii) Criminal Asylum: Dundrum.
- (iii) Chartered Hospitals: St. Patrick's.
- (iv) Private Mental Hospital: Farnham House (for Female Nurses only).

(4) CHANNEL ISLANDS.
Jersey Mental Hospital.

(5) FEDERATED MALAY STATES.
Central Mental Hospital, Tanjong Rambutan, Perak.

(6) INDIA.
Ranchi Mental Hospital for Europeans, Kankè, Province of Bihar and Orissa.

(7) SOUTHERN RHODESIA.
Ingutsheni, Bulawayo.

(8) SYRIA.
Lebanon Hospital.

FOR TRAINING THOSE NURSING MENTAL DEFECTIVES.

(1) ENGLAND.
- (i) State Institutions: Rampton, Moss Side.
- (ii) Certified Institutions: Aston Hall, Nr. Derby; Botleys Park, Surrey; Brentry, Bristol; Brockhall, Blackburn; Bromham House, Nr. Bedford; Brunswick House, Mistley, Essex (for Male Nurses); Calderstones; Cell Barnes Colony, Herts; Clerks Croft, Surrey; Coldeast Colony, Nr. Southampton; Coleshill Hall; Cranage Hall, Holmes Chapel, Cheshire; Farmfield, Horley, Surrey; Great Barr Park Colony; Harmston Hall Colony (with Holbeach, Bourne and Caistor ancillary premises), Nr. Lincoln; Hensol Castle, Pontyclun, Glam.; Hortham, Bristol; Leicester Frith Institution; Leybourne Grange Colony, Kent; Little Plumstead Hall Colony (with Heckingham ancillary premises), Norfolk; Middlesex Colony, Shenley; Monyhull Colony; Pewsey Colony, Wilts; Royal Albert Institution; Royal Earlswood; Royal Eastern Counties; St. Catherine's Institution, Doncaster; St. Andrew's Colony, Morpeth; Sandhill Park (with ancillary premises); Silverton House, Northumberland (for Female Nurses); South Ockenden Colony, Essex; South Side, Streatham; Stoke Park Colony, Bristol; Stretton Hall, Leicester; The Manor, Epsom; Thornhill, Derby; Western Counties Institution.

(iii) Approved Institutions: Darenth Park, Leavesden, Caterham, Fountain (for Female Nurses only).
(iv) Certified Houses: Normansfield.

(2) SCOTLAND.
Baldovan; Gogarburn, Edinburgh; Lennox Castle; Royal Scottish National Institution; Stoneyetts.

FOR TRAINING FOR THE CERTIFICATE IN OCCUPATIONAL THERAPY.

ENGLAND.
North Riding Mental Hospital, York.
Chester Mental Hospital, Upton, Chester.
Cardiff City Mental Hospital, Whitchurch, Glam.
Lancashire County Mental Hospital, Whittingham.
The Old Manor, Salisbury.

The Library and Secretary's Office.

11 CHANDOS STREET, LONDON, W. 1.
Telephone: Langham 1495.

Secretary and Assistant Librarian.—Miss M. HIGGINS.

Publications.

From MESSRS. ADLARD & SON, LTD.:

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Enquiry (History) Form for use in Mental Hospitals. In three sizes. Prices and specimen forms on application.

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"Handbook for Mental Nurses." 7th edn. 1923. Price 6/-.
"Manual for Mental Deficiency Nurses." 1931. Price 6/-.
"Occupational Therapy": Addendum to "Handbook". 1938. Price 6*d*.

From the REGISTRAR, Littleton Hall, Brentwood, Essex.

"Syllabuses", for the Examinations for the Certificates of Proficiency in Mental Nursing and in Nursing Mental Defectives. Price 2*d*. each. Postage ½*d*.
"Syllabuses", for the Examination for the Certificate of Proficiency in Occupational Therapy. Price 2*d*. each. Postage ½*d*.
"Regulations and Rules for the Nursing Examinations." Revised, 1938. Price 1*s*. each. Postage 1*d*.
"Examination Papers, 1928–38." Price 1*s*. 6*d*. each. Postage 1*d*.

Honours Roll.

Year.	Gaskell Medal and Prize.	Bronze Medal and Prize.
1883	—	J. Wiglesworth.*
1884	—	S. R. Macphail.
1885	—	T. D. Greenlees.*
1886	—	—
1887	J. E. D. Mortimer.	J. Wiglesworth.
1888	—	—
1889	T. B. Hyslop.	—
1890	G. M. Robertson.	J. C. Mackenzie. W. J. Smythe.
1891	—	—
1892	Nathan Raw. G. R. Wilson.	G. M. Robertson.
1893	—	A. W. Campbell.
1894	—	C. Beadles.
1895	G. W. F. Macnaughton.	—
1896	W. R. Dawson.	J. Turner.
1897	C. Hubert Bond.	—
1898	—	J. R. Lord.
1899	—	F. G. Crookshank.
1900	Maurice Craig.	C. C. Easterbrook.
1901	W. H. B. Stoddart.	—
1902	G. H. Grills.	—
1903	—	—
1904	—	A. A. D. Townsend.
1905	—	—
1906	J. M. Rutherford.	C. J. Shaw.
1907	—	—
1908	—	S. C. Howard.
1909	H. Devine.	C. F. F. McDowall.
1910	—	H. Morton.
1911	J. G. P. Phillips.	G. H. Garnett.
1912	W. Boyd.	—
1913	W. R. Thomas.	D. McKinley Reid.
1914	—	J. C. Wootton.
1915	—	—
1916	—	—
1917	J. C. Woods.	—
1918	—	—
1919	J. Walker.	R. Eager.
1920	—	—
1921	—	—
1922	—	W. S. Dawson.
1923	J. T. H. Madill.	—
1924	Mary Barkas.	—
1925	W. S. Dawson.	—
1926	G. de M. Rudolf.	P. K. McCowan.
1927	Elizabeth Casson.	—
1928	F. R. Martin.	—
1929	Alexander Walk.	—
1930	G. W. T. H. Fleming.	Duncan Macmillan.
1931	—	J. H. Ewen.
1932	Muriel L. M. Northcote.	W. R. Ashby.
1933	Louis Minski. Desmond Curran.	D. N. Parfitt.
1934	William Blyth.	H. C. Beccle.
1935	—	Arthur Guirdham.
1936	S. W. Hardwick.	D. K. Bruce.
1937	—	E. S. Stern.
1938	E. H. Kitching.	F. T. Thorpe.
1939	Eliot Slater. J. A. Hobson.	G. Tayleur Stockings.

* Prize only.

Medals and Prizes.

The Gaskell Gold Medal and Prize.

(Value not less than £30.)

This Medal and Prize was established, at the Annual Meeting held on August 9, 1886, in honour of Samuel Gaskell, Esq., F.R.C.S., at one time Medical Superintendent of the County Asylum, Lancaster, and afterwards for 17 years a Commissioner in Lunacy. Upon his death on March 16, 1886, his sister, Mrs. Holland, gave £1000 to the Association, and other members of the family contributed further sums amounting to £340. The interest of this sum is given annually as a prize to the candidate who most distinguishes himself in an Examination in the subjects hereunder mentioned.

The examination must be held in England according to the terms of the Trust.

(1) Candidates must produce evidence: (*a*) Of having attained the age of 23. (*b*) Of having been qualified Medical Officers in one or more mental hospitals or clinics in psychiatry in the United Kingdom or elsewhere in the British Empire for at least two years. (*c*) Of possessing the Certificate in Psychological Medicine of this Association or a degree or diploma in Psychological Medicine of one of the Universities or Examining Boards having the power to grant medical qualifications registrable in the British Isles or elsewhere in the British Empire.

(2) Candidates will be examined in: (*a*) Psychology. (*b*) Anatomy, Histology and Physiology of the Nervous System, reproductive and endocrine glands; Pathology of the above, especially in relation to mental disorders. (*c*) The diagnosis, prognosis, treatment and legal relations of mental disorders. (*d*) Clinical cases.

An entry fee of £3 3*s*. is charged, returnable to bona-fide candidates.

The Bronze Medal and Prize.

(Value Ten Guineas.)

The Bronze Medal and Prize was established at the Annual Meeting held on August 2, 1882, and is awarded to any assistant medical officer of a mental hospital (public or private) for the best dissertation on a clinical or pathological subject relating to mental disorders.

The following is an abstract of the conditions:

(1) The dissertation to be written in English.

(2) Each dissertation to be distinguished by a motto or device, and accompanied by a sealed envelope containing the name and residence of the author, and having on the outside a motto or device corresponding with that on the dissertation.

(3) The dissertation shall not exceed 10,000 words in length.

(4) The dissertation and every accompanying drawing and preparation will become the property of the Association, to be published in the Journal at the discretion of the Editors.

(5) The dissertations not approved, with their accompanying drawings and preparations, will, upon application within one year, be returned, together with the sealed envelopes unopened; if not claimed within one year they will become the property of the Association.

(6) The dissertations for the year must be delivered to the Registrar before April 30.

(7) No prize will be awarded if none of the dissertations is of sufficient merit.

Divisional Prizes for Assistant Medical Officers.

(Two Prizes of £10 and £5 respectively.)

The proposal to award Divisional Prizes under the conditions set out below emanated from the Irish Division and was adopted at the Annual Meeting held on July 13, 1911.

(1) Two prizes of £10 and £5 respectively will be awarded annually by the Association (provided sufficient merit be shown) for the best paper read during the preceding calendar year at a Divisional Meeting by an Assistant Medical Officer or Assistant Physician in a Psychiatric or Neurological Institution or Service. (*See also Regulation* No. 7.)

(2) Competitors must be members of the Association.

(3) Only one paper by a competitor can be entered during any competitive year. The same applies to a paper entered by more than one author.*

(4) Only papers certified by the Secretary of the Division (in the absence of the Secretary, the Chairman of the Meeting) to have been read at a meeting of the Division and to be eligible for this competition can be entered. Divisional Secretaries are to withhold their certificates in cases where there has occurred material alterations or additions.

(5) Papers certified as eligible for the competition shall be forwarded to the Registrar not later than April 30 of the following year. They shall be submitted to the Examiners for the Certificate in Psychological Medicine for report and then adjudicated on by the President. Publication shall not invalidate a paper for adjudication.†

(6) The results shall be announced, and the prizes awarded, if any, by the President at the Annual Meeting in the year following the competitive year.

(7) Papers by more than one author can be entered and any prize awarded will be divided among the authors.

(8) If in any competitive year, one or two papers only are submitted for competition the Council may withhold either or both prizes; or it may, after considering the report of the Adjudicator, and if in its opinion the paper or papers are of outstanding merit, award a first or second or both prizes, at its discretion.

The Certificate in Psychological Medicine.

This Certificate was founded at the Annual Meeting held on August 4, 1885, *and the first examinations were held in* 1886.

Candidates must be at least twenty-one years of age, and must produce a certificate of having had at least three months' clinical experience of mental disorders, or of having attended a course of lectures on insanity and the practice of a mental hospital (where there is clinical teaching) for a like period, or they shall give such proof of experience in mental disorders as shall, in the opinion of the President, be sufficient.

The examination is held yearly, and is in three parts: (1) Written. (2) Oral. (3) Practical.

Candidates must be registered under the Medical Act (1858) before the certificate is bestowed.

The fee for the examination is £3 3s., and intending candidates should communicate with the Registrar, who will supply date and place of examination.

Candidates failing in the examination may present themselves at the next or subsequent examinations on payment of a fee of £1 1s.

* This means that the joint authors (though separately eligible) cannot enter another paper in the competitive year.

† The original MS., certified in accordance with Regulation No. 4, is to be submitted. Only under exceptional circumstances can a certified reprint of a published paper be accepted, but a reprint, where possible, should accompany the certified original MS.

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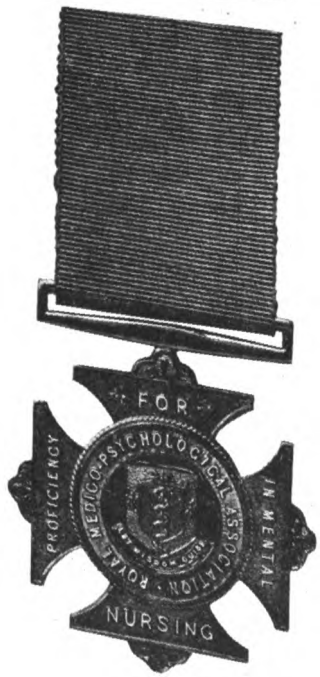
The Insignia of the Nursing Certificate.

The Certificate of Proficiency in Mental Nursing was founded at the Annual Meeting held on July 24, 1890.

The Nursing Medal.



The Nursing Badge.

The Nursing Badge was founded at the Annual Meeting held on July 11, 1928.

Honorary Certificate in Mental Nursing.

1928. H.R.H. The Princess Royal.

The Campbell Clark Gold Medal and Prize.

This Prize was instituted in 1933 in memory of the late Dr. Campbell Clark, and is awarded in May and November of each year to the candidate, whether male or female, who obtains the highest number of marks at the Examination for the Certificate of Proficiency in Mental Nursing. It is provided that only candidates who have completed the whole of their training in one institution are eligible. The value of the prize is Three Guineas, together with the Medal.

Winners of the Campbell Clark Medal.

1933, May.	Arthur Barnett Hindson, Cambridge Mental Hospital.
,, Nov.	Florence Barber, Maudsley Hospital.
1934, May.	Cissie Morris, Bexley Mental Hospital.
,, Nov.	John Humphries, Belfast Mental Hospital.
1935, May.	Thelma Mary Preece, Powick Mental Hospital.
,, Nov.	Ronald Nears, Claybury Mental Hospital.
1936, May.	Winifred Amelia Hill, Erdington House.
,, Nov.	Norah Peck, Brentwood Mental Hospital.
,, ,,	Frederick Austin, Hull City Mental Hospital.
1937, May.	Mabel Nelson Castling, Durham Mental Hospital.
,, Nov.	Alfred Stanley Earp, Rubery Hill Mental Hospital.
1938, May.	Trixie M. B. Padmanabha, Devon Mental Hospital.
1938, Nov.	Frank Holden, Smithdown Road Hospital.
,, ,,	Josephine M. Burrow, Wilts County Mental Hospital.
1939. May.	Mabel G. Scott, Belfast Mental Hospital.

Honorary Certificate in Mental Nursing.

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1938, May. Trixie M. B. Padmanabha, Devon Mental Hospital.
1938, Nov. Frank Holden, Smithdown Road Hospital.
,, ,, Josephine M. Burrow, Wilts County Mental Hospital.
1939. May. Mabel G. Scott, Belfast Mental Hospital.

List of Chairmen.

1841. Dr. Blake, Nottingham General Asylum.
1842. Dr. de Vitré, Lancaster Asylum.
1843. Dr. Conolly, Hanwell Asylum.
1844. Dr. Thurnam, The Retreat.
1847. Dr. Wintle, Warneford House.
1848. William Ley, M.R.C.S., Littlemore Asylum.
1851. Dr. Conolly, Hanwell Asylum.
1852. Dr. Wintle, Warneford House.

List of Presidents.

1854. A. J. Sutherland, M.D., St. Luke's Hospital, London.
1855. J. Thurnam, M.D., Wilts County Asylum.
1856. J. Hitchman, M.D., Derby County Asylum.
1857. Forbes Winslow, M.D., Sussex House, Hammersmith.
1858. John Conolly, M.D., Hanwell Asylum.
1859. Sir Charles Hastings, D.C.L., Worcester.
1860. J. C. Bucknill, M.D., Devon County Asylum.
1861. Joseph Lalor, M.D., Richmond Asylum, Dublin.
1862. John Kirkman, M.D., Suffolk County Asylum.
1863. David Skae, M.D., Royal Asylum, Edinburgh.
1864. Henry Munro, M.D., Brook House.
1865. Wm. Wood, M.D., Kensington House.
1866. W. A. F. Browne, M.D., Commissioner in Lunacy for Scotland.
1867. C. A. Lockhart Robertson, M.D., Haywards Heath Asylum.
1868. W. H. O. Sankey, M.D., Sandywell Park, Cheltenham.
1869. T. Laycock, M.D., Edinburgh.
1870. Robert Boyd, M.D., Wells Asylum.
1871. Henry Maudsley, M.D., The Lawn, Hanwell.
1872. Sir James Coxe, M.D., Commissioner in Lunacy for Scotland.
1873. Harrington Tuke, M.D., Chiswick House.
1874. T. L. Rogers, M.D., Rainhill Asylum.
1875. J. F. Duncan, M.D., Dublin.
1876. W. H. Parsey, M.D., Warwick County Asylum.
1877. G. Fielding Blandford, M.D., London.
1878. Sir J. Crichton-Browne, M.D., Lord Chancellor's Visitor in Lunacy.
1879. J. A. Lush, M.D., Fisherton House.
1880. G. W. Mould, M.R.C.S., Royal Asylum, Cheadle.
1881. D. Hack Tuke, M.D., London.
1882. Sir W. T. Gairdner, M.D., Glasgow.
1883. W. Orange, M.D., State Criminal Lunatic Asylum, Broadmoor.
1884. Henry Rayner, M.D., Hanwell Asylum.
1885. J. A. Eames, M.D., District Asylum, Cork.
1886. Sir Geo. H. Savage, M.D., Bethlem Royal Hospital.
1887. Sir Fred. Needham, M.D., Barnwood House.
1888. Sir T. S. Clouston, M.D., Royal Asylum, Edinburgh.
1889. H. Hayes Newington, F.R.C.P., Ticehurst House.
1890. David Yellowlees, M.D., Royal Asylum, Glasgow.
1891. E. B. Whitcombe, M.R.C.S., City Asylum, Birmingham.
1892. Robert Baker, M.D., The Retreat.
1893. J. Murray Lindsay, M.D., Derby County Asylum.
1894. Conolly Norman, F.R.C.P.I., Richmond Asylum, Dublin.
1895. David Nicolson, *C.B.*, M.D., State Criminal Lunatic Asylum, Broadmoor.
1896. William Julius Mickle, M.D., Grove Hall.
1897. Thomas W. McDowall, M.D., Northumberland Asylum.
1898. A. R. Urquhart, M.D., James Murray's Royal Asylum, Perth.
1899. J. B. Spence, *O.B.E.*, M.D., Burntwood Asylum, Lichfield.
1900. Fletcher Beach, M.B., London.
1901. Oscar T. Woods, M.D., District Asylum, Cork.
1902. J. Wiglesworth, M.D., Rainhill Asylum.

1903. Ernest W. White, *C.B.E.*, M.B., City of London Asylum, Stone.
1904. R. Percy Smith, M.D., London.
1905. T. Outterson Wood, M.D., London.
1906. Sir Robert Armstrong-Jones, *C.B.E.*, M.D., Claybury Asylum.
1907. P. W. MacDonald, M.D., Dorchester County Asylum.
1908. Chas. A. Mercier, M.D., Flower House.
1909. W. Bevan-Lewis, M.Sc., West Riding Asylum, Wakefield.
1910. Sir John Macpherson, M.D., Commissioner in Lunacy for Scotland.
1911. Wm. R. Dawson, *O.B.E.*, M.D., Inspector of Lunatic Asylums, Dublin.
1912. J. Greig Soutar, M.B., Barnwood House.
1913. James Chambers, M.D., The Priory.
1914–18. David G. Thomson, *C.B.E.*, M.D., Norfolk County Asylum.
1918. John Keay, *C.B.E.*, M.D., Bangour Village.
1919. Bedford Pierce, M.D., The Retreat.
1920. William F. Menzies, M.D., Cheddleton Mental Hospital.
1921. Sir Hubert Bond, *K.B.E.*, M.D., Commissioner, Board of Control.
1922. G. M. Robertson, M.D., Royal Mental Hospital, Morningside, Edinburgh.
1923. Edwin Goodall, *C.B.E.*, M.D., Cardiff City Mental Hospital.
1924. Michael J. Nolan, L.R.C.P.&S.Irel., Downpatrick Asylum.
1925. Sir Frederick W. Mott, *K.B.E.*, M.D., London.
1926. John R. Lord, *C.B.E.*, M.D., Horton Mental Hospital, Epsom.
1927. Hamilton Marr, *C.B.*, M.D., Commissioner, General Board of Control for Scotland.
1928. J. Shaw Bolton, D.Sc., M.D., West Riding Mental Hospital, Wakefield.
1929. Nathan Raw, *C.M.G.*, M.D., F.R.C.S.E., F.R.S.E., Lord Chancellor's Visitor in Lunacy.
1930. T. Saxty Good, *O.B.E.*, M.A., M.R.C.S., L.R.C.P., Oxford County and City Mental Hospital, Littlemore.
1931. R. R. Leeper, L.R.C.P.I., F.R.C.S.I., St. Patrick's Hospital, Dublin.
1932. R. B. Campbell, M.D., F.R.C.P.E., Stirling District Mental Hospital, Larbert.
1933. Frank Douglas Turner, M.B., M.R.C.S., L.R.C.P., Royal Eastern Counties Institution, Colchester.
1934. Daniel F. Rambaut, M.A., M.D., St. Andrew's Hospital, Northampton.
1935. Reginald Worth, *O.B.E.*, M.B., Springfield Mental Hospital.
1936. M. A. Collins, *O.B.E.*, M.D., B.S., M.R.C.S., L.R.C.P., Canterbury.
1937. Douglas McRae, M.D., F.R.C.P.E., Glengall Hospital, Ayr.
1938. John Rutherford Gilmour, M.B., C.M., F.R.C.P.E., Scalebor Park, Burley-in-Wharfedale.
1939. A. Helen A. Boyle, M.D., L.R.C.P.&S., Hove, Sussex.

List of Maudsley Lecturers.

1920. Sir J. Crichton-Browne, LL.D., D.Sc., M.D., F.R.S.
1921. Sir F. W. Mott, *K.B.E.*, LL.D., M.D., F.R.C.P., F.R.S.
1922. Sir M. Craig, *C.B.E.*, M.A., M.D., F.R.C.P.
1923. Charles Kirk Clarke, LL.D., M.D.
1924. J. Carswell, F.R.F.P.S.
1925. Joseph Shaw Bolton, D.Sc., M.D., F.R.C.P.
1926. George M. Robertson, M.D., F.R.C.P.E., F.R.C.S.E.
1927. Edwin Goodall, *C.B.E.*, M.D., F.R.C.P.
1928. Sir John Macpherson, *C.B.*, M.D., F.R.C.P.E.
1929. Charles E. Spearman, Ph.D., F.R.S.
1930. The Hon. Mr. Justice McCardie.
1931. Sir Hubert Bond, *K.B.E.*, LL.B., D.Sc., M.D., F.R.C.P.
1932. Sir Edward Farquhar Buzzard, Bart., *K.C.V.O.*, M.A., M.D., F.R.C.P.
1933. Adolf Meyer, M.D.
1934. The Right Hon. Lord Macmillan, M.A., LL.D.
1935. Lewis C. Bruce, *M.C.*, M.D., F.R.C.P.E., M.P.C.
1936. Sir Walter Langdon Brown, M.A., M.D., F.R.C.P.
1937. F. L. Golla, M.A., M.B., B.Ch., F.R.C.P.
1938. D. K. Henderson, M.D., Ch.B., F.R.C.P.E.
1939. E. Mapother, M.D., F.R.C.P., F.R.C.S.

1903. Ernest W. White, *C.B.E.*, M.B., City of London Asylum, Stone.
1904. R. Percy Smith, M.D., London.
1905. T. Outterson Wood, M.D., London.
1906. Sir Robert Armstrong-Jones, *C.B.E.*, M.D., Claybury Asylum.
1907. P. W. MacDonald, M.D., Dorchester County Asylum.
1908. Chas. A. Mercier, M.D., Flower House.
1909. W. Bevan-Lewis, M.Sc., West Riding Asylum, Wakefield.
1910. Sir John Macpherson, M.D., Commissioner in Lunacy for Scotland.
1911. Wm. R. Dawson, *O.B.E.*, M.D., Inspector of Lunatic Asylums, Dublin.
1912. J. Greig Soutar, M.B., Barnwood House.
1913. James Chambers, M.D., The Priory.
1914-18. David G. Thomson, *C.B.E.*, M.D., Norfolk County Asylum.
1918. John Keay, *C.B.E.*, M.D., Bangour Village.
1919. Bedford Pierce, M.D., The Retreat.
1920. William F. Menzies, M.D., Cheddleton Mental Hospital.
1921. Sir Hubert Bond, *K.B.E.*, M.D., Commissioner, Board of Control.
1922. G. M. Robertson, M.D., Royal Mental Hospital, Morningside, Edinburgh.
1923. Edwin Goodall, *C.B.E.*, M.D., Cardiff City Mental Hospital.
1924. Michael J. Nolan, L.R.C.P.&S.Irel., Downpatrick Asylum.
1925. Sir Frederick W. Mott, *K.B.E.*, M.D., London.
1926. John R. Lord, *C.B.E.*, M.D., Horton Mental Hospital, Epsom.
1927. Hamilton Marr, *C.B.*, M.D., Commissioner, General Board of Control for Scotland.
1928. J. Shaw Bolton, D.Sc., M.D., West Riding Mental Hospital, Wakefield.
1929. Nathan Raw, *C.M.G.*, M.D., F.R.C.S.E., F.R.S.E., Lord Chancellor's Visitor in Lunacy.
1930. T. Saxty Good, *O.B.E.*, M.A., M.R.C.S., L.R.C.P., Oxford County and City Mental Hospital, Littlemore.
1931. R. R. Leeper, L.R.C.P.I., F.R.C.S.I., St. Patrick's Hospital, Dublin.
1932. R. B. Campbell, M.D., F.R.C.P.E., Stirling District Mental Hospital, Larbert.
1933. Frank Douglas Turner, M.B., M.R.C.S., L.R.C.P., Royal Eastern Counties Institution, Colchester.
1934. Daniel F. Rambaut, M.A., M.D., St. Andrew's Hospital, Northampton.
1935. Reginald Worth, *O.B.E.*, M.B., Springfield Mental Hospital.
1936. M. A. Collins, *O.B.E.*, M.D., B.S., M.R.C.S., L.R.C.P., Canterbury.
1937. Douglas McRae, M.D., F.R.C.P.E., Glengall Hospital, Ayr.
1938. John Rutherford Gilmour, M.B., C.M., F.R.C.P.E., Scalebor Park, Burley-in-Wharfedale.
1939. A. Helen A. Boyle, M.D., L.R.C.P.&S., Hove, Sussex.

List of Maudsley Lecturers.

1920. Sir J. Crichton-Browne, LL.D., D.Sc., M.D., F.R.S.
1921. Sir F. W. Mott, *K.B.E.*, LL.D., M.D., F.R.C.P., F.R.S.
1922. Sir M. Craig, *C.B.E.*, M.A., M.D., F.R.C.P.
1923. Charles Kirk Clarke, LL.D., M.D.
1924. J. Carswell, F.R.F.P.S.
1925. Joseph Shaw Bolton, D.Sc., M.D., F.R.C.P.
1926. George M. Robertson, M.D., F.R.C.P.E., F.R.C.S.E.
1927. Edwin Goodall, *C.B.E.*, M.D., F.R.C.P.
1928. Sir John Macpherson, *C.B.*, M.D., F.R.C.P.E.
1929. Charles E. Spearman, Ph.D., F.R.S.
1930. The Hon. Mr. Justice McCardie.
1931. Sir Hubert Bond, *K.B.E.*, LL.B., D.Sc., M.D., F.R.C.P.
1932. Sir Edward Farquhar Buzzard, Bart., *K.C.V.O.*, M.A., M.D., F.R.C.P.
1933. Adolf Meyer, M.D.
1934. The Right Hon. Lord Macmillan, M.A., LL.D.
1935. Lewis C. Bruce, *M.C.*, M.D., F.R.C.P.E., M.P.C.
1936. Sir Walter Langdon Brown, M.A., M.D., F.R.C.P.
1937. F. L. Golla, M.A., M.B., B.Ch., F.R.C.P.
1938. D. K. Henderson, M.D., Ch.B., F.R.C.P.E.
1939. E. Mapother, M.D., F.R.C.P., F.R.C.S.

Membership of the Association.

South-Eastern Division:			
Honorary	16		
Ordinary	352	368	
South-Western Division:			
Honorary	3		
Ordinary	151	154	
Northern and Midland Division:			
Honorary	...		
Ordinary	201	201	
Scottish Division:			
Honorary	..		
Ordinary	98	98	
Irish Division:			
Honorary	1		
Ordinary	87	88	
India:			
Ordinary		30	
Other Countries:			
Honorary	15		
Corresponding	51	114	
Ordinary	48		
Total Membership:			
Honorary	35		
Corresponding	51	1,053	
Ordinary	967		

HONORARY MEMBERS.

1932. Armstrong-Jones, Sir Robert, *C.B.E.*, D.Sc., M.D., B.S., F.R.C.P., F.R.C.S., F.S A., *D.L., J.P.*, 27, Phillimore Gardens, W. 8 (and Plas Dinas, Carnarvon, North Wales). (*Ord. Mem. since* 1882 ; *Gen. Sec.*, 1897–1906 ; PRESIDENT, 1906–7.)

1900. Blumer, G. Alder, M.D., L.R.C.P.Edin., Superintendent-Emeritus, Butler Hospital; 196, Blackstone Boulevard, Providence, R.I., U.S.A. (*Ord. Mem.*, 1890.)

1928. Bond, Sir Hubert, *K.B.E.*, D.Sc., M.D.Edin., LL.B.Lond., F.R.C.P., M.P.C., Senior Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1 ; Emeritus Lect. on Psychiat., Middlx. Hosp. (*Ord. Mem.*, 1892 ; *General Secretary*, 1906–12 ; PRESIDENT, 1921–22.)

1900. Bresler, Johannes, Sanitätsrat Dr., Director of the Provincial Mental Hospital, Kreuzburg, Oberschlesien, Germany ; Editor, *Psychiatrisch-neurologische Wochenschrift.* (*Corr. Mem.*, 1896.)

1932. Briggs, L. Vernon, M.D., 64, Beacon Street, Boston, Mass., U.S.A. (*Corr. Mem. since* 1923.)

1934. Brock, Sir Laurence G., *C.B.*, Chairman of the Board of Control, Hobart House, Grosvenor Place, London, S.W. 1.

1925. Chamberlain, Rt. Hon. Neville, *M.P.*, Prime Minister, 10, Downing Street, London, S.W. 1.

1937. Claude, Prof. Henri, Professor of Psychiatry, University of Paris; 11, Rue Ampère, Paris, France.

1909. Collins, Sir Wm. Job, *K.C.V.O.*, B.Sc., M.D., M.S., F.R.C.S., 1, Albert Terrace, Regent's Park, London, N.W. 1.

1936. Darwin, Ruth, *C.B.E.*, Senior Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1.

1924. Dawson, Lt.-Col. W. R., *O.B.E.*, B.A., M.D., B.Ch.Dubl., F.R.C.P.Irel., D.P.H., M.P.C., 18, Brock Street, Bath. (*Ord. Mem.*, 1894 ; PRESIDENT, 1911–12 ; *Co-Editor of Journal*, 1920–21.)

1936. Doll, Edgar A., Ph.D., Director of Research at the Vineland Training School, Vineland, New Jersey ; President of the American Association on Mental Deficiency.

1938. Goodall, Edwin, *C.B.E.*, M.D., B.S.Lond., F.R.C.P., M.P.C., " Fairlawn " Kingsway, Hove, Sussex. *Asst. Editor*, 1894–5, and *Co-Editor of Journal*, 1895–98 ; PRESIDENT, 1923–24 ; *Ord. Mem. since* 1889.)

1922. l'Hermitte, Dr. Jacques Jean, Médecin de l'Hospice Paul Brousse, Paris ; 9, rue Marbeuf, Paris (VIII[e]), France.

1930. Janet, Pierre, M.D., Member of the Institute of France ; Professor of Psychology, College of France ; 54, Rue de Varenne, Paris (VII[e]), France.

1930. von Jauregg, Hofrat Prof. Julius R. Wagner, M.D., late Professor of Psychiatry, University of Vienna ; 1, Landesgerichtstr. 18, Vienna.

1935. Keay, John, *C.B.E.*, M.D., C.M., F.R.C.P., " Champions ", Beaminster, Dorset. (*Ord. Mem.* 1886 ; PRESIDENT, 1918 ; *Chairman, Educational Committee*, 1920–27.)

1937. Kirkland, J., *O.B.E.*, F.R.I.B.A., c/o. Dr. E. A. Roberts, 34, Lowndes Street, S.W. 1.

1928. Macmillan, Rt. Hon. Lord, *G.C.V.O.*, M.A., LL.D., 44, Millbank, S.W. 1.

1910. Macpherson, Sir John, *C.B.*, M.D., C.M., F.R.C.P.Edin., " Hillside ", Cleeve, nr. Bristol. (*Ord. Mem.*, 1886 ; PRESIDENT, 1910–11.)

1921. Maudsley, Sir Henry Carr, *K.C.M.G., C.B.E.*, M.D., B.S., F.R.C.P., Consulting Physician Melbourne Hospital, Victoria ; 8, Collins Street, Melbourne.

1937. Menzies, William F., B.Sc., M.D., C.M.Edin., F.R.C.P.Lond., " Three Trees ", Theobald Street, Radlett, Herts.

1926. Meyer, Adolf, M.D., Psychiatrist in Chief, Phipps Psychiatric Clinic, Johns Hopkins Hospital, Baltimore, Md., U.S.A.

1931. Nolan, Michael James, L.R.C.P.I., L.R.C.S.I., *J.P.*, Consulting Visitor-in-Lunacy to the Lord Chief Justice of Northern Ireland, and to the Chief Justice, Eire ; Slieve Dhu, Bryansford Road, Newcastle, Belfast, Ireland. (*Ord. Mem. since* 1888; PRESIDENT, 1924–5.)

1922. Pactet, Dr. François Florentin, Médecin Honoraire des Asiles de la Seine ; 35, Grande Rue, Châtenay, Seine, France.

1927. Rolleston, Sir Humphry Davy, *Bt.*, *G.C.V.O.*, *K.C.B.*, D.C.L., LL.D., D.Sc., M.D., F.R.C.P., " Martins ", Haslemere, Surrey.

1929. Sherrington, Sir Charles Scott, *O.M.*, *G.B.E.*, M.A., LL.D., D.Sc., M.D., F.R.C.P., F.R.C.S., F.R.S., "Broomside ", Valley Road, Ipswich, Suffolk.

1927. Smith, Robert Percy, M.D., B.S.Lond., F.R.C.P., 42, Albion Street, London, W. 2. (*Ord. Mem.*, 1885 ; *General Secretary*, 1896–97 ; *Chairman, Educational Committee*, 1899–1903 ; PRESIDENT, 1904–05.)

1901. Toulouse, Dr. Edouard, Médecin des Asiles de la Seine ; 1, Rue Cabanis, Paris (XIV^{e}), France.

1934. Whitwell, James Richard, M.B.Edin., 43, Lancaster Close, W. 2 ; 16, Westgate Road, Newbury, Berkshire. *Ord. Mem. since* 1889 ; *Acting Hon. Librarian and Chairman, Library Committee, since* 1927 ; *Hon. Librarian since* 1928.)

1923. Willis, Sir Frederick James, *K.B.E.*, *C.B.*, Church House, Bramley, Guildford

1926. Winkler, C., M.D., 35, Heerenstraat, Utrecht, Holland. (*Corr. Mem.*, 1924.)

1936. Wood, Rt. Hon. Sir Kingsley, M.P., Minister of Air, Whitehall, S.W. 1.

CORRESPONDING MEMBERS.

1928. Bliss, Malcolm Andrews, M.D., Consultant in Neuro-Psychiatry, St. Luke's Hospital; 301, Himboldt Buildings, St. Louis, Minn., U.S.A.
1911. Boedeker, Geheimer Sanitätsrat, Prof. Justus Karl Edmund, Director, Zehlenhof Asylum; 18, Kolnrigs-Allee, Berlin-Grünewald.
1929. Bouman, K. Herman, M.D., Professor of Psychiatry and Director of the University Psychiatric Clinic, Jan Luykenstraat 24, Amsterdam.
1929. Buscaino, V. M., M.D., Professor of Psychiatry, University of Catania, Sicily.
1897. Buschan, Sanitätsrat Dr. med. et phil. G., Friedrich Carlstrasse 7, Stettin, Germany.

1930. Campbell, Charles Macfie, M.D., Professor of Psychiatry, Harvard Medical School; Director, Boston Psychopathic Hospital; 74, Fenwood Road, Boston, Massachusetts, U.S.A.
1927. Charpentier, René, M.D., Vice-Président de la Société Médico-Psychologique de Paris; 119, rue Perronet, Neuilly s/Seine (Seine), France.
1936. Cheney, Clarence O., Medical Director of the Westchester Division, New York Hospital, 121, Westchester Avenue, White Plains, New York, U.S.A.
1935. Combemale, Pierre, Professor of Psychiatry in the University of Lille, Médecin-Chef à l'Asile de Bailleul, Nord, France.
1904. Coroleü, Wilfrid, Medico forense del distrito de la Barceloneta, Aribau, 31, Barcelona, Spain.
1896. Cowan, F. M., M.D., 109, Perponcherstraat, The Hague, Holland.

1929. Ebaugh, Franklin G., A.B., M.D., Professor of Psychiatry, University of Colorado; Director, Colorado Psychiatric Hospital; 4200, East Ninth Avenue, Denver, Colorado, U.S.A.
1930. Evensen, Dr. Hans, Medical Director, Gaustad State Hospital, Vinderen, Norway; Commissioner in Legal Medicine for Norway; President, Norwegian Psychiatric Society.

1911. Falkenberg, Sanitätsrat, Dr. Wilhelm, Berlin-Friedenau, Ringstr. 5.
1907. Ferrari, Giulio Cesare, M.D., Director, Manicomio Provinciale, Imola, Bologna, Italy.
1930. Flournoy, Dr. Henri, 6, Rue de Monnetier, Geneva, Switzerland.
1911. Friedländer, Prof. Dr. Adolf Albrecht, Haus Sonnblick, Littenweiler, bei Freiburg i/Baden, Germany.

1931. Génil-Perrin, Dr., Chief Physician, Seine Department Mental Hospitals; General Secretary, French League for Mental Hygiene; 99, Avenue La Bourdonnais, Paris (VII).
1938. Gjessing, R., Dikemark Sykehus, Asker, pr. Oslo, Norway.
1901. Gommès, Dr. Marcel, 5, Rue Parrot, Paris (XII^{e}).

1930. Haskovec, Prof. Dr. Ladislav, Professor of Nervous Diseases in the Charles University, Prague, Czecho-Slovakia.
1931. Hincks, Clarence Meredith, A.B., M.D., General Director of the National Committee for Mental Hygiene, 450, Seventh Avenue, New York, U.S.A.

1928. Kappers, C. U. Ariëns, M.D., Director, Netherlands Central Institution for Brain Research, Amsterdam.
1936. Klaesi, Prof. Jakob, Director, University Psychiatric Clinic, Waldau, Berne, Switzerland.
1934. Kraus, G., Provinciaal Ziekenhuis, Santpoort, by Haarlem, Holland.

1936. Maier, Prof. H. W., Director, University Psychiatric Clinic, Burgholzli, Zurich, Switzerland.
1932. May, James V., M.D., 36, Adams Avenue, Watertown, Mass., U.S.A.

1930. Miyake, Dr. Koichi, Professor of Psychiatry, Tokio Imperial University; Director, Tokio Municipal Matsuzawa Psychopathic Hospital, Japan.
1931. Moreno, Dr. Samuel Ramirez, Director, Manicomio General, Mexico City.
1922. Morowoka, Dr. T., Owada, 102, Shibuya, Tokyo, Japan.

1929. Pameijer, J. H., M.D., Inspector of State Mental Hospitals, Bildersstraat 22, The Hague.
1928. Pighini, Giacomo, M.D., Professor of Psychiatry and Director, Laboratori Scientifici, Instituto Psichiatrico di S. Lazzaro, S. Maurizio, Reggio Emilia, Via De Amicis 10, Italy.
1909. Pilcz, Prof. Dr. Alexander, VIII/2 Alserstrasse 43, Vienna.
1929. Pratt, G. K., M.D., Assistant Medical Director, National Committee for Mental Hygiene, 80, Myrtle Avenue, Westport, Connecticut, U.S.A.

1937. Répond, Dr. A., Maison de Santé de Malévoz, Monthey, Valais, Switzerland.
1931. Riedel, Dr. Gustavo, Director, Hospital-Psychopathic Colony of Engenbo de Dentro, Rio de Janeiro, Brazil; Hon. President, Brazilian League for Mental Hygiene; Vice-President, Brazilian Society of Psychiatry.
1931. Roemer, Dr. med. Hans, Director, Institute for Mental Diseases, Illenau, Baden, Germany; Secretary, German Association for Mental Hygiene; Secretary, Health Welfare Committee, Baden.
1931. Ruggles, Dr. Arthur H., Medical Superintendent, Butler Hospital, Providence, R.I., U.S.A.; Lecturer in Psychiatry, Yale University, New Haven; Chairman, Executive Committee of the National Committee for Mental Hygiene.

1922. Sano, Dr., late Directeur de la Colonie de Gheel, Belgium.
1929. Scheer, Prof. W. M. van der, M.D., Psychiatrisch-Neurologische Kliniek, Groningen, Holland.
1934. Simon, Hermann, Direktor der Provinzialheilanstalt, Gütersloh, Westphalia, Germany.
1930. Strecker, Edward A., M.D., Professor of Nervous and Mental Diseases, Jefferson Medical College; 111, North Forty-ninth Street, Philadelphia, U.S.A.
1929. Stuurman, F. J., M.D., Secretary, Dutch Association for Psychiatry and Neurology; Oegstgeest, near Leyden, Holland.
1935. Sveinsson, Thordur, Medical Superintendent, Gamle Kleppur Asylum, Reykjavik, Iceland.

1927. Targowla, René, M.D., *Chev. Leg. Hon.*, 169, Rue de L'Université, Paris (VII^e).
1929. Thom, Douglas A., M.D., Professor of Mental Hygiene, Tuft Medical School; 520, Commonwealth Avenue, Boston, Mass., U.S.A.
1935. Tómasson, Helgi, Medical Superintendent, Nýja Spitalanum á Kleppi, Reykjavik, Iceland.

1930. Weygandt, Dr. phil. et med. Wilhelm, Professor of Psychiatry and Director, Psychiatric Clinic, University of Hamburg; Friedrichsbergerstr 60, Hamburg.
1929. Wiersma, E. D., late Professor of Psychiatry and Director of the University Psychiatric Clinic, Groningen, Holland.
1930. Williams, Frankwood E., D.Sc., M.D.; Editor, *Mental Hygiene and Mental Hygiene Bulletin*; 44, West 12th Street, New York City.

ORDINARY MEMBERS OF THE ASSOCIATION.

Alphabetical List of Ordinary Members of the Association on January 1, 1940, with the year in which they joined.

1928. Abd-el-Hakeem, Mohammed, M.B., B.Ch.Cairo, D.P.M., Assistant Medical Officer, Mental Hospital, Abbassia, Cairo, Egypt.

1910. Adam, George Henry, M.R.C.S., L.R.C.P., Resident Physician, Malling Place, West Malling, Kent.

1931. Adamson, James Weeden Woodhams, M.D.Durh., M.R.C.S., L.R.C.P., L.S.A., Commissioner of the Board of Control (England and Wales), Hobart House, Grosvenor Place, London, S.W. 1.

1919. Adey, J. K., M.B., C.M.Melb., F.R.A.C.P., Receiving House, Royal Park, Melbourne, Victoria, Australia.

1923. Ainsworth, Cyrus Gerald, M.A., LL.B., M.B., B.Ch.Camb., M.R.C.S., L.R.C.P., Graylingwell Mental Hospital, Chichester.

1935. Aird, Patrick Joseph, M.B., B.Ch., B.A.O.N.U.I., D.P.M., D.P.H., Assistant Medical Officer, Grangegorman Mental Hospital, Dublin.

1931. Allan, Samuel Miller, M.D., Ch.B.Glasg., D.P.M., Medical Superintendent, Devon County Mental Hospital, Exminster, Devon.

1932. Allen, James Stewart, B.Sc., M.B., Ch.B.Belf., D.P.M., Medical Superintendent, St. Catherine's Institution, Loversall, Doncaster.

1926. Albiston, Norman Arthur, M.B., B.S.Syd., D.P.M., 61, Collins Street, Melbourne, Australia.

1924. Alexander, Douglas Reid, *M.C.*, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, The Manor, Epsom, Surrey.

1922. Alexander, Marion Cameron, M.B., B.Ch., B.A.O.Belf., Dipl. Psych. Edin., Assistant Medical Officer, Storthes Hall Mental Hospital, Kirkburton, near Huddersfield.

1899. Allman, Dorah Elizabeth, M.B., B.Ch.R.U.I., Karavanagh, 52, Sandymount Avenue, Dublin.

1935. Anderson, Edward W., M.D., M.R.C.P., D.P.M., c/o Midland Bank, Dartford, Kent.

1929. Anderson, John Colquhoun, B.Sc., M.B., Ch.B.Glasg., Dipl. Psych., 68, Highburgh Road, Glasgow, W. 2.

1938. Anderson, Rupert George, M.D.Edin., D.P.M.Lond., Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1.

1918. Anderson, William Kirkpatrick, M.D., Ch.B., F.R.F.P.S.Glasg., Lect. on Ment. Dis., Andr. Coll., Glasg.; 2, Woodside Crescent, Glasgow.

1938. Andrews, Gordon Frank, M.R.C.S., L.R.C.P., Assistant Medical Officer, Severalls Hospital, Colchester, Essex.

1912. Annandale, James Scott, M.B., Ch.B.Aberd., D.P.M., Medical Superintendent, Kingseat Mental Hospital, Newmachar, Aberdeen.

1938. Annesley, Dudley Thomas, M.B., B.Ch.Dubl., Assistant Medical Officer, Severalls Hospital, Colchester, Essex.

1904. Archdale, Mervyn Alexander, M.B., B.S.Durh., D.P.M., Medical Superintendent, Almora Hall, Middleton-St.-George, Durham. (*Chairman, N. and M. Division*, 1938–40.)

1903. Armitage, Bernard William Francis, M.A., M.R.C.S., L.R.C.P., Assistant Physician, Bethlem Royal Hospital, Monk's Orchard, Eden Park, Beckenham, Kent.

1930. Armstrong, Robert William, B.Sc., M.D., B.Ch.Belf., D.P.M., Medical Superintendent, County and City Mental Hospital, Littlemore, Oxford. (*Chairman, S.W. Division*, 1938–40.)

1935. Arnott, Desmond William Henry, M.B., Ch.M., F.R.A.C.P., D.P.M.Sydney, "Harley", 143, Macquarie Street, Sydney, Australia.

1930. Ashby, William Ross, M.A., M.D., B.Ch.Cantab., M.R.C.S., L.R.C.P., D.P.M., Pathologist, St. Andrew's Hospital, Northampton.

1934. Aslett, Henry Edward Cullinan, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Rauceby Mental Hospital, Sleaford, Lincs.

1927. Atkin, Isaac, M.D., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Knowle Mental Hospital, Fareham, Hants.

1922. Back, Frederick, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Sunderland Mental Hospital, Cherry Knowle, Ryhope, Durham.

1938. Bailey, Kenneth Cyril, M.A., M.B., B.Ch., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Warlingham Park Hospital, Upper Warlingham, Surrey.
1926. Bailey, Josiah Reginald, M.B., Ch.B.Glasg., Medical Superintendent, Gogarburn Certified Institution, Corstorphine, Edinburgh.
1937. Bain, Archibald James, M.B., Ch.B.Edin., D.P.M.Leeds, Senior Assistant Medical Officer, City Mental Hospital, Humberstone, Leicester.
1906. Baird, Harvey, M.D., Ch.B.Edin., Medical Superintendent, Periteau House, Winchelsea, Sussex.
1934. Bamford, Charles Barry, M.D., Ch.B., D.P.M.Dubl., Medical Superintendent, Gateshead Mental Hospital, Stannington, Morpeth, Northumberland.
1922. Banbury, Percy, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Borough Mental Hospital, Ipswich.
1930. Barber, Leonard, M.D., B.S.Durh., L.R.C.P.&S.Edin., L.R.F.P.&S.Glasg., D.P.M., Deputy Medical Superintendent, Brookwood Hospital; "The Orchard", Knaphill, Surrey.
1934. Barbour, William Johnstone, M.D., Ch.B., D.P.M., Medical Superintendent, Borough Mental Hospital, Rowditch, Derby.
1922. Barclay, Rachel Mary, M.A., LL.B., M.D.Edin., Dipl. Psych., 2, W. Crosscauseway, Edinburgh.
1938. Bardon, Desmond Terence, M.B., B.Ch., B.A.O., Assistant Medical Officer, St. Patrick's Hospital, Dublin.
1904. Barham, Guy Foster, M.A., M.D., B.Ch.Camb., M.R.C.S., L.R.C.P., Tresilian, Gorran Haven, Cornwall.
1919. Barkas, Mary Rushton, M.Sc.N.Z., M.D., B.S., M.R.C.S., L.R.C.P., D.P.M., Taihoa, Tapu, Thames, New Zealand.
1927. Barkas, Thomas Cook, *O.B.E.*, M.B., B.S.Durh., Resident Medical Officer, Middleton Hall, Middleton St. George, co. Durham.
1923. Barnes, Francis Gregory Lawson, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Long Grove Hospital, Epsom, Surrey.
1935. Barnes, John Francis Lovel, M.A., M.R.C.S., L.R.C.P., Hill End Hospital, St. Albans, Herts.
1939. Barua, Hem Chandra, M.B., Superintendent, Mental Hospital, Tezpur, Assma, India.
1901. Baskin, J. Lougheed, M.D., L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Warming Hall, Aylesbury, Bucks.
1932. Bates, Ralph Marshall, F.R.C.S., D.P.M., Resident Medical Officer, Stoke Park Colony; Purdown House, Stapleton, Bristol.
1933. Beasley, Henry Eric, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Resident Medical Officer, Middlesex Colony, Shenley.
1921. Beaton, Thomas, *O.B.E.*, M.D.Lond., F.R.C.P., Medical Superintendent, City Mental Hospital, Milton, Portsmouth. Lect. on Ment. Dis., Bethlem Royal Hosp. (*Assistant Editor*, 1926–27, *and Co-Editor of Journal*, 1927–31.)
1932. Beccle, Harold Charles, M.B., B.S., M.R.C.P., D.P.M., Deputy Medical Superintendent, Springfield Mental Hospital, S.W. 17.
1913. Bedford, Percy William Page, M.D., Ch.B., Dipl. Psych.Edin., Medical Superintendent, Dorset County Mental Hospital, Herrison, near Dorchester.
1934. Beggs, John, M.A., M.B., Ch.B., B.A.O.Dubl., Senior Assistant Physician, The Warneford, Oxford.
1922. Bell, Andrew Allan, M.B., Ch.B., F.R.F.P.S.Glasg., D.P.M., Medical Superintendent, Dundee Mental Hospital, Westgreen, Dundee.
1934. Bell, Gavin John, M.B., B.S.Lond., D.P.M., Assistant Medical Officer, Park Prewett Mental Hospital, Basingstoke, Hants.
1931. Bell, George Macdonald, M.B., Ch.B.Edin., Medical Superintendent, Ladysbridge Mental Hospital, Banff.
1933. Benjacar, Edgar, M.D.Malta, Assistant Medical Officer, Royal Eastern Counties Institution, Colchester; The Turner Village, Turner Road, Mile End, Colchester.
1931. Bennet, Edward Armstrong, *M.C.*, M.A., M.D., D.P.M., Physician, The Tavistock Clinic, London; 97, Harley Street, London, W. 1.
1914. Bennett, James Wodderspoon, M.R.C.S., L.R.C.P., "Marsden", Babbacombe Road, Torquay, S. Devon.
1937. Benson, Gerald Edward Meade, M.A., B.M., B.Ch., M.R.C.S., L.R.C.P., Resident Medical Officer, Fiddington House, Market Lavington, Devizes, Wilts.
1914. Benson, John Robinson, F.R.C.S., Resident Physician, Fiddington House, Market Lavington, Wilts, and Laverstock House, Salisbury. (*Chairman, S.W. Division*, 1936–38.)

1939. Beresford, Cecil Clee, M.B., B.S.Lond., L.R.C.P., D.P.M., Senior Assistant Physician and Deputy Medical Superintendent, The Retreat, York; 132, Lawrence Street, York.

1899. Beresford, Edwyn Henry, M.R.C.S., L.R.C.P., 20, Campion Road, Putney, London, S.W.15.

1922. Berkeley-Hill, Owen Alfred Rowland, M.A., M.D., B.Ch.Oxon, M.R.C.S., L.R.C.P.Lond., Lt.-Col. *I.M.S.* (retired), "Hillstow", Tatisilwai, Ranchi District, Bihar, India.

1912. Berncastle, Herbert Melbourne, M.R.C.S., L.R.C.P., Toorak, 36, Birdhurst Rise, S. Croydon.

1938. Berrington, William Pye, M.B., B.Ch., B.A.O.Belf., D.P.M.Lond., Assistant Medical Officer, West Park Hospital, Epsom, Surrey.

1939. Betts, George Arnold, M.R.C.S., L.R.C.P., Assistant Medical Officer, County and City Mental Hospital, Hereford.

1932. Bhathena, Sorab Jamasji, Lt.-Col. *I.M.S.* (retired), L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., L.M.Dubl., c/o Lloyds Bank, Ltd., Bombay, India.

1938. Bhattacharjya, Bidyapati, M.B., B.S.Pat., M.R.C.P.Lond.&Edin., M.R.C.S.Eng., D.P.M., Officer Commanding, 10 Indian General Hospital, Egypt.

1934. Biggart, John Henry, M.D., Professor of Pathology, Queens University, Belfast: 2, Malone Park, Belfast.

1920. Birch, William Somerset, *M.C.*, M.R.C.S., L.R.C.P., Medical Superintendent, The Mental Hospital, Bridgetown; "Rosemont", Bridgetown, Barbados, British West Indies.

1894. Blachford, James Vincent, *C.B.E.*, M.D., B.S.Durh., M.R.C.S., L.R.C.P.Lond., M.P.C., Milverton House, Long Ashton, Somerset.

1935. Blacker, Carlos Paton, *M.C.*, M.A., D.M.Oxon., M.R.C.P., General Secretary, Eugenics Society, 69, Eccleston Square, London, S.W. 1.

1898. Blair, David, M.A., M.D., C.M.Glasg., 3*a*, Eton Terrace, Edinburgh.

1938. Blair, Donald Alexander Sangster, M.A., M.B., Ch.B.Cantab., M.R.C.S., L.R.C.P., D.P.M.Lond., Assistant Medical Officer, Cane Hill Hospital, Coulsdon, Surrey.

1939. Blake, B. S., L.R.C.P.&S.I., Central Criminal Asylum, Dundrum, Co. Dublin.

1919. Blake, Stanley, L.R.C.P.&S.Irel., Deputy Resident Medical Superintendent, Portrane Mental Hospital, Donabate, co. Dublin.

1939. Bleaden, Frank Autridge, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Brighton County Borough Mental Hospital, Haywards Heath, Sussex.

1932. Blyth, William, M.D., Ch.B.Glasg., D.P.M., F.R.F.P.S., Senior Physician, Royal Scottish National Institution, Larbert, Stirlingshire.

1934. Bogle, Harriette Grenelle, M.D., Ch.B.Edin., D.P.M., Assistant Medical Officer, Holloway Sanatorium, Virginia Water, Surrey.

1900. Bolton, Joseph Shaw, D.Sc., M.D., B.S.Lond., F.R.C.P., Emeritus Professor of Mental Diseases, University of Leeds; "Merevale", Brownswood Road, Beaconsfield, Bucks. (PRESIDENT, 1928–29.)

1935. Boome, Edward James, M.B., Ch.B., M.R.C.P., D.P.H., T.D., Divisional Medical Officer, L.C.C., and Visiting Medical Officer, Farmfield Certified Institution; Greystacks, Hill View Road, Woking, Surrey.

1937. Bonnell, Hugh Emrys, B.Sc.Wales, M.R.C.S., L.R.C.P., Visiting Pathologist, Runwell Hospital, Wickford, Essex; 16, Queenswood Court, King's Avenue, London, S.W. 4.

1937. Bonnell, Jane, M.Sc., A.I.C., M.R.C.S., L.R.C.P., Assistant Medical Officer, Harmston Hall, Harmston, Lincoln.

1934. Booth, Edith Marion, M.B., Ch.B., Assistant Medical Officer, Bucks County Mental Hospital, Stone, near Aylesbury.

1922. Bostock, John, M.B., B.S., M.R.C.S., L.R.C.P., F.R.A.C.P., D.P.M., Lauriston, Wickham Terrace, Brisbane, Queensland, Australia.

1918. Bower, Cedric William, L.M.S.S.A., Physician-Superintendent, Springfield House, near Bedford. (*Chairman, S.E. Division*, 1938–39.)

1926. Boyd, William, M.B., Ch.B.Edin., D.P.H., D.P.M., Medical Superintendent, Fife and Kinross District Asylum, Cupar, Fife.

1898. Boyle, A. Helen A., M.D.Brux., L.R.C.P.&S.Edin., 5, The Drive, Hove, Sussex. (*President*, 1939–40.)

1933. Boyle, Eric Patrick, M.B., Ch.B.Edin., D.P.M.Eng., Deputy Medical Superintendent, Worcester County and City Mental Hospital, Powick, Worcester.

1926. Braithwaite, Joseph, M.B., Ch.B.Edin., D.P.M., Assistant Medical Officer, Cumberland and Westmorland Mental Hospital, Garlands, Carlisle.

1922. Bramwell, Edwin, M.D., F.R.C.P.Edin.&Lond., F.R.S.Edin., Physician, Royal Infirmary, and Prof. of Clin. Med., Univ. of Edin., 23, Drumsheugh Gardens, Edinburgh.

1911. Brander, John, M.D., Ch.B.Edin., F.R.C.P., D.P.M., Medical Superintendent, Friern Hospital, New Southgate, London, N. 11.
1925. Brennan, Richard Dominick, M.B., B.Ch.N.U.I., D.P.M., Assistant Medical Officer, District Mental Hospital, Waterford.
1930. Bristowe, Hubert C., M.D.Lond., M.R.C.S., L.R.C.P., M.P.C., Hon. Major *R.A.M.C.* (retired), 3, Upper Belgrave Road, Clifton, Bristol.
1937. Brody, Morris Benjamin, M.B., Ch.B., Assistant Physician, Runwell Hospital, Wickford, Essex.
1938. Brooks, Matthew James, M.R.C.S.Eng., L.R.C.P.Lond., Assistant Medical Officer, Severalls Hospital, Colchester, Essex.
1924. Brown, Basil William, M.B., B.S.Lond., L.M.S.S.A., D.P.M., The Priory, Roehampton, London, S.W. 15.
1905. Brown, Harry Egerton, *O.B.E.*, M.D., Ch.B.Glasg., M.P.C., " Green Gates ", Henderson Road, Pietermaritzburg, Natal, S. Africa.
1908. Brown, Robert Dods, M.D., Ch.B., F.R.C.P.Edin., D.P.H., Dipl. Psych., Physician-Superintendent, Royal Mental Hospital, Aberdeen.
1935. Brown, Roger Crosbie, M.R.C.S., L.R.C.P., Junior Deputy Medical Superintendent, State Criminal Lunatic Asylum, Broadmoor, Crowthorne, Berks.
1916. Brown, William, D.Sc.Lond., M.A., M.D., B.Ch.Oxon., F.R.C.P., Wilde Reader in Mental Philosophy, Univ. Oxford ; 88, Harley Street, London, W. 1.
1939. Browne, James, M.B., B.Ch., B.A.O., Assistant Medical Officer, Botleys Park Colony, Chertsey, Surrey.
1935. Brownlees, Thomas John Kilpatrick, M.R.C.S., L.R.C.P., Assistant Medical Officer, Devon Mental Hospital, Exminster, near Exeter.
1917. Bruce, Alexander Ninian, D.Sc., M.D., F.R.C.P.Edin., Lect. on Neurol., Univ. of Edin. ; 8, Ainslie Place, Edinburgh.
1932. Bruce, David Charles, M.B., Ch.B.Edin., Dipl. Psych. Edin., Medical Superintendent, Criminal Lunatic Department and State Institution for Defectives, Perth.
1928. Bruce, David Kennedy, M.B., Ch.B.Glasg., D.P.M., Senior Assistant Medical Officer, Storthes Hall Mental Hospital, Kirkburton, near Huddersfield.
1927. Brunlees, Oswald, L.R.C.P.&S.Edin., 75, Denmark Villas, Hove, Sussex.
1913. Brunton, George Llewellyn, M.D., Ch.B.Edin., Medical Superintendent, City Mental Hospital, Mapperley Hill, Nottingham.
1939. Buckle, Donald Fergus, M.B., B.S.Melb., D.P.M., c/o National Bank of Australia, George Street, Sydney, New South Wales.
1939. Buhrmann, Maatjevera, M.B., Ch.B., Capetown, Medical Officer, Fort Napier Institution, Pietermaritzburg, Natal, S. Africa.
1933. Bunbury, Doris Elizabeth, M.B., B.S.Lond., M.R.C.P., D.P.M., 15, Devonshire Place, London, W. 1.
1928. Burke, Noel Hawley Michael, M.R.C.S., L.R.C.P., D.P.M., D.M.R.E.Camb., Medical Superintendent, Cell Barnes Colony, St. Albans, Herts.
1932. Burns, Robert Henderson, B.A.Cantab., M.R.C.S., L.R.C.P., Assistant Medical Officer, Claybury Hospital, Woodford Bridge, Essex.
1936. Burrows, Thomas Eggleston, B.A.Cantab., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Hereford County and City Mental Hospital, Burghill, Hereford.
1935. Burt, Hutchison, M.B., Ch.B.Glasg., D.P.M.Leeds, Assistant Medical Officer, West Riding Mental Hospital, Wakefield.
1924. Bushe, Charles Kendal, *O.B.E.*, B.A., M.D., B.Ch.Dubl., Surg.-Rear-Admiral R.N., (retired), Hill End Hospital, St. Albans, Herts.
1921. Buzzard, Sir Edward Farquhar, Bart., *K.C.V.O.*, M.A., M.D., B.Ch.Oxon., F.R.C.P., Regius Professor of Medicine, Oxford University ; 85, Banbury Road, Oxford.

1928. Calder, Flora Hannah Macdonald, M.A., M.D., D.P.H.Edin., Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1.
1921. Caldicott, Charles Holt, *M.B.E.*, M.B., M.R.C.S., L.R.C.P., Grantbourne, Chobham, Surrey.
1928. Caldwell, William Alexander, M.R.C.P., M.R.C.S., D.P.M., Medical Superintendent, West Park Hospital (L.C.C.), Epsom, Surrey.
1938. Calvert, Preston Craine, M.R.C.S., L.R.C.P., Junior Assistant Medical Officer, County Mental Hospital, Herrison, Dorchester, Dorset.
1939. Cameron, Alexander David C. S., M.B., Ch.B., Bangour Mental Hospital, Broxburn, West Lothian.
1925. Cameron, Donald Ewen, M.B., Ch.B.Glasg., D.P.M., Worcester State Hospital, Worcester, Mass., U.S.A.
1936. Cameron, Kenneth, M.B., Ch.B., Dipl. Psych., Assistant Physician, Edinburgh Royal Mental Hospital, Morningside, Edinburgh.

1936. Campbell, Margaret Catherine, M.B., Ch.B.Glas., Assistant Medical Officer, West Riding Mental Hospital, Wakefield.
1897. Campbell, Robert Brown, M.D., C.M., F.R.C.P.Edin., 15, Douglas Crescent, Edinburgh 12. (*Secretary, Scottish Division*, 1910–20, *and Chairman*, 1929–30; PRESIDENT, 1932–33.)
1932. Cannon, Alexander, M.A., M.D., Ph.D., D.P.M., 53, Welbeck Street, London, W. 1.
1930. Cannon, H. C. A. Tandy, Surgeon Lt.-Commander *R.N.* (Ret.), L.R.C.P.&S.I., Resident Physician, Springwell House, Hayes End, Middlesex.
1936. Cant, John Arthur Pinney, M.B., Ch.B.Bir., Waltham House, Coleshill, near Birmingham.
1927. Carey, Catherine, M.B., B.Ch.N.U.I., Assistant Medical Officer, District Mental Hospital, Cork.
1938. Carlyle-Gall, Carlyle Marchant, M.R.C.S., L.R.C.P., D.P.M., 37, University Road, Belfast.
1932. Carroll, Denis Charles, M.A.Cantab., M.R.C.S., L.R.C.P., Proud's Farm, Thaxted, Essex.
1933. Carruthers, Peter Walter, M.B., Ch.B.Edin., Assistant Medical Officer, The Old Manor, Salisbury.
1935. Carse, Joshua, M.D., D.P.M., Medical Superintendent, Graylingwell Mental Hospital, Chichester.
1939. Carson, James, M.B., Ch.B., D.P.M., Senior Assistant Medical Officer, Brighton County Borough Mental Hospital, Haywards Heath, Sussex.
1928. Cassin, Patrick Joseph, M.D., B.Ch.N.U.I., D.M.D., Resident Medical Superintendent, Mental Hospital, Kilkenny, Ireland.
1922. Casson, Elizabeth, M.D., Ch.B.Brist., D.P.M., Dorset House, Clifton, Bristol 8.
1934. Cates, Bernard, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M.Lond., Assistant Physician, City of London Mental Hospital, Stone, near Dartford, Kent.
1928. Cates, Henry Joseph, M.D.Lond., D.P.H., Medical Superintendent, Northwoods House, Winterbourne, Bristol.
1932. Chalmers, Edith, M.B., Ch.B.Glasg., Assistant Medical Officer, Royal Scottish National Institution, Larbert, Stirlingshire.
1937. Chalmers, John, M.B., Ch.B.Glasg., Deputy Medical Superintendent, Glengall Hospital, Ayr.
1911. Chambers, Walter Duncanon, M.A., M.D., Ch.B., F.R.C.P.Edin., M.P.C., Physician-Superintendent, James Murray's Royal Asylum; Murray House, Perth. (*Chairman, Scottish Division*, 1939–40.)
1932. Chapman, William Noel James, M.B., Ch.B., D.P.H., Dipl. Psych. Edin., Medical Superintendent, Lanark District Asylum, Hartwood.
1939. Charlton, Ernest Peter Herries, M.B., B.S., Assistant Medical Officer, Bexley Hospital (L.C.C.), Bexley, Kent.
1928. Chennell, Eileen Anne, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Brooke House, Clapton, London, E. 5.
1923. Chevens, Leslie Charles Frederick, M.R.C.S., L.R.C.P., D.P.M., Cookshayes, Moreton-hampstead, Devon.
1937. Child, John Peto, B.M., B.Ch.Oxon., M.R.C.P., Assistant Medical Officer, St. Alfege's Hospital, Greenwich, London, S.E. 10.
1917. Chisholm, Percy, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Medical Superintendent, Queen Mary Hospital, Hanmer Springs, New Zealand.
1907. Chislett, Charles Game Angus, M.B., Ch.B., F.R.F.P.S Glasg., Medical Superintendent, Lennox Castle Certified Institution, Lennoxtown, Stirlingshire. (*Chairman, Scottish Division*, 1938–39.)
1921. Cholmeley, Montague Adye, M.R.C.S., L.R.C.P., D.P.M., 43, Upper Richmond Road, London, S.W. 15.
1937. Christie, Thomas, M.D., Ch.B., Medical Officer, H.M. Prison, Wormwood Scrubs; 22, Brewster Gardens, North Kensington, London, W. 10.
1937. Clark, James Thomson Doran, M.B., Ch.B.Edin., Medical Officer, Wyke House, Isleworth, Middlesex.
1907. Clarke, Geoffrey, M.D.Lond., Baldwyns, 14, Elgin Road, Bournemouth.
1907. Clarkson, Robert Durward, B.Sc., M.D., C.M., F.R.C.P.Edin., Lect. on Ment. Deficiency, Univ. of Edin.; Little Cambus, Doune, Perthshire. (*Chairman, Scottish Division*, 1935–36.)
1931. Clegg, John Leonard, M.D., Ch.B., D.P.H., D.P.M., Deputy Medical Superintendent, Worcestershire Mental Hospital, Bromsgrove.
1934. Clifford, Louis Seymour, L.R.C.P.I.&L.M., L.R.C.S.I.&L.M., Assistant Medical Officer, Criminal Lunatic Asylum, Dundrum, co. Dublin.
1938. Coats, Percy Murray, M.D., B.S.Dur., Medical Officer, H.M. Prison, Liverpool.
1933. Colahan, Arthur Nicholas Whistler, M.B., Ch.B., 12, De Montfort Street, Leicester.

1900. Cole, Sydney John, M.A., M.D., B.Ch.Oxon., Alphen, Sea Lane, Goring-by-Sea, Worthing, Sussex.

1930. Coleman, Stanley Maurice, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Cornwall Mental Hospital, Bodmin.

1906. Collier, Walter Edgar, M.R.C.S., L.R.C.P.Lond., Ailsa Cottage, Parkfield, Seal, Sevenoaks, Kent.

1903. Collins, Michael Abdy, *O.B.E.*, M.D., B.S.Lond., M.R.C.S., L.R.C.P., Ministry of Pensions, Medical Services Division; Burwood House, Whitstable Road, Canterbury. (*General Secretary*, 1912–18; *Vice-Chairman, Educational Committee*, 1919–27; *Chairman, S.E. Division*, 1932–33; PRESIDENT, 1936–37.)

1934. Conlon, Thomas Joseph, L.R.C.P.I.&L.M., D.P.M., Assistant Medical Officer, District Mental Hospital, Enniscorthy, co. Wexford.

1921. Connell, Ernest Henry, M.B., Ch.B.Edin., D.P.M., 9, Redford Crescent, Colinton, Edinburgh.

1920. Connell, Oliver George, *M.C.*, L.R.C.P.&S.Irel., Medical Superintendent, St. Andrew's Hospital, Thorpe, Norwich.

1914. Connolly, Victor Lindley, *M.C.*, M.B., B.Ch.Belf., D.P.M., Medical Superintendent, Hants County Mental Hospital, Park Prewett, Basingstoke.

1927. Cook, Leslie Colin, M.B., B.Ch., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Bexley Hospital (L.C.C.), Bexley, Kent.

1930. Cooper, Hugh Astley, M.B., B.S.Lond., M.R.C.P., D.P.M., Medical Superintendent, County Mental Hospital, Moulsford, Wallingford, Berks.

1928. Copeland, Cecil Leonard, M.B., Ch.B.Liverp., D.P.M., Deputy Medical Superintendent, County Mental Hospital, Chester.

1938. Copeland, Neville, M.B., Ch.B., Assistant Medical Officer, County Mental Hospital, Brentwood, Essex.

1903. Cormac, Harry Dove, M.B., M.S.Madras, D.P.M., Medical Superintendent, Cheshire County Mental Hospital, Parkside, Macclesfield; Lect. on Ment. Dis., Univ. of Manch.; Parkside House, Macclesfield. (*Chairman, N. and M. Division*, 1931–32.)

1891. Corner, Harry, M.D., M.R.C.S., L.R.C.P., M.P.C., Jersey Farm, Sandridge, near St. Albans, Herts.

1910. Coupland, William Henry, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Flat 8, Manor Court, Leigham Avenue, High Road, Streatham, London, S.W. 16.

1932. Courtney, Patrick J., M.D.N.U.I., Assistant Medical Officer, Donegal Mental Hospital, Letterkenny.

1931. Couston, Alastair Gordon, L.R.C.P.&S.Edin., Sunnyside Mental Hospital, Christchurch, New Zealand.

1936. Cox, Alice, M.B., Ch.B.Glasg., 65, Lister Building, 195, Jeppe Street, Johannesburg, Transvaal, S. Africa.

1911. Cox, Donald Maxwell, *M.C.*, M.R.C.S., L.R.C.P.Lond., Deputy Medical Superintendent, Hereford County Mental Hospital, Burghill.

1938. Cox, Mary, M.B., B.Ch., B.A.O., Assistant Medical Officer, Rubery Hill Mental Hospital, Birmingham.

1926. Coyne, William Joseph, M.D., B.Ch.N.U.I., D.P.M., Resident Medical Superintendent, District Mental Hospital, Monaghan, Ireland.

1937. Craigie, Hugh Brechin, M.B., Ch.B., Assistant Medical Officer, County Mental Hospital, Lancaster.

1911. Crichlow, Charles Adolphus, M.B., Ch.B.Glasg., Senior Assistant Medical Officer, Bangour Village, Uphall, Linlithgowshire.

1930. Crichton-Miller, Hugh, M.A., M.D.Edin., M.D.Pavia, Hon. Senior Physician, The Tavistock Clinic; 6, Devonshire Place, London, W. 1.

1915. Crosthwaite, Frederick Douglas, M.B., Ch.B.Edin., D.P.H., Physician Superintendent, Witrand Institute for Feeble-minded, Potchefstroom, Transvaal, S. Africa.

1923. Crow, Norah Annie, M.A.Edin., M.D., B.S.Lond., "Kingsclere", Harrington Road, Brighton.

1937. Crowe, Philip Michael, M.B., Ch.B., D.P.M., Assistant Medical Officer, Cheshire County Mental Hospital, Parkside, Macclesfield.

1935. Crowley, Timothy, M.B., Ch.B.Edin., Hallington Hall, Blythebridge, Stoke-on-Trent.

1933. Curran, Desmond, M.B., B.Ch.Camb., F.R.C.P., D.P.M., Physician and Lect. on Psych. Med., St. George's Hospital; 14, Wimpole Street, London, W. 1.

1933. Curran, James Thomas, M.B., Ch.B.Glasg., Deputy Medical Superintendent, Lennox Castle Certified Institution, Lennoxtown, Stirlingshire.

1935. Curran, Thomas Patrick, M.B., Ch.B., B.A.O., D.P.M., Deputy Medical Superintendent, County Mental Hospital, Prestwich, near Manchester.
1936. Cuthbert, Theordore Martin, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Sunderland Mental Hospital; "Field House", Cherry Knowle, Ryhope, co. Durham.
1930. Cutts, George Lambert, M.R.C.S., L.R.C.P., L.D.S., D.P.M., Deputy Medical Superintendent, Friern Hospital, New Southgate, N. 11.

1934. Daly, Patricia Mary Josephine, M.B., B.Ch., B.A.O.N.U.I., D.P.H., Assistant Medical Officer, Portrane Mental Hospital, Donabate, co. Dublin.
1935. Danby, Thomas Anyan, M.B., Ch.B.Vict., D.P.H., Capt. R.A.M.C.(T.A.), Medical Superintendent, Sandhill Park, Bishop's Lydeard, Taunton; "Wayside", Bishop's Lydeard, Taunton.
1907. Daniel, Alfred Wilson, B.A., M.D., B.Ch.Camb., M.R.C.S., L.R.C.P., Red Roofs, 25, Lauderdale Drive, Petersham, Surrey. (*Secretary, Educational Committee*, 1920–27.)
1926. Darlington, Arthur, B.A., M.B., B.Ch.Dubl., D.P.H., D.P.M., Deputy Medical Superintendent, Somerset and Bath Mental Hospital, Wells.
1930. Das, Banarsi, M.B., B.S.Punjab, D.P.M., Superintendent, Mental Hospital, Agra, India. (*Secretary, Indian Division since* 1938.)
1925. Davidson, Thomas Wishart, M.B., Ch.B.Glasg., D.P.M., Deputy Medical Superintendent and Pathologist, City Mental Hospital, Humberstone, Leicester.
1922. Davie, Thomas Macnaughton, *M.C.*, M.D., Ch.B.Edin., Ph.D., D.P.M., Barrister-at-Law, Medical Superintendent, East Riding Mental Hospital, Beverley, Yorks.
1935. Davies, Isaac John, M.B., B.Ch., B.Sc.Wales, D.P.M., Senior Assistant Medical Officer, Cardiff City Mental Hospital, Whitchurch, Glam.
1931. Davies, Sidney, M.B., B.S.Lond., L.M.S.S.A., D.P.M., Medical Superintendent, Joint Counties Mental Hospital, Carmarthen.
1928. Davies, Stuart Wyndham, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Hensol Castle, nr. Pontyclun, Glam.
1921. Davies-Jones, Charles William Saunderson, M.B., Ch.B.Edin., Medical Superintendent, Isle of Wight Mental Hospital, Whitecroft, Newport.
1938. Davis, Robert Brocklesby, M.B.Cantab., M.R.C.S., L.R.C.P., Capt. I.M.S., Specialist in Mental Diseases, Northern Command; c/o Indian Military Hospital, Rawalpindi, India.
1920. Dawson, William Siegfried, M.A., M.D., B.Ch.Oxon., F.R.C.P., F.R.A.C.P., D.P.M., Professor of Psychiatry, University of Sydney; B.M.A. House, 135, Macquarie Street, Sydney, New South Wales, Australia.
1937. Dax, Eric Cunningham, B.Sc.Lond., L.M.S.S.A., Senior Assistant Medical Officer, Netherne Hospital, Coulsdon, Surrey.
1926. Deane, Frederick John, M.B., Ch.B.Edin., D.P.M., 24, Cyprus Avenue, Belfast.
1935. Dedman, James Baillie, M.B., Ch.B.Edin., D.P.M., Assistant Medical Officer, Cornwall Mental Hospital, Bodmin, Cornwall.
1925. Delany, John James, L.R.C.P.&S.Irel., D.P.M., 68, Wellington Road, Dublin.
1905. Devine, Henry, *O.B.E.*, M.D., B.S.Lond., F.R.C.P., M.P.C., The Ridge, Virginia Water, Surrey. (*Assistant Editor*, 1916–1920, *and Co-Editor of Journal*, 1920–27.)
1936. De Vine, Michael George, M.B., B.Ch.N.U.I., 126, Harley Street, London, W. 1.
1904. Devon, James, L.R.C.P.&S.Edin., F.R.F.P.S.Glasg., 67, Great King Street, Edinburgh.
1932. Dewar, Douglas Campbell, M.B., Ch.B.Glasg., L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., D.P.M.Lond., Assistant Medical Superintendent, Renfrew District Asylum, Dykebar, Paisley.
1925. Dhunjibhoy, Jal Edulji, M.B., B.S.Bomb., Lt.-Col. *I.M.S.*, Medical Superintendent, The Indian Mental Hospital, Kanké, Ranchi, Bihar and Orissa, India; c/o Lloyds Bank, 6, Pall Mall, London, S.W. 1.
1938. Diamond, Thomas Patrick, M.B., B.Ch., B.A.O., Assistant Medical Officer, Rubery Hill Mental Hospital, Birmingham.
1921. Dick, Alexander, *M.C.*, M.B., Ch.B.Glasg., Medical Superintendent, Stoneyetts Certified Institution, Chryston, Lanarkshire.
1936. Dickson, Robert F. G., L.R.C.P.&S.I., D.P.H., Senior Assistant Medical Officer, Down County Mental Hospital, Downpatrick, Ireland.
1915. Dillon, Frederick, M.D., Ch.B.Edin., Medical Superintendent, Northumberland House, Finsbury Park, London, N. 4.
1909. Dillon, Kathleen, L.R.C.P.&S.Irel., Assistant Medical Officer, District Asylum, Mullingar.

1938. Doherty, Patrick, M.B., B.Ch., B.A.O., D.P.M., Assistant Medical Officer, Mental Hospital, Waterford.
1892. Donelan, John O'Conor, L.R.C.P.&S.Irel., M.P.C., Sylvan, Foxrock, co. Dublin. (*Chairman, Irish Division*, 1931–33.)
1928. Douglas-Morris, Ernest Mannering, L.M.S.S.A., Neurologist, Ministry of Pensions Clinic, Nottingham; Tykeford Abbey Nursing Home, Newport Pagnell, Bucks.
1919. Drake-Brockman, Henry George, M.R.C.S., L.R.C.P.Lond., Medical Superintendent, St. Luke's Hospital, Middlesbrough.
1933. Drummond, Peter, M.B., Ch.B., Medical Superintendent, Mid-Wales Counties' Mental Hospital; Chancefield, Talgarth, Breconshire.
1921. Drury, Kenneth Kirkpatrick, *M.C.*, B.A., M.D., B.Ch.Dubl., D.P.M., Medical Superintendent, Leicestershire and Rutland Mental Hospital, Narborough, near Leicester. (*Secretary, Educational Committee since* 1936.)
1907. Dryden, Arthur Mitchell, M.B., Ch.B.Edin., Medical Superintendent, Glasgow District Mental Hospital, Gartloch, Gartcosh.
1899. Dudley, Francis, L.R.C.P.&S.Irel., "Hilton", Keyberry Park, Newton Abbott, Devon.
1926. Duncan, Archibald Glen, M.D., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Essex County Mental Hospital, Severalls, Colchester.
1937. Dunlevy, Annie Josephine, L.R.C.P.&S.I., Assistant Medical Officer, Portrane Mental Hospital, Donabate, Dublin.
1923. Dunne, John, M.B., B.Ch.R.U.I., D.M.D., Resident Medical Superintendent, Grangegorman Mental Hospital, Dublin, N.W. 5.
1932. Dymock, Thomas, M.D., Ch.B.Glasg., Senior Assistant Medical Officer, Lanark District Mental Hospital, Hartwood, Shotts, Lanarkshire.

1906. Eager, Richard, *O.B.E.*, M.D., Ch.B.Aberd., M.P.C., Crossways, Countess Weir, near Exeter.
1931. Earl, Charles James Cecil, F.R.C.P.I., D.P.M., Medical Superintendent, Monyhall Colony, near Birmingham.
1921. East, Guy Rowland, M.D., B.S., B.Hy.Durh., D.P.H., Medical Superintendent, Northumberland County Mental Hospital, Cottingwood, Morpeth.
1907. East, Wm. Norwood, M.D.Lond., F.R.C.P., M.P.C., "Rhododendrons", Crowthorne, Berks.
1895. Easterbrook, Charles C., M.A., M.D., F.R.C.P.Edin., M.P.C., *J.P.*, Murrayfield Private Hotel, Murrayfield, Edinburgh.
1931. Eaves, Elizabeth Cowper, M.D., B.S., D.P.M.Lond., Honorary Neuro-pathologist, South Yorkshire Mental Hospital, Wadsley, Sheffield; Lect. on Physiol., Univ. of Sheffield; 2, The Mount, Glossop Road, Sheffield, 10.
1924. Eddison, Herbert Wilfred, M.A., M.D.Camb., M.R.C.S., L.R.C.P., D.P.M., 9, The Crescent, Plymouth.
1937. Edel, Ernst, M.D.Berlin, 63, South Hill Park, London, N.W. 3.
1895. Edgerley, Samuel, M.A., M.D., C.M.Edin., M.P.C., Holly Bank, Menston, Leeds. (*Chairman, N. and M. Division*, 1934–36.)
1897. Edwards, Francis Henry, M.D.Brux., M.R.C.P.Lond., "Cherchefelle", Reigate, Surrey.
1924. Edwards, Thomas Lloyd, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., D.P.M., Assistant Medical Officer, Glamorgan County Mental Hospital, Bridgend.
1919. Eggleston, Henry, M.B., B.S.Durh., M.P.C., c/o Standard Bank of S. Africa, 10, Clement's Lane, E.C. 4.
1936. Elphinstone, John Henry, M.R.C.S., L.R.C.P., L.M.S.S.A., Windsor Hotel, Lancaster Gate, London, W. 2.
1901. Erskine, Wm. J. Adams, M.D., C.M.Edin., The Orchard, Ravenmeols Lane, Formby, near Liverpool.
1925. Esson, Walter Louis, M.A., M.B., Ch.B.Aberd., 21, Oldham Road, Miles Platting, Manchester.
1895. Eurich, Frederick Wilhelm, M.D., C.M.Edin., Emeritus Prof. of For. Med., Univ. of Leeds; Lanshawe Cottage, Dibden Purlieu, Southampton.
1939. Eustace, Anthony, M.B., B.Ch., L.M., St. Edmondsbury, Lucan, Dublin.
1934. Eustace, Henry Jocelyn, M.B., B.Ch., B.A.O.Dubl., Assistant Medical Officer, Hampstead, Glasnevin, Dublin.
1909. Eustace, William Neilson, L.R.C.P.&S.Irel., Lisronagh, Glasnevin, Dublin.
1918. Evans, Albert Edward, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.H., Lord Chancellor's Visitor in Lunacy; 11, Weymouth Avenue, Mill Hill, N.W. 7.

1927. Ewan, Grey Lamont, *J.P.*, B.Sc., M.B., Ch.M.Sydney, D.P.M., Medical Superintendent, The Mental Hospital, Stockton, nr. Newcastle, New South Wales.
1930. Ewen, John Harold, M.R.C.P.E., D.P.M., Medical Superintendent, Springfield Hospital, Tooting, London, S.W. 17.
1914. Ewing, Cecil Wilmot, L.R.C.P.&S.Irel., D.P.M., Green Bank, Edward Road, Walton St. Mary, Clevedon, Somerset.

1929. Fairbairn, William Ronald Dodds, M.A., M.D., Ch.B.Edin., Dipl. Psych., 18, Lansdowne Crescent, Edinburgh.
1925. Fairweather, Anne, M.D., B.S.Durh., D.P.M., The Red House, Haydon Bridge, Northumberland.
1933. Faull, John Langdon, M.R.C.S., L.R.C.P., D.P.M., 61, Cotham Brow, Bristol.
1908. Fenton, Henry Felix, M.B., Ch.B.Edin., Medical Superintendent, Worcester County and City Mental Hospital, Powick.
1930. Fenwick, Philip Cuthbert Collingwood, L.M.S.S.A., Deputy Medical Superintendent, East Sussex Mental Hospital, Hellingly.
1937. Ferguson Henry Robb, M.B., Ch.B., D.P.M., Senior Assistant Physician, Royal Earlswood Institution, Redhill, Surrey.
1928. Finiefs, Leonidas Aristodimos, M.D.Paris, M.R.C.S., L.R.C.P., Deputy Medical Superintendent, Three Counties Mental Hospital, Arlesey, Beds.
1938. Finkleman, Benedict, M.B., Ch.B., M.Sc.Vict., D.P.M., Assistant Medical Officer, Lancashire County Mental Hospital, Winwick, Warrington.
1938. Fisher, Henry, M.D.Berl., L.R.C.P.Edin., L.R.C.S.Edin., L.R.F.P.&S.Glas., D.P.M., Assistant Medical Officer, Mapperley Hospital, Nottingham.
1930. Fisher, John William, M.R.C.S., L.R.C.P., D.P.H., D.P.M., Assistant Medical Officer, Devon Mental Hospital, Exminster, S. Devon; Glen Lea, 58, Oldway Road, Paignton, S. Devon.
1903. Fitzgerald, Alexis, L.R.C.P.&S.Irel., Medical Superintendent, District Mental Hospital, Waterford.
1929. FitzGerald, Edward Joseph, M.D., B.Ch.N.U.I.
1908. Fitzgerald, James Francis, L.R.C.P.&S.Irel., Resident Medical Superintendent, District Mental Hospital, Clonmel, co. Tipperary.
1928. Fitzgerald, John, M.D., B.Sc.N.U.I., D.P.M., D.P.H., Resident Medical Superintendent, Mental Hospital, Mullingar.
1930. Fitzgerald, Nora May, M.B., B.Ch., B.A.O., Mental Hospital, Mullingar.
1933. Fitzgerald, Otho William Strangman, M.A., M.D., B.Ch.Dubl., D.P.M., Assistant Medical Officer, Shenley Mental Hospital, Shenley, Herts.
1921. Fleming, Gerald William Thomas Hunter, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Barnwood House, Gloucester. (*Assistant Editor*, 1931–32, *Co-Editor*, 1932–38, *Managing Editor of Journal since* 1938.)
1904. Fleming, Wilfried Louis Remi, M.R.C.S., L.R.C.P., *J.P.*, Suffolk House, Pirbright, Surrey.
1925. Flind, James, M.D., Ch.B.Glasg., D.P.M., Deputy Medical Superintendent, Peckham House, London, S.E. 15.
1937. Foley, Timothy Laurence, B.A., M.B., B.Ch., B.A.O., L.M., Assistant Medical Officer, Mental Hospital, Sligo.
1930. Forbes, Donald John, M.B., Ch.B.St.And., Medical Superintendent, Baldovan Certified Institution; Craigmill House, by Dundee.
1927. Ford Robertson, William Marsden, M.D., Ch.B.Edin., Director, West of Scotland Neuro-Psychiatric Research Institute; 28, Hamilton Park Avenue, Glasgow, W. 2.
1926. Forrester, Robert Cairns, M.B., Ch.B.Edin., D.P.M., Deputy Medical Superintendent, City of London Mental Hospital, Stone, Dartford.
1939. Forsythe, Thomas Ronald, M.B., Ch.B.Sheffield, D.P.M., Commissioner, Board of Control.
1925. Fox, Francis Elliot, B.A.Camb., M.R.C.S., L.R.C.P., Medical Superintendent, Brislington House, Bristol.
1920. Fox, J. Tylor, M.A., M.D., B.Ch.Camb., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Lingfield Epileptic Colony; The Homestead, Lingfield, Surrey.
1923. Franklin, Marjorie Ellen, M.B., B.S., M.R.C.S., L.R.C.P.Lond., D.P.M., Physician, London Clinic for Psycho-Analysis; 86, Harley Street, London, W. 1.
1919. Fraser, Kate, B.Sc., M.D., Ch.B.Glasg., D.P.H., Deputy Commissioner, General Board of Control, Scotland; 25, Palmerston Place, Edinburgh.
1928. Fraser, William, B.Sc., M.B., Ch.B.Glasg., D.P.H., D.P.M., Deputy Medical Superintendent, North Riding Mental Hospital, York.

1935. French, Margaret, M.B., B.S., Wick Lodge, Catsey Lane, Bushey, Herts.
1937. Freudenberg, Rudolf, M.D.Freiburg, Advisory Physician, Moorcroft House, Hillingdon, Middlesex.
1936. Frew, John McIntyre, M.B., Ch.B.Glas., D.P.M., Assistant Medical Officer, North Riding Mental Hospital, York.
1937. Frost, Isaac, B.Sc., M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Friern Hospital, New Southgate, London, N. 11.
1938. Furniss, Frank Webster, M.A.Cantab., M.R.C.S., L.R.C.P., Medical Superintendent, Whittington Hall Institution, Old Whittington, Chesterfield.

1928. Gallagher, Charles Eddie, M.R.C.S., L.R.C.P., " Killiecrankie ", 196, Main Road, Sidcup, Kent.
1932. Galloway, James Forbes, M.D.Liverp., Ch.B., M.R.C.S., L.R.C.P., D.P.M., D.P.H., Public Health Department, Municipal Buildings, Halifax Road, Dewsbury, Yorks.
1928. Gardner, Dorothy Margaret, M.B., B.Ch.Belf., D.P.H., Assistant Medical Officer, Belfast Mental Hospital, Purdysburn, Belfast.
1938. Gardner, Lionel Dalrymple, B.Sc., M.B., Ch.B., Assistant Medical Officer, Hawkhead Mental Hospital, Glasgow, S.W. 2.
1938. Garner, Algernon Ronald, M.R.C.S., L.R.C.P., Assistant Medical Officer, Severalls Hospital, Colchester, Essex.
1931. Garrod, Marjorie, M.R.C.S., L.R.C.P., Hon. Medical Registrar, The Tavistock Clinic; " Bankcroft ", Douglas Road, Harpenden, Herts.
1912. Garry, John William, M.B., B.Ch.N.U.I., Assistant Medical Superintendent, District Mental Hospital, Ennis, co. Clare.
1896. Geddes, John William, M.B., C.M.Edin., 4, Ambrose House, Worthing.
1930. Gemmell, Daniel Topping, L.R.C.P.&S.I., L.R.T.P.&S.G., D.P.M., Dornhurst, Halstead, Essex.
1938. Geraghty, Daniel Joseph, M.B., B.Ch., B.A.O., D.P.M., Assistant Medical Officer, Grangegorman Mental Hospital, Dublin.
1919. Gifford, John, B.A.Cape, M.B., Ch.B.Edin., D.P.M., Medical Superintendent, Lancashire County Mental Hospital, Prestwich.
1931. Gilchrist, Thomas, L.R.F.P.&S.Edin., L.R.F.P.S.Glasg., Assistant Medical Officer, Park Prewett Mental Hospital, Basingstoke.
1931. Gill, Samuel Ernest, M.D.Lond., D.P.H. 3, Buckingham Place, Seven Dials, Brighton, 1.
1938. Gillespie, John Eustace O'Neill, M.A., M.D.Dublin, D.P.M., Oster House Hospital, St. Albans, Herts.
1921. Gillespie, Robert Dick, M.D., Ch.B.Glasg., F.R.C.P., D.P.M., Physician and Lect. on Psych. Med., Guy's Hosp.; 16, Chester Terrace, Regent's Park, London, N.W. 1.
1920. Gillis, Kurt, M.B., Ch.B.Edin., Physician Superintendent, Mental Hospital, Grahamstown, South Africa.
1938. Gillman, Simeon W., M.R.C.S., L.R.C.P., Assistant Medical Officer, Warwickshire and Coventry Mental Hospital, Hatton, near Warwick.
1938. Gilmour, David, M.B., Ch.B.Edin., Deputy Medical Superintendent, Murray Royal, Perth.
1897. Gilmour, John Rutherford, M.B., C.M., F.R.C.P.Edin., M.P.C., " The Fairway ", Overstrand, Norfolk. (*Secretary, N. and M. Division*, 1920–8, *and Chairman*, 1929–31; *President*, 1938–39.)
1906. Gilmour, Richard Withers, M.B., B.S.Durh., M.R.C.P., Wilsley House, Holme Lacy, Hereford.
1929. Glaister, John Norman, M.B., B.S., M.R.C.S., L.R.C.P.Lond., Physician, British Hospital for Nervous and Mental Disorders; 2, Devonshire Place, London, W. 1.
1936. Glass, Joseph Vincent, M.B., B.Ch., B.A.O.N.U.I., D.P.M., Assistant Medical Officer, District Mental Hospital, Carlow, Ireland.
1923. Golla, Frederick Lucien, M.A., M.B., B.Ch.Oxon., F.R.C.P., Medical Director, Burden Neurological Institute, Stapleton, Bristol; Newlands, Frenchay, nr. Bristol. (*Chairman, Research and Clinical Committee since* 1931.)
1897. Good, Thomas Saxty, *O.B.E.*, M.A.Oxon., M.R.C.S., L.R.C.P., Lect. on Psychiat., Univ. of Oxford; 14, Upland Park Road, Oxford. (PRESIDENT, 1930–31.)
1920. Gordon, George, M.B., B.Ch.Glasg., 25, Park Crescent, London, W. 1.
1928. Gordon, Ronald Grey, D.Sc., M.D., F.R.C.P.Edin., 23, Queen Square, Bath.

1901. Gostwyck, Cecil Hubert Gostwyck, M.B., Ch.B., F.R.C.P.Edin., Dipl. Psych., M.P.C. Medical Superintendent, Moss Side State Institution, Maghull, near Liverpool.
1923. Gough, Isabel Falconer, M.B., Ch.B., L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., D.P.M., Shepherds, Cranbrook, Kent.
1928. Grace, Pierce, L.R.C.P.&S.I., Resident Medical Superintendent, District Mental Hospital, Portlaoighise (Maryborough), Leix.
1938. Grace, Richard Fairfax T., M.D., Ch.B.Edin., M.R.C.P., Part-time Medical Officer, Maudsley Hospital; Clinical Assistant, The Tavistock Clinic; 50, Wimpole Street, London, W. 1.
1933. Graham, John James, M.B., Ch.B., D.P.M., White Lodge, Guildford Road, Lightwater, Surrey.
1914. Graham, Norman Bell, *M.C.*, B.A.R.U.I., M.B., B.Ch.Belf., D.P.M., Senior Assistant Medical Officer, Purdysburn Villa Colony, Belfast.
1918. Graham, Samuel John, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Resident Medical Superintendent, Purdysburn Villa Colony, Belfast.
1937. Graham, William, L.R.C.P., L.R.C.S., L.R.F.P.S.G., Senior Assistant Medical Officer, Royal Albert Institution, Lancaster.
1908. Graham, William Shepherd, M.B., B.Ch.R.U.I., Medical Superintendent, Somerset and Bath Mental Hospital, Cotford, near Taunton.
1921. Grant, Alastair Robertson, M.D., Ch.B.Aberd., Medical Superintendent, Lancashire County Mental Hospital, Whittingham, Preston.
1927. Grant, Florence Margaret (*née* Gamble), M.D., B.S., M.R.C.P., D.P.M., 306, St. James's Court, Buckingham Gate, London, S.W. 1.
1925. Grant, John King, M.B., Ch.B.Aberd., Dipl. Psych., Medical Superintendent, Dykebar Mental Hospital, Paisley, Renfrewshire.
1930. Grant, Penuel Grant, M.B., Ch.B., D.P.H., Assistant Medical Officer, City Mental Hospital, Fishponds, Bristol.
1928. Graves (*née* Sykes), Kathleen Annie Harvey, M.D., B.S.Lond., M.B., Ch.B.Liverp., D.P.M., Rubery Hill, Birmingham.
1915. Graves, Thomas Chivers, B.Sc., M.D., B.S.Lond., F.R.C.S., M.R.C.V.S., Medical Superintendent, Rubery Hill and Hollymoor Mental Hospitals, Northfield, Brimingham. (*President-Elect*, 1939–40.)
1916. Gray, Cyril, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Senior Assistant Medical Officer, City Mental Hospital, Gosforth, Newcastle-upon-Tyne.
1938. Gray George Edward, M.B., B.Ch., B.A.O., Assistant Medical Officer, Belfast Mental Hospital, Belfast.
1928. Gray, James, M.D., ChB.Edin., Viewmount, Munlochy, Ross-shire.
1934. Greaves, Marion, M.R.C.S.Eng., L.R.C.P.Lond., D.P.M., Assistant Medical Officer, Cassel Hospital, Swaylands, Penshurst, Kent.
1909. Greene, Thomas Adrian, L.R.C.P.&S.Irel., *J.P.*, Gocean, Killyleagh, co Down. (*Chairman, Irish Division*, 1937–40.)
1936. Greener, Joan Ethne, M.B., Ch.B., D.P.M., D.P.H., 174, Birmingham Road, Wylde Green, Sutton Coldfield, Warwickshire.
1922. Gregorson, Albert William, M.D., Ch.B., F.R.F.P.S.Glasg., 17, Forestdale, Southgate, London, N. 14.
1927. Grierson, Hugh Arrowsmith, *M.C.*, M.B., B.S.Lond., Medical Officer, H.M. Prison, Brixton, London, S.W. 2.
1926. Griffiths, Gwenvron Mary, M.D.Lond., M.R.C.P., 56, Wimpole Street, London, W. 1.
1934. Griffiths, Henry John, M.R.C.S., L.R.C.P., 9, Crown Villas, Morriston, Swansea.
1901. Grills, Galbraith Hamilton, M.D., B.Ch.R.U.I., D.M.D., M.P.C., Medical Superintendent, Cheshire County Mental Hospital, Upton, Chester. (*Chairman, N. and M. Division*, 1936–38.)
1935. Guirdham, Arthur, M.A., D.M.Oxon., D.P.M., Medical Superintendent, Bailbrook House, Batheaston, Bath.
1922. Guppy, Francis Henry, *M.C.*, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Brighton Mental Hospital, Haywards Heath, Sussex.
1938. Guttmann, Erich, M.D.Munich, The Maudsley Hospital, Denmark Hill, London, S.E. 5.

1932. Hagedorn, Egmont Oscar, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., 441, Pasir Panjang Road, Singapore.
1939. Haggar, Norman James, M.R.C.S., L.R.C.P., Assistant Medical Officer, Bucks County Mental Hospital, Stone, Aylesbury.
1939. Haldane, Frederick Paterson, M.B., Ch.B., Assistant Physician, Runwell Hospital, Wickford, Essex.

1928. Hamilton, John Gerard, M.D., B.S., M.R.C.S., L.R.C.P., D.P.M., Senior Assistant Physician, Bethlem Royal Hospital, Monks Orchard. Eden Park, Beckenham, Kent.

1920. Hancock, Allen Coulter, *M.C.*, M.B., B.S., M.R.C.S., L.R.C.P., D.P.H., D.P.M., Medical Superintendent, Kent County Mental Hospital, Barming Heath, Maidstone.

1929. Handley, Richard, M.B., Ch.B.Manch., D.P.M., Medical Director, David Lewis Epileptic Colony, Warford, Alderley Edge, Cheshire.

1923. Hardcastle, Douglas Noel, M.R.C.S., L.R.C.P., D.P.M., 62, Queen Anne Street, London, W. 1; Haymeads Emergency Hospital, Bishops Stortford, Herts.

1920. Harding, Edward Palmer, L.R.C.P.&S.Irel., Deputy Medical Superintendent, East Riding Mental Hospital, Beverley.

1934. Hardwick, Sydney Walpole, M.D., B.Sc.Lond., M.R.C.P., D.P.M., Deputy Medical Superintendent, West Park Hospital, Epsom, Surrey.

1936. Harke, Wilfred Vaughan, M.R.C.S., L.R.C.P., D.P.M., Physician, Department for Functional Disorders, Royal Victoria and West Hants Hospital, Bournemouth; 23, Browning Avenue, Boscombe, Hants.

1920. Harper, Raymond Sydney, M.R.C.S., L.R.C.P., 36, First Avenue, Hove, Sussex.

1904. Harper-Smith, George Hastie, M.A., M.D.Camb., M.R.C.S., L.R.C.P., Green Meadow, Wivelsfield Green, Sussex.

1938. Harris, Arthur, B.A., M.D.Munich, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, St. Bernard's Hospital, Southall; 94, Bryanston Court, George Street, London, W. 1.

1939. Harris, Cyril Robert, M.B., B.Ch.Dubl., D.P.M., Senior Assistant Medical Officer, Holloway Sanatorium, Virginia Water, Surrey.

1924. Harris, John Stuart, M.D., Ch.B.Edin., M.R.C.P., D.P.M., Medical Superintendent, Claybury Hospital, Woodford Bridge, Essex.

1928. Harris, Noel Gordon, M.D., B.S., M.R.C.S., L.R.C.P., D.P.M., 414, Harley Street, London, W. 1.

1898. Harris-Liston, Llewellyn, M.D.Brux., M.R.C.S., L.R.C.P., L.S.A., The Hall, Glan-y-don, Colwyn Bay, N. Wales.

1930. Harrison, Geoffrey J., L.R.C.P.&S.I., Assistant Medical Officer, Lancs County Mental Hospital, Winwick, Warrington, Lancs.

1928. Harrowes, William McConnachie, M.D., Ch.B.Glasg., D.P.M., Medical Superintendent, New Saughton Hall, Polton, Midlothian.

1905. Hart, Bernard, M.D.Lond., F.R.C.P., Physician and Lect. on Ment. Dis., Univ. Coll. Hosp.; 79, Harley Street, London, W. 1.

1930. Haslam-Fox, Edward Arthur, M.B., Ch.B.Edin., D.P.M., Medical Superintendent, Cranage Hall, Holmes Chapel, Cheshire.

1935. Haughie, Thomas McFadden, M.B., Ch.B., D.P.H., Assistant Medical Officer, County Mental Hospital, Whittingham, Preston, Lancs.

1923. Hayes, Edmund Duncan Tranchell, B.A., M.D., B.Ch.Dubl., D.P.M., Medical Superintendent, County Mental Hospital, Berry Wood, Northampton.

1920. Haynes, Horace Guy Lankester, M.R.C.S., L.R.C.P., Littleton Hall, Brentwood, Essex. (*Secretary, Parliamentary Committee*, 1929–36; *Chairman, S.E. Division*, 1934–36; *Registrar since* 1938.)

1936. Haynes, William Noël Lankester, M.R.C.S., L.R.C.P., M.P.C., Capt., R.A.M.C. c/o Glyn Mills & Co., Holts Branch, Kirkland House, Whitehall, London, S.W. 1.

1939. Hayward, Edwin William, M.A.Cantab., F.R.C.S.Edin., L.M.S.S.A., Lieut., R.A.M.C., Principal Medical Officer, Jodhpur, India.

1938. Hayward, Lilian Ann, M.B., Ch.B.Edin., D.P.M., Assistant Medical Officer, Warwickshire and Coverntry Mental Hospital, Hatton, near Warwick.

1935. Hayward, Sydney Thomas, M.B., B.S.Lond., M.R.C.S., L.R.C.P., Arthington, Barton Road, Torquay.

1938. Haworth, Norah A., M.A.Camb., M.R.C.S., L.R.C.P., D.P.M., 69, Gloucester Court, Kew Road, Kew.

1927. Healey, Frederick Henry, B.Sc., M.D., Ch.B.Birm., D.P.M., Medical Superintendent, Hellesdon Hospital, Norwich.

1933. Hegarty, Denis, M.B., B.Ch., B.A.O. N.U.I., D.P.M., Assistant Medical Officer, Portrane Mental Hospital, Donabate, co. Dublin.

1932. Hemphill, Robert Edward, M.B., B.Ch., B.A.O.Dubl., D.P.M., Assistant Medical Officer, City Mental Hospital, Bristol.

1920. Henderson, Cyril John, M.B.Durh., Medical Superintendent, The Royal Albert Institution, Lancaster.

1929. Henderson, David, M.D., Ch.B.Glasg., Assistant Medical Officer and Pathologist, Stafford County Mental Hospital, Cheddleton; The Hollies, Cheddleton, near Leek.

1916. Henderson, David Kennedy, M.D., Ch.B.Edin., F.R.F.P.S.Glasg., Physician-Superintendent, Edinburgh Royal Mental Hospital, Morningside; Professor of Psychiatry, University of Edinburgh; Tipperlinn House, Edinburgh.

1923. Henderson, Norman Keane, B.A., LL.B.Camb., M.B., Ch.B.Edin., D.P.H., D.P.M., Medical Superintendent, Rauceby Mental Hospital, Sleaford, Lincs.

1930. Hennelly, Thomas John, M.D., B.Ch., B.A.O.N.U.I., D.P.M., Medical Superintendent, Cardiff City Mental Hospital, Whitchurch, Glamorgan; Lecturer in Mental Diseases, Welsh National School of Medicine

1924. Herbert, James Ewart, M.B., B.Ch.R.U.I., Senior Assistant Medical Officer, District Asylum, Omagh.

1938. Herd, James Alan, M.B., Ch.B.Man., M.R.C.S., L.R.C.P., Assistant Medical Officer, Leavesden Hospital, Abbots Langley, Watford, Herts.

1925. Heron, John, M.B., Ch.B.Edin., D.P.M., British Dispensary, 35, Raffles Place, Singapore.

1929. Hewitt, Edward John Campbell, M.D., Ch.B.Edin., D.P.M., Deputy Medical Superintendent, Shenley Mental Hospital, Shenley, Herts.

1938. Higgins, Niall B., M.B., B.Ch., B.A.O., D.P.M., Assistant Medical Officer, Mental Hospital, Mullingar.

1937. Hill, Horace Bryden, M.B., B.S.Lond., M.R.C.P., Medical Officer, Laverstock House, Salisbury.

1937. Hill, John Denis Nelson, M.B., B.S., M.R.C.S., L.R.C.P., St. Thomas's House, Lambeth Palace Road, London, S.E. 1.

1933. Hilliard, Leslie Theodore, M.A., M.B., B.Ch., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Tooting Bec Hospital, London, S.W. 17.

1931. Hills, Harold William, M.D., B.S.Lond., M.R.C.P., D.P.M.Camb., "Cotsmoor", Rodborough Common, Stroud, Glos.

1932. Hingston, Cicely Lamorna, *M.B.E.*(Mil.), M.R.C.S., L.R.C.P., Hon. Visiting Physician, Lady Chichester Hospital, Hove; 29, The Drive, Hove, Sussex.

1930. Hobson, Jack Abbott, B.Sc., M.B., Ch.B., D.P.M., Assistant Physician, Woodside Hospital, Muswell Hill, London, N. 10.

1939. Hodge, Ralph Sessions, M.R.C.S. L.R.C.P. Hon. Medical Psychologist, West End Hospital for Nervous Diseases; Hon. Physician, Crewkerne Hospital; The Abbey, Crewkerne, Somerset.

1935. Holmes, Cedric, L.R.C.P., L.R.C.S.Edin., L.R.F.P.S.Glasg., L.D.S.Liverp., Assistant Medical Officer, County Mental Hospital, Chester.

1929. Holmes, Eric Gordon, M.A., M.B., B.Ch.Camb., Lect. in Biochem., Univ. Camb.; Biochemical Laboratory, Cambridge.

1925. Honan, Bernard Francis, L.R.C.P.&S.Irel., D.P.M., Medical Superintendent, District Mental Hospital, Cork.

1920. Hooper, Reginald Arthur, M.B., B.S.Durh., Medical Superintendent, City Mental Hospital, Fulford, York.

1929. Hopkins, Edwin Lancelot, *M.C.*, M.R.C.S., L.R.C.P., D.P.H., D.P.M., Medical Superintendent, County Mental Hospital, Mickleover, Derby.

1926. Hopwood, Joseph Stanley, M.B., B.S., M.R.C.S., L.R.C.P., Deputy Medical Superintendent, State Criminal Lunatic Asylum, Broadmoor.

1935. Horsley, John Stephen, M.R.C.S., L.R.C.P., Senior Assistant Medical Officer, Dorset Mental Hospital, Dorchester.

1926. Hosie, William, M.B., Ch.B.Glasg., 2, Chester Road, Northwich, Cheshire.

1894. Hotchkis, Robert Dunmore, M.A.Glasg., M.D., B.S.Durh., M.R.C.S., L.R.C.P.Lond., M.P.C., Rathmore, Kennedy Gardens, St. Andrews, Fifeshire.

1934. Howie, James Erskine, M.D.Liverp., M.R.C.S., L.R.C.P., D.P.M., Hollins Drive, Winwick, Warrington, Lancs.

1904. Hughes, William Stanley, M.B., B.S., M.R.C.S., L.R.C.P., Medical Superintendent, Salop County Mental Hospital, Bicton Heath, Shrewsbury.

1932. Hull, Eric Randal, M.B., B.Ch., B.A.O., D.P.M., Deputy Medical Superintendent, Calderstones, Whalley, near Blackburn, Lancs.

1931. Hunter, Constance Primrose Helena, L.R.C.P.&S.Edin., D.P.H.Edin., Secretary, Scottish Association for Mental Welfare, 25, Palmerston Place, Edinburgh; St. Catherine's, Linlithgow.

1897. Hunter, David, M.A., M.B., B.Ch.Camb., L.S.A., Medical Superintendent, The Coppice, Nottingham. (*Secretary, S.E. Division*, 1910–1913).

1928. Hunter, James Dewar Hunter, M.B., Ch.B.N.Z., Dipl. Psych., Senior Assistant Medical Officer, Mental Hospital, Seacliff, Otago, New Zealand.

1939. Hunter, Robert Munro Manson, B.Sc., M.B., Ch.B., D.P.H., Assistant Medical Officer, Herrison Hospital, Dorchester.
1935. Hurley, Theodore Egan, M.B., B.S., D.P.M., Assistant Medical Officer, Knowle Mental Hospital, Fareham, Hants.
1938. Hutton, Effie Lilian, M.B., B.S.Lond., D.P.M., Research Medical Officer, Malaria Therapy Centre, Horton Hospital, Epsom.
1931. Hutton, Eustace, M.R.C.S., L.R.C.P., Deputy Medical Superintendent, North Wales Counties' Mental Hospital, Denbigh.
1911. Hutton, Isabel Emslie, M.D., Ch.B.Edin., Hon. Physician, British Hospital for Mental and Nervous Disorders; 6, Montagu Place, London, W. 1.

1926. Illingworth, Reginald Ernest, L.R.C.P.&S., L.D.S.Edin., D.Psy.Durh., Deputy Medical Superintendent, Northumberland County Mental Hospital, Cottingwood, Morpeth.
1915. Ingall, Frank Ernest, F.R.C.S., D.P.H., 36, Albert Road, Ashford, Kent.
1926. Ironside, Archibald Jennings, M.A., M.B., Ch.B.Aberd., Assistant Physician Superintendent, Fort Napier Institution, Pietermaritzburg, Natal, S. Africa.
1932. Irvine, Francis Philip, M.B., Ch.B.Liverp., Assistant Medical Officer, East Sussex Mental Hospital, Hellingly.
1906. Irwin, Peter Joseph, L.R.C.P.&S.Irel., Medical Superintendent, District Mental Hospital, Limerick.

1936. Jackson, Winifred M., M.B., B.Ch., B.A.O.Belf., Assistant Medical Officer, Erdington House, Birmingham.
1927. Jacobson, Jack Nathan, M.R.C.S., L.R.C.P., D.P.M., D.M.R.E.Camb., Deputy Medical Superintendent, Fountain Hospital, London, S.W. 17.
1914. James, George William Blomfield, *M.C.*, M.D., B.S.Lond., L.S.A., D.P.M., Physician, Moorcroft House, Hillingdon, Uxbridge; Lect. on Ment. Dis., St. Mary's Hosp.; 124, Harley Street, London, W. 1. (*Secretary, Parliamentary Committee*, 1926–29.)
1935. James, Gwilym Treharne, B.Sc., M.B., B.Ch., Assistant Medical Officer, Dorset Mental Hospital, Herrison, Dorchester.
1939. James, Stanley George, M.D., M.Ch., M.R.C.P., D.P.M., Deputy Medical Superintendent, Rampton State Institution, Retford, Notts.
1922. Jarrett, Reginald Fitzroy, F.R.F.P.S.Glasg., L.M.S.S.A., Medical Superintendent, Leybourne Grange Colony, West Malling, Kent.
1938. Jefferson, Gertrude M., M.R.C.S., L.R.C.P., D.P.M., 33, Belfield Road, Didsbury, Manchester.
1908. Jeffrey, Geo. Rutherford, M.D., Ch.B.Glasg., F.R.C.P., F.R.S.Edin., M.P.C., 11, Langland Gardens, Hampstead, London, N.W. 3.
1938. Jeffrey, Manfred, M.B., Ch.B.Glasg., Assistant Medical Officer, Wadsley Mental Hospital, Sheffield.
1925. Jenkins, John Alexander, M.B., Ch.B.Glasg., Medical Superintendent, Mental Hospital, Larbert, Stirlingshire.
1924. Jenkins, Reginald Edward, L.M.S.S.A., Willow Hayne, London Road, N. Cheam, Surrey.
1935. Johnson, James Stanley, M.B., B.S.Durh., D.P.M.Leeds, Assistant Medical Officer, Durham County Mental Hospital, Winterton, Stockton-on-Tees.
1928. Johnston, James McLauchlan, M.B., Ch.B.Edin., Lyndhurst, Primrose Bank Road, Edinburgh, 5.
1936. Johnston, John Moore, M.B., B.Ch., B.A.O.Dub., Resident Medical Superintendent, The Mental Hospital, Omagh, co. Tyrone, Ireland.
1935. Jones, Maxwell Shaw, M.B., Ch.B., D.P.M., Assistant Physician, Royal Edinburgh Hospital for Mental and Nervous Disorders, Morningside, Edinburgh.
1936. Jones, Norman Howard, M.R.C.S., L.R.C.P., Apartment Haus, Steinengraben 51, Basel, Switzerland.
1938. Jones, Thomas Brinley, M.R.C.S., L.R.C.P., D.P.M., Bridge Home Institution, Witham; Carlow, London Road, Witham, Essex.

1934. Keane, Clarence Augustine, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, The Mental Hospital, Berry Wood, Northampton.
1927. Kearney, Joseph, M.B., B.Ch.N.U.I., D.P.M., Resident Medical Superintendent, Mental Hospital, Letterkenny, Donegal.
1907. Keene, George Henry, M.D., B.Ch.Dubl., 61, Cowper Road, Rathmines, Dublin.
1909. Keith, William Brooks, *M.C.*, M.D., Ch.B.Aberd., M.P.C., Medical Superintendent, St. Audry's Hospital, Melton; Redwald House, Melton, Suffolk. (*Secretary, Parliamentary Committee*, 1921–26; *Chairman, S.E. Division*, 1936–7.)
924. Kelly, Daniel Lane, L.R.C.P.&S.Irel., Inspector of Mental Hospitals, Local Government Department; 52, Grosvenor Road, Rathgar, Dublin.

1930. Kelly, John Vincent, M.B., B.Ch., D.P.M., Assistant Medical Officer, District Mental Hospital, Castlebar, Ireland.
1939. Kelly, Patrick Joseph, L.R.C.P.&S.I., L.M., D.P.M., Assistant Medical Officer, Mental Hospital, Limerick.
1936. Kennedy, Alexander, M.D., B.S.Lond., M.R.C.P., 124, Wicken Avenue, Cheam, Surrey.
1931. Kennedy, Robert Stewart, M.B., Ch.B., D.P.M., Medical Superintendent, West Riding Mental Hospital, Wadsley, Sheffield.
1938. Kennedy, William Graeme, M.B., Ch.B.St. And., Capt. I.M.S., Specialist in Mental Diseases, Eastern Command; Indian Military Hospital, Lucknow.
1938. Kenton, Colman, M.R.C.S., L.R.C.P., Assistant Medical Officer, County Mental Hospital, Rainhill, Lancs.
1902. Kerr, Neil Thomson, M.B., C.M.Edin., *J.P.*, Ardsenaig, Ardrishaig, Argyll. (*Chairman, Scottish Division*, 1930–31.)
1920. Key, Gordon James, M.B., Ch.B.Aberd., Medical Superintendent, Mental Hospital, Grahamstown, C.P., South Africa.
1923. el Kholy, Mohamed Kamel, M.R.C.S., L.R.C.P., D.P.M., Medico-Legal Office, Post Office Buildings, Alexandria, Egypt.
1920. Kimber, William Joseph Teil, M.R.C.S., L.R.C.P., D.P.M., Medical Director, Hill End Hospital and Clinic, St. Albans. (*Secretary, Educational Committee*, 1927–30.)
1903. King, Frank Raymond, B.A.Camb., M.R.C.S., L.R.C.P., Medical Superintendent, Peckham House, Peckham, London, S.E. 15.
1902. King-Turner, Arthur Charles, M.B., C.M.Edin., Medical Superintendent, The Retreat, Fairford, Gloucestershire.
1935. Kingston, Frank Edward, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, West Riding Mental Hospital, Menston, nr. Leeds.
1915. Kirwan, Richard R., M.B., B.Ch.R.U.I., Assistant Medical Officer, West Riding Mental Hospital, Menston, Leeds.
1933. Kirwan, William Joseph, M.B., B.Ch., B.A.O.N.U.I., D.P.M., City Mental Hospital, Winson Green, Birmingham.
1936. Kitching, Edwin Howard, M.B., Ch.B.Leeds, M.R.C.S., M.R.C.P., D.P.M., Psychiatrist, Manchester Royal Infirmary; 22, St. John Street, Manchester, 3.
1939. Knight, Gwendoline Dorothy, M.R.C.S., L.R.C.P., D.P.M., Leeds, Assistant Medical Officer, The Retreat, York.
1919. Knight, Mary Reid, M.A., M.B., Ch.B.Glasg., Assistant Medical Officer, Paisley Mental Hospital, Riccartsbar.
1937. Knox, John Stuart, M.R.C.S., L.R.C.P., D.P.M., Junior Deputy Medical Superintendent, Broadmoor Criminal Lunatic Asylum, Crowthorne, Berks.

1914. Ladell, Robert George Macdonald, M.B., Ch.B.Vict., Queens Hospital, Birmingham.
1923. Laing, John Kidd Collier, M.B., B.S.Melb., D.P.M., Medical Superintendent, Darenth Park, Dartford, Kent.
1935. Lalkaka, Kaikhushru Ardeshir J., M.B., B.S.Bombay, Hon. Psychiatrist to Bai Yamunabai Nair Hospital; "Nishat", Darabsha Road, off Nepean Sea Road, Bombay, 6.
1925. Landers, John Joseph, M.B., B.Ch.N.U.I., D.P.H. 26, Lyford Road, Wandsworth Common, London, S.W. 18.
1935. Langdon-Down, Mary, M.B., B.S.Lond., Assistant Medical Officer, Normansfield, Teddington; Lansdowne, Holmesdale Road, Teddington.
1896. Langdon-Down, Reginald L., M.A., M.B., B.Ch.Camb., Normansfield, Teddington, Middlesex.
1938. Larkin, Edward Henry, M.B., B.S., D.P.M., Deputy Medical Superintendent, West Ham Mental Hospital, Goodmayes, Essex.
1925. Lascelles, William James, M.D., B.Ch.Belf., D.P.M., Assistant Medical Officer, Claybury Hospital, Woodford Bridge, Essex.
1935. Last, Samuel Leopold, M.D.Berlin, L.R.C.P., L.R.C.S.Edin., L.R.F.P.S.Glasg., D.P.M., Penarth, Runwell, nr. Wickford, Essex.
1937. Laughland, William Walker, M.B., Ch.B., Capt. I.M.S., Indian Military Hospital, Almora, U.P.
1935. Laval, Evariste, M.B., C.M.Edin., Park End, Egham, Surrey.
1935. Laverty, Samuel John, B.A., M.B., Ch.B., B.A.O., L.M., D.P.M., Medical Superintendent, Harmston Hall Colony, Lincoln; Medical Adviser, Lincolnshire Joint Board for the Mentally Defective.
1929. Laws, John Joseph, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Horton Hospital, Epsom.
1936. Leckie, James, B.Sc., M.B., Ch.B., Assistant Physician, Royal Mental Hospital, Aberdeen.

1915. Leech, Henry Brougham, B.A., M.D., B.Ch.Dubl., 55, Kenilworth Road, Leamington, Warwickshire. (*Acting Registrar*, 1923–24.)
1909. Leech, John Frederick Wolseley, B.A., M.D., B.Ch.Dubl., D.P.M., Medical Superintendent, Wilts County Mental Hospital, Devizes.
1899. Leeper, Richard R., F.R.C.S., L.R.C.P.Irel., M.P.C., Medical Superintendent, St. Patrick's Hospital, Dublin. (*Secretary, Irish Division*, 1911–29, *and Chairman*, 1929–31; PRESIDENT, 1931–32.)
1906. Leggett, William, B.A., M.D., B.Ch.Dubl., Medical Officer, Smithston Mental Hospital, Greenock.
1927. Levinson, Reuben, M.B., Ch.B.Edin., D.P.H., D.P.M., 58, Wimpole Street, London, W. 1.
1937. Lewis, Arthur Picton Rossiter, B.Sc.Lond., M.R.C.S.Eng., L.R.C.P.Lond., Medical Officer, H.M. Prison Service; 162, Du Cane Road, Shepherd's Bush, London, W. 12.
1933. Lewis, Aubrey Julian, M.D.Adelaide, F.R.C.P., Clinical Director, Maudsley Hospital, London, S.E. 5.
1930. Lewis, Edmund Oliver, M.A.Camb., D.Sc.Lond., M.R.C.S., L.R.C.P., Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1. (*Secretary, Mental Deficiency Committee since* 1935.)
1916. Lewis, Edward, F.R.F.P.S.Glasg., L.R.C.P.&S.Edin., Medical Superintendent, Hensol Castle Institution, Pontyclun, Glamorgan.
1924. Lewis, John Biddulph Strafford, M.A., M.D.Camb., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, St. Bernard's Hospital, Southall, Middlesex.
1931. Liddell, John Kenneth Crawford, M.B., Ch.B.Edin., D.P.M., Senior Assistant Medical Officer, Barnwood House, Gloucester.
1920. Lilly, George Austen, *M.C.*, M.A., M.D.Camb., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Cane Hill Hospital, Coulsdon, Surrey.
1939. Ling, Thomas Mortimer, M.D.Oxf., M.R.C.P., Medical Officer, Bristol Police; 50, Pembroke Road, Clifton, Bristol.
1927. Lindsay, Thomas, M.D., F.R.C.S.Edin., D.P.M., Medical Superintendent, Caterham Hospital (L.C.C.); The Pines, Caterham, Surrey. (*Chairman, South-Eastern Division*, 1939–40.)
1933. Linklater, George James Irvine, *O.B.E.*, M.D., M.R.C.P.E., D.P.H., D.T.M., Assistant M.O.H., Edinburgh; Westland House, Eskbank, Midlothian.
1908. Litteljohn, Edward Salterne, M.R.C.S., L.R.C.P., Medical Superintendent, The Manor, Epsom.
1938. Littlewood, James, M.B., Ch.B., D.P.M., Assistant Medical Officer, Parkside Mental Hospital, Macclesfield.
1935. Lloyd, John Ernest Seton, M.D., Ch.B.Liverp., M.R.C.P., D.P.M., Barrister-at-Law, Medical Superintendent, The Fountain Hospital, Tooting, London, S.W. 17.
1936. Lloyd, John Stanley, M.D., F.R.C.S.Edin., Hayes Park, Hayes, Middlesex.
1934. Lockwood, Madeline Rose, M.R.C.S., L.R.C.P., D.P.M., Resident Medical Superintendent, Fenstanton, Christchurch Road, Streatham Hill, London, S.W. 2.
1922. Logan, Frederick Colquhoun, M.B., Ch.B., F.R.F.P.S.Glasg., Medical Superintendent, County and City Mental Hospital, Gloucester; Lindi, Horton Road, Gloucester.
1932. Logan, William Robert, M.B., Ch.B., Assistant Superintendent, Mental Hospital, Singapore.
1924. Lornie, Peter, *O.B.E.*, M.D., Ch.B.Edin., Senior Assistant Medical Officer, Monmouth County Mental Hospital, Abergavenny.
1924. Lothian, Douglas B. M., M.B., Ch.B., F.R.C.P.Edin., D.P.M., Medical Superintendent, Down Mental Hospital, Downpatrick, N. Ireland.
1923. Lovell, Clement, *M.C.*, M.D., B.S.Lond., Pathologist, Bethlem Royal Hospital, Monk's Orchard, Beckenham, Kent; Beach Road, Emsworth, Hants.
1931. Lowenfeld, Margaret Frances Jane, M.R.C.S., L.R.C.P., Hon. Medical Director, The Children's Clinic for the Treatment and Study of Nervous and Delicate Children; 1, Weymouth House, Hallam Street, London, W. 1.
1906. Lowry, James Arthur, M.D., B.Ch.R.U.I., Medical Superintendent, Surrey County Mental Hospital, Brookwood.
1928. Lowson, William, M.B., Ch.B.St. Andr., Medical Officer, Moat House, Tamworth; 9, Colehill, Tamworth, Staffordshire.
1926. Lucas, Edmund Stanley Sayer, M.R.C.S., L.R.C.P., Major, *I.M.S.*, c/o Grindlay & Co., Bombay, India.
1938. Lucas, Saul Harold, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Leavesden Hospital, Abbots Langley, Watford, Herts.
1930. Lyons, Bernard, M.B., B.Ch., B.A.O.N.U.I., Medical Superintendent, Ballinasloe Mental Hospital, co. Galway.
1936. Lyons, John Francis, L.R.C.P.&S.I., D.P.H., D.P.M., L.M.Rot., Medical Superintendent, Hortham Colony, Almondsbury, near Bristol.

1920. McAlister, William Malcolm, M.A., M.B., Ch.B., F.R.C.P.Edin., Dipl. Psych., Medical Superintendent, Bangour Village, West Lothian; Lect. on Psychiat., Univ. of Edin. (*Secretary, Scottish Division, since* 1935.)

1906. Macarthur, John, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, County Mental Hospital, Bracebridge Heath, Lincs.

1923. Macaulay, Douglas Ian Otto, M.D., Ch.B.Edin., D.P.M., Medical Superintendent, Chiswick House, Pinner, Middlesex.

1939. Macaulay, Joseph Langham, M.D., L.C.P.&S.Quebec, Medical Superintendent, Bishopstone House, Bedford.

1936. McBroom, Robert P. J., M.B., Ch.B.Glasg., Wedgewood, Cadzow Street, Motherwell.

1880. MacBryan, Henry Crawford, L.R.C.P.&S.Edin., *2a*, Clifton Road, Weston-super-Mare, Somerset.

1926. MacCallum, Alexander Grigor, M.B., Ch.B.Glasg., 8, Becmead Avenue, Streatham, London, S.W. 16.

1929. Maccallum, Archibald Montgomery, M.B., Ch.B.Glasg., Assistant Medical Officer, Ipswich Mental Hospital, Ipswich.

1929. MacCalman, Douglas Robert, M.D., Ch.B.Glasg., 128, Harley Street, London, W. 1.

1929. McCartan, William, M.D.Belf., M.R.C.P., D.P.H., D.P.M., Medical Superintendent, Brighton Mental Hospital, Haywards Heath, Sussex.

1934. McCarthy, Cornelius J., M.B., B.Ch., B.A.O.N.U.I., B.Sc., D.P.H., D.P.M., Grangegorman Mental Hospital, co. Dublin.

1900. McClintock, John, L.R.C.P.&S.Edin., Resident Medical Superintendent, Grove House, Church Stretton, Salop.

1931. McConnell, Joyce, M.B., B.S.Lond., D.P.M., Assistant Medical Officer, Long Grove Hospital, Epsom.

1927. McCoull, George, M.D., B.S.Durh., L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Medical Superintendent, Prudhoe Hall Colony for Mental Defectives; Tyne View, Prudhoe-on-Tyne.

1936. McCowan, Alexander Knight, M.B., Ch.B., D.P.M., Assistant Medical Officer and Pathologist, Chartham Mental Hospital, Canterbury, Kent.

1920. McCowan, Peter Knight, M.D., Ch.B.Edin., F.R.C.P.Lond., D.P.M., Barrister-at-Law; Physician Superintendent, Crichton Royal, Dumfries. (*Secretary, Research and Clinical Committee, since* 1931.)

1926. McCowan, Mrs. P. K. (*née* Northcote), M.D., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Crichton House, Crichton Royal, Dumfries.

1932. McCulley, William John, B.Sc., M.B., Ch.B., D.P.M., St. Andrew's Hospital, Thorpe, Norwich.

1936. McCulloch, Andrew Stenhouse, M.B., Ch.B.Edin., Dipl. Psych. Edin., Assistant Medical Officer, Lanark District Asylum, Hartwood.

1921. McCutcheon, Archibald Munn, M.B., Ch.B., F.R.F.P.S.Glasg., Shepperton, 40, Selly Wick Road, Selly Hill, Birmingham, 29.

1931. McDiarmid, Neil, M.B., Ch.B.Glasg., Medical Superintendent, Three Counties Mental Hospital, Arlesey, Beds.

1901. MacDonald, James Hogg, M.B., Ch.B., F.R.F.P.S.Glasg., Medical Superintendent, Glasgow District Asylum, Hawkhead, Cardonald, Glasgow; Lect. on Psychol. Med., Univ. of Glasgow. (*Chairman, Scottish Division*, 1932–33.)

1911. MacDonald, Ranald, *O.B.E.*, M.D., Ch.B.Edin., D.P.M., Medical Superintendent, Coton Hill Mental Hospital, Stafford.

1928. Macdonald, Robert William, M.B., Ch.B.Glasg., Medical Officer, Ministry of Pensions, Queen Alexandra Hospital, Cosham, Hampshire.

1905. MacDonald, William Fraser, M.B., Ch.B.Edin., M.P.C., Olive Lodge, Polworth Terrace, Edinburgh 11.

1928. McDougall, John, M.B., Ch.B.Glasg., Medical Superintendent, Perth District Asylum, Murthly.

1906. McDowall, Colin Francis Frederick, M.D., B.S.Durh., M.R.C.S., L.R.C.P., Medical Superintendent, Ticehurst House, Ticehurst, Sussex. (*Secretary, Library Committee, since* 1922.)

1895. Macfarlane, Neil M., *C.B.E.*, M.D., C.M.Aberd., Laurelhill, 10, Nonoti Avenue, Durban, Natal, South Africa.

1924. Macfarlane, Robert Melvin, M.D., Ch.B.Edin., D.P.H., D.P.M., Jamnagar House, Staines, Middlesex. (*Secretary, S.E. Division since* 1935; *Secretary, Parliamentary Committee since* 1936.)

1923. McGarvey, John, M.B., B.Ch.Belf., D.P.M., Medical Superintendent, Somerset and Bath Mental Hospital, Wells.

1928. MacGilp, Finlay Duncan, M.B., Ch.B. St.Andr., Deputy Medical Superintendent, Durham County Mental Hospital, Winterton, Ferry Hill, co. Durham.
1934. McGlashan, Alice, M.B., Ch.B., D.P.H., Assistant Medical Officer, County Mental Hospital, Prestwich, Manchester.
1925. McGlashan, William Reid, M.A., M.B., Ch.B.Aberd., D.P.M., Physician to the Mental Health Services, Health Office, Lukis House, Grange, Guernsey.
1925. MacGown, Agnes Mildred, M.B., Ch.B.Edin., D.P.M., Assistant Medical Officer and Pathologist, Bangour Village, Uphall, Linlithgowshire.
1921. McGrath, Mathew Joseph, M.B., B.Ch.R.U.I., D.P.M., Deputy Medical Superintendent, West Riding Mental Hospital; The Gables, Bar Lane, Stanley, near Wakefield.
1938. McGrath, William Michael, M.B., B.Ch., B.A.O., D.P.M., Assistant Medical Officer, Leavesden Hospital, Abbots Langley, Watford, Herts.
1938. MacGregor, James MacWilliam, L.R.C.P.&S.E., L.R.F.P.S.G., Assistant Medical Officer, Worcestershire Mental Hospital, Barnsley Hall, Bromsgrove.
1902. McGregor, John, M.B., Ch.B.Edin., Ardchoille, Llantrisant Road, Llandaff, Glamorgan.
1938. McGuiness, John Plenderleith, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Assistant Medical Officer, Carlton Hayes Hospital, Narborough, near Leicester.
1931. McIlroy, William Ernest, M.B., Ch.B., B.A.O., D.P.M., Assistant Medical Officer, Bracebridge Mental Hospital, Lincoln.
1924. McInnes, John, M.B., Ch.B.Glasg., D.P.M., Medical Superintendent, City Mental Hospital, Willerby, Hull.
1932. McInnes, Robert Gow, L.R.C.P.&S.Edin., M.R.C.P.Edin., Physician-Superintendent, The Warneford, Oxford; Gabriels, Hill Top Road, Oxford.
1924. Mackay, George William John, M.B., Ch.B.Edin., D.P.M., Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1.
1929. MacKay, John, M.D., Ch.B.Glasg., D.P.M., Deputy Medical Superintendent, Somerset and Bath Mental Hospital, Cotford, Norton Fitzwarren, Taunton.
1914. Mackay, Magnus Ross, *M.C.*, M.B., Ch.B.Edin., Medical Superintendent, Newport, Borough Mental Hospital, Caerleon, Mon.
1936. MacKeith, Stephen Alexander, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Graylingwell Hospital, Chichester, Sussex.
1937. Mackenzie, Donald Lachlan, M.B., Ch.B., D.P.M., Assistant Medical Officer, County Mental Hospital, Rainhill, Lancs.
1927. Mackenzie, Ivy, M.A., B.Sc., M.D., F.R.F.P.S.Glasg., Consulting Physician, Glasgow District Board of Control; 10, Woodside Terrace, Glasgow, C. 3.
1911. Mackenzie, John Cosserat, M.B., Ch.B.Edin., Assistant Medical Officer, Stafford Mental Hospital, Burntwood, Lichfield.
1927. Mackenzie, Murdo, M.D., B.S. Lond., M.R.C.P., 122, Harley Street, London, W. 1.
1930. Mackenzie, Myra, M.B., Ch.B.Aberd., Medical Superintendent, The Lawn, Lincoln.
1934. Mackenzie, Norman Fraser, M.B., Ch.B.Edin., Deputy Medical Superintendent, Brockhall Certified Institution for Mental Defectives, Langho, near Blackburn.
1903. Mackenzie, Theodore Charles, M.D., Ch.B., F.R.C.P.Edin., M.P.C., Druim, Inverness.
1935. McLaren, Robert Gordon Alexander, M.D., Ch.B.Aberd., B.Hy.Durh., D.P.H., D.P.M., Deputy Medical Superintendent, County Mental Hospital, Whittingham, Preston.
1934. McLeman, John, M.B., Ch.B.Edin., 9, Margaret Street, Greenock, Renfrewshire.
1927. Macleod, John, M.B., Ch.B.Edin., Assistant Medical Officer, Glasgow District Mental Hospital, Woodilee, Lenzie, N.B.
1921. Macleod, Neil, M.D.Edin., D.P.M., 121, Clifton, York.
1938. MacMahon, James Francis, M.A., M.D., D.P.M., Deputy Medical Superintendent, Leavesden Hospital, Abbots Langley, Watford, Herts.
1925. McManus, Hugh Charles, M.B., Ch.B.Vict., D.P.M., 7, King Edward Avenue, Blackpool.
1930. McMenamin, Francis de Sales, *M.C.* M.B., Ch.B.Edin., 38, Lower Baggot Street, Dublin.
1931. Macmillan, Donald MacPhail, M.B., Ch.B.Glasg., D.P.M., Medical Superintendent, Great Barr Park Colony, near Birmingham.
1929. Macmillan, Duncan, B.Sc., M.D., M.R.C.P.Edin., D.Psych., Deputy Medical Superintendent, Nottingham City Mental Hospital; Thorneywood Mount, Nottingham.
1925. MacNiven, Angus, M.B., Ch.B.Glasg., M.R.C.P.Edin., D.P.M., Physician Superintendent, Glasgow Royal Mental Hospital; 2, Whittingehame Gardens, Glasgow, W. 2. (*Secretary, Scottish Division*, 1934-35.)
1910. MacPhail, Hector Duncan, *O.B.E.*, M.A., M.D., Ch.B.Edin., Medical Superintendent, City Mental Hospital, Gosforth, Newcastle-upon-Tyne; Lect. on Psychol. Med., Univ. of Durh.
1922. Macphail, Iain Ross, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Wye House, Buxton.

1901. McRae, Douglas, M.D., C.M., F.R.C.P.Edin., *J.P.*, Duich, West Linton, Peeblesshire. (*Assistant Editor*, 1915–20, *and Co-Editor of Journal since* 1920; *Chairman, Scottish Division*, 1931–32; *Vice-Chairman, Educational Committee*, 1933–1937; PRESIDENT, 1937–38.)

1922. McWilliam, William, M.D., Ch.B., F.R.F.P.S.Glasg., D.P.M., Medical Superintendent, District Asylum, Inverness.

1923. Maddox, Isabella Anne (*née* Gillespie), M.B., B.Ch.Edin.. D.P.M., Oxhey Grove, Hatch End, Middlesex.

1925. Madgwick, John Reginald Alexander, M.D.Lond., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Long Grove Hospital, Epsom, Surrey.

1923. Madill, Joseph Thomas Herbert, B.A.R.U.I., M.B., B.Ch.Edin., F.R.F.P.S.Glasg., D.P.M., M.P.C., Medical Superintendent, Cumberland and Westmorland Mental Hospital, Carlisle.

1931. Magrath, Donald, M.B., Ch.B.Birm., M.R.C.S., L.R.C.P.Lond., D.P.H., D.P.M., Deputy Medical Superintendent, Botleys Park Colony, Ottershaw, Surrey.

1929. Mahony, Elizabeth Maud, M.B., Ch.B., B.A.O.N.U.I., Assistant Medical Officer, Mental Hospital, Monaghan, Ireland.

1928. Main, Dorothy Mary, M.B., Ch.B.Glasg., Assistant Medical Officer, City Mental Hospital, Willerby, Hull.

1931. Malloy, Joseph Holder, M.D.St. And., D.P.M., Deputy Medical Superintendent, Staffordshire County Mental Hospital, Cheddleton.

1939. Mantani Khushaldas Jawahirmal, M.B., B.S., D.O., Superintendent, Sir C. J. Mental Hospital, Hyderabad, Sind, India.

1908. Mapother, Edward, M.D., B.S.Lond., F.R.C.P.Lond., F.R.C.S.Eng., Professor of Psychiatry, University of London, and Lect. in Psych. Med., King's Coll. Hosp.; 19, Queen Anne Street, London, W. 1.

1903. Marnan, John, B.A., M.B., B.Ch.Dubl., 2, Horton Road, Gloucester.

1929. Marsh, Rex Godfrey Blake, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Bromham House Colony, near Bedford.

1938. Marshall, Gilbert, B.A., M.B., B.Ch., D.P.H.Dub.Univ., Pembroke House, Markethill, co. Armagh.

1939. Marshall, John Kemsley, D.M., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, St. Ebba's Hospital, Epsom, Surrey.

1926. Martin, Alexander Reid, M.B., B.Ch.Belf., D.P.M., 24, Gramercy Park, New York City, U.S.A.

1922. Martin, Frederick Robertson, M.D., Ch.B.Glasg., D.P.M., 6, Grove Road, Sutton, Surrey.

1930. Martin, John James Black, M.A., M.D., B.Ch., M.R.C.P., D.P.M., Medical Superintendent, Fishponds Mental Hospital, Bristol.

1907. Martin, Mary Edith, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., L.S.A., M.P.C., 9, The Drive, Hove, Sussex.

1914. Martin, Samuel Edgar, M.B., Ch.B.Edin., Barrister-at-Law, Medical Superintendent, The Old Manor, Salisbury. (*Secretary, S.W. Division, since* 1930.)

1921. Masefield, William Gordon, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Essex County Mental Hospital, Brentwood. (*Secretary, Educational Committee*, 1930–36; *Hon. General Secretary since* 1936.)

1938. Mason, James Johnston, M.B., Ch.B.Edin., Medical Superintendent, Brentry Colony, Westbury-on-Trym, Bristol.

1937. Mason, William McLaren, L.R.C.P.&S.Edin.&Glasg., Assistant Medical Officer, Midlothian and Peebles Asylum, Rosslynlee, Midlothian.

1911. Mathieson, James Moir, M.B., Ch.B.Aberd., Assistant Medical Officer, South Yorks Mental Hospital, Wadsley, Sheffield.

1939. Mathur, Din Dayal, M.B., B.S., Superintendent of Jail, Bharatpur State, India.

1934. Maudsley, Henry Fitzgerald, *M.C.*, M.D.Melb., M.R.C.P., F.R.A.C.P., D.P.M.Lond., Hon. Neurologist, Melbourne General Hospital; 8, Collins Street, Melbourne, Victoria, Australia.

1932. Maxwell, Robert Warnock, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Berry Wood Mental Hospital, Northampton.

1934. Maybin, Nora, M.B., B.Ch., B.A.O., D.P.H., 17, Antrim Road, Lisburn, co. Antrim.

1939. Mayer-Gross, W., M.D.Heidelberg, M.R.C.P., L.R.C.S.Edin., Crichton Royal, Dumfries.

1938. Meade-King, Michael Liddon, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Springfield Hospital, Beechcroft Road, London, S.W. 17.

1939. Meenan, John M., M.B., B.Ch., B.A.O., L.M., D.P.M., Assistant Medical Officer, Mental Hospital, Grangegorman, Dublin.

1937. Mellett, Michael Kevin, M.B., B.Ch., B.A.O.N.U.I., Assistant Medical Officer, West Riding Mental Hospital, Menston, near Leeds.

1932. Menzies, Archibald, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., 65, Dixon Avenue, Glasgow, S. 2.

1926. Menzies, Duncan, M.A., M.B., Ch.B.Aberd., D.P.M., Deputy Medical Superintendent, Plymouth Mental Hospital, Ivybridge, Devon.

1932. Methven, James Black, M.B., Ch.B.Edin., Assistant Medical Officer, Somerset County Council; Cambridge House, Flax Bourton, Bristol.

1937. Meyer, Alfred, M.D.Bonn., Assistant to the Pathologist, L.C.C. Central Pathological Laboratory, Maudsley Hospital, Denmark Hill, London, S.E. 5.

1910. Middlemiss, James Ernest, F.R.F.P.S.Glasg., M.R.C.S., L.R.C.P.Lond., M.P.C., "The Crest", Scott Hall Road, Chapel-Allerton, Leeds.

1928. Mill, Laura Margaret Dorothea, M.B., Ch.B.Glasg., 25, Palmerston Place, Edinburgh.

1929. Miller, Emanuel, M.A.Camb., M.R.C.S., L.R.C.P., D.P.M., Hon. Director, East London Child Guidance Clinic; 23, Park Crescent, London, W. 1.

1930. Miller, Frederick Richard Lanfear, M.R.C.S., L.R.C.P., D.T.M.&H., 169, New Church Road, Hove 3, Sussex.

1924. Miller, Robert Stewart, M.D., Ch.B.Glasg., Lebanon Hospital for Mental Diseases, P.O. Box 92, Asfuriyeh, near Beyrout, Syria.

1938. Millman, Cyril Guy, M.R.C.S.Eng., L.R.C.P., Deputy Medical Superintendent, Cell Barnes Colony, St. Albans, Herts.

1931. Milmo, Dermod Hubert Francis, M.B., B.Ch.Dubl., D.P.H., Assistant Medical Officer, Caterham Hospital (L.C.C.), Caterham, Surrey.

1938. Milner, Kenneth Oswald, M.D., Ch.B.Leeds, M.R.C.S., L.R.C.P., D.P.M., Medical Officer, H.M. Prison, Pentonville, London, N. 7.

1933. Minshull, Michael John Wilmott, B.M., B.Ch.Oxon., 10, Estcourt Avenue, Leeds 6.

1923. Minski, Louis, M.D., B.S.Durh., M.R.C.P., D.P.M., Deputy Medical Superintendent, St. Ebba's Hospital, Epsom, Surrey.

1922. Molony, Charles Bernard, M.B., Ch.B.N.U.I., D.P.M., Medical Superintendent, Enniscorthy Mental Hospital, co. Wexford.

1910. Monnington, Richard Caldicott, M.D., Ch.B.Edin., D.P.H., D.P.M., Neurologist, Ministry of Pensions; 33, New Street, Salisbury.

1915. Monrad-Krohn, G. H., B.A., M.D., B.S.Oslo, F.R.C.P., M.R.C.S.Eng., M.P.C., Prof. of Med., Royal Frederick University, Oslo; Rikshospitalet, Oslo, Norway.

1935. Montgomery, Neil McEachran, M.D., D.P.M., Senior Medical Officer, Storthes Hall Mental Hospital, Kirkburton, near Huddersfield.

1939. Moore, John Norman Parker, B.A., M.D., B.Ch., B.A.O., St. Patrick's Hospital, Dublin.

1925. Moran, Patrick, M.B., B.Ch.N.U.I., D.P.M., Resident Medical Superintendent, Ardee Mental Hospital, Ardee, co. Louth. (*Secretary, Irish Division since* 1937.)

1917. Morris, Bedlington Howel, M.B., B.S.Durh., Inspector-General of Hospitals, South Australia; "Tros-y-Parc", Pembroke Street, St. Peter's, Adelaide, South Australia.

1925. Morris, John Vincent, B.A., M.B., B.Ch.Dubl., Medical Superintendent, Little Plumstead Hall, near Norwich.

1939. Morton, Richard Bertram, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, County Mental Hospital, Brentwood, Essex.

1896. Mould, Gilbert Edward, M.R.C.S., L.R.C.P., The Grange, Rotherham, Yorks.

1934. Moulson, Norman, M.D.Lond., D.P.M., Medical Superintendent, Cefn Coed Hospital, Swansea.

1914. Moyes, John Murray, M.B., Ch.B.Edin., D.P.M., Ardcaein, Shantallow, Londonderry.

1919. Mules, Annie Shortridge, M.R.C.S., L.R.C.P., Court Hall, Kenton, South Devon.

1907. Mules, Bertha Mary, M.D., B.S.Durh., Court Hall, Kenton, South Devon.

1939. Mulligan, Mary Frances, L.R.C.S.I., Assistant Medical Officer, Mental Hospital, Mullingar.

1929. Mullin, Bartholomew Joseph, *M.C.*, L.R.C.P.&S.Irel., D.P.H., D.P.M., Medical Superintendent, Wonford House Hospital, Exeter.

1929. Munro, Thomas Arthur, M.B., Ch.B., M.R.C.P.Edin., Dipl. Psych., Hon. Psychiatrist, Royal Eastern Counties Institution, Colchester, Essex.

1925. Murdoch, James Wilson, M.B., Ch.B.Aberd., Medical Superintendent, Central Mental Hospital, Tanjong Rambutan, Perak, Federated Malay States.

1931. Murray, Helen Sara Euphemia, M.B., Ch.B.Edin., Cedar Grange, Caterham, Surrey.

1932. Murray, John Raymund, M.D., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Banstead Hospital (L.C.C.), Sutton.

1937. Napier, Francis James, M.R.C.S., L.C.R.P., D.P.M., Deputy Medical Superintendent, Carlton Hayes Hospital, Narborough, near Leicester.
1939. Nevin, Samuel, B.Sc., M.D., M.R.C.P., Director of the Central Pathological Laboratory and Pathologist to the London County Council's Mental Health Services; Professor of Mental Pathology, University of London; 11, Upper Wimpole Street, London, W. 1.
1920. Nicol, William Drew, M.B., B.S.Lond., F.R.C.P., D.P.M., Medical Superintendent, Horton Hospital, Epsom; Lect. on Psychiatry, London School of Medicine for Women.
1923. Nicole, J. Ernest, L.M.S.S.A., D.P.M., Medical Superintendent, Lancashire County Mental Hospital, Winwick, Warrington.
1938. Nightingale, Geoffrey Slingsby, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Brentwood Mental Hospital, Brentwood, Essex.
1920. Nix, Sidney, M.D., B.S.Durh., L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Deputy Medical Superintendent, Graylingwell Mental Hospital, Chichester.
1938. Noble, John Henry, M.D., M.R.C.P., Visiting Medical Officer, Leicester Frith Institution; 119, Loughborough Road, Leicester.
1922. Noble, Ralph Athelstane, M.B., Ch.M.Syd., M.R.C.P., F.R.A.C.P., D.P.M., 86, Brook Street, Grosvenor Square, London, W. 1.
1909. Norman, Hubert James, M.B., Ch.B.Edin., D.P.H., Medical Superintendent, Camberwell House Mental Hospital, London, S.E. 5; Lect. on Ment. Dis., Westm. Hosp.; Northcotes, 79, West Hill, Sydenham, London, S.E. 26.
1938. Norman, Ronald Melville, M.D., Ch.B., D.P.M., Senior Assistant Medical Officer, Stoke Park Colony, Bristol; Medical Assistant to the Burden Mental Research Trust; 25, Victoria Square, Clifton, Bristol.
1932. Norris, Frank Edwin, M.R.C.S.Eng., L.R.C.P., D.P.M., Medical Officer, H.M. Prison; 164, Du Cane Road, London, W. 12.
1939. Nuthall, Robert Nuthall, M.R.C.S., L.R.C.P., The Homestead, Orpington, Kent.

1930. O'Brien, Eveleen J., M.B., B.Ch., B.A.O.N.U.I., D.P.M., D.P.H., Assistant Medical Officer, Grangegorman Mental Hospital, co. Dublin.
1929. O'Connell, Daniel Joseph, M.D., B.Ch., D.P.M., Assistant Medical Officer, St. Andrew's Hospital, Northampton.
1934. O'Connor, Joseph, M.D., N.U.I., Assistant Medical Officer, Ardee Mental Hospital, Ardee, co. Louth.
1937. O'Dea, John Francis, B.Sc., M.B., B.Ch., B.A.O., D.P.H., D.P.M., L.M., Assistant Medical Officer, Mental Hospital, Clonmel, co. Tipperary.
1924. Odlum, Doris Maude, M.A.Oxon., B.A.Lond., M.R.C.S., L.R.C.P., D.P.H., 42, Harley Street, London, W. 1.
1938. Ogden, William, M.R.C.S.Eng., L.R.C.P., D.P.M.,, Assistant Medical Officer, Bexley Hospital (L.C.C.), Bexley, Kent.
1918. Ogilvie, William Mitchell, M.B., C.M.Aberd., "Monymusk", 2, Riselaw Terrace, Edinburgh.
1911. Oliver, Norman Henry, M.R.C.S., L.R.C.P., Barrister-at-Law, Medical Superintendent, Ministry of Pensions Hospital; Northumberland House, Richmond, Surrey.
1938. O'Meara, Louisa Mary, M.B., B.Ch., B.A.O., D.P.H., D.P.M., Richmond House, Millbrook, Jersey, C.I.
1936. Orchard, Ethel Adelaide, L.R.C.P.&S.Edin., Byron Court, Mecklenburgh Square, London, W.C. 1.
1924. O'Reilly, James Joseph, M.B., B.Ch.Belf., D.P.M., Medical Superintendent, City Mental Hospital, Winson Green, Birmingham.
1930. O'Riordan, John Joseph, M.B., Ch.B., D.P.M., Assistant Medical Officer, North Riding Mental Hospital, York.
1902. Orr, David, M.D., C.M.Edin., M.P.C., 24, Grange Road, Edinburgh.
1910. Orr, James Henry Cubitt, M.D., Ch.B.Edin., Medical Superintendent, Midlothian and Peebles Asylum, Rosslyn Castle.
1933. Osburne, John Carr, M.B., B.Ch., B.A.O.N.U.I., Medical Superintendent, Lindville Private Mental Hospital, Cork.
1936. O'Sullivan, Daniel Joseph, M.B., B.Ch., B.A.O.N.U.I., Assistant Medical Officer, Grangegorman Mental Hospital, Dublin.
1932. O'Sullivan, Edward N. M., B.A., M.B., B.Ch., B.A.O., D.P.M.N.U.I., Resident Medical Superintendent, District Mental Hospital, Killarney.
1935. Owen, David Rhyd, B.Sc., M.B., B.Ch.Wales, Medical Superintendent, Glamorgan County Mental Hospital, Bridgend; Angelton, Bridgend, Glam.

1928. Paddle, Kenneth Cecil Laurence, *M.C.*, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Botleys Park Colony; Copse Lea, Tringham Close, Ottershaw, Chertsey, Surrey.

1938. Page, Leonard Gilbert Millar, M.R.C.S.Eng., L.R.C.P., Senior Medical Officer, City of Norwich Mental Hospital; "Gorsefield", Drayton, Norwich.

1930. Page, William Robert, B.A., M.B., Ch.M.Sydney, F.R.A.C.P., D.P.M.Lond., Hon. Psychiatrist, Sydney Hospital and St. Vincent's Hospital, Sydney; 221, Macquarie Street, Sydney, N.S.W., Australia.

1937. Pakenham-Walsh, Robert, B.A., B.M., B.Ch., D.P.M., Assistant Medical Officer, County Mental Hospital, Lancaster.

1936. Palmer, Harold Anstruther, M.B., B.Ch., M.R.C.P., D.P.M., Senior Physician, Woodside Hospital, Woodside Avenue, N. 10.

1927. Pal, Sachindra Bhushan, B.A., L.M.S.Calc., Senior Assistant Physician, Central Mental Hospital, Tanjong Rambutan, Federated Malay States.

1933. Panton, John Barrie, L.R.C.P.Edin., Assistant Medical Officer, County Mental Hospital, Stafford.

1927. Parasuram, Govindarajpuram Rampattar, B.A., L.M.S.Madras, M.R.C.P.Edin., Deputy Medical Superintendent, Government Mental Hospital, Madras.

1932. Parfitt, David Neil, B.Sc., M.D., B.S.Lond., M.R.C.P., D.P.M., Medical Superintendent, Warwick County Mental Hospital, Hatton.

1938. Parker, Jean Brown, M.B., Ch.B., Deputy Medical Superintendent, Riccartsbar Mental Hospital, Paisley.

1931. Parker, William Patrick Hugh, L.R.C.P.&S.I., Assistant Medical Superintendent, Mental Hospital, Toowoomba, Queensland, Australia.

1920. Parkin, George Gray, M.D., Ch.B.Vict., Grocott, Petersfield Road, Boscombe, Bournemouth.

1916. Patch, Charles James Lodge, *M.C.*, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Lt.-Col. *I.M.S.*, 39, Jail Road, Lahore, India; c/o Lloyds Bank, 6, Pall Mall, London, S.W. 1. (*Chairman, Indian Division*, 1938–40.)

1929. Paterson, Arthur Spencer, M.A.Oxon., M.D., Ch.B., F.R.C.P.Edin., M.R.C.P.Lond., 18, Harley St., London, W. 1.

1930. Paton, Thomas, M.D., Ch.B.Glasg., D.P.M., Deputy Medical Superintendent, St. Audry's Hospital, Melton, Suffolk.

1937. Patterson, Alexander Stafford, M.B., B.Ch., B.A.O.Belf., Assistant Medical Officer, Leybourne Grange Colony, West Malling, Kent.

1928. Patterson, Edward Cecil, M.B., B.Ch.Belf., Croom Lodge, Perry Hill, London, S.E. 6.

1931. Paul, Arthur Blackwell, M.A., M.B., B.Ch.Camb., Consulting Physician, Cheshire County Mental Hospital, Chester; Hon. Physician, Chester Royal Infirmary; Greyfriars House, Greyfriars, Chester.

1929. Pearce, John Dalziel Wyndham, M.A., M.D., Ch.B.Edin., M.R.C.P., D.P.M., Medico-Psychologist, London County Council; 13, Harley Street, London, W. 1.

1931. Pearce, May I., M.D., Ch.B.Birm., D.P.M., 17, Abbey Road, Harborne, Birmingham, 17.

1920. Pearn, Oscar Phillips Napier, M.R.C.S., L.R.C.P., L.S.A., D.P.M., Deputy Medical Superintendent, Cane Hill Hospital, Coulsdon, Surrey.

1931. Pearson, Kate Young, M.B., Ch.B., 2, Montgomery Street, Kirkcaldy, Fife.

1913. Penny, Robert Augustus Greenwood, M.R.C.S., L.R.C.P., Deputy Medical Superintendent, Devon County Mental Hospital, Exminster.

1933. Penrose, Lionel Sharples, M.A., M.D.Camb., M.R.C.S., L.R.C.P., The Ontario Hospital, London, Ontario, Canada. (*Co-Editor of Journal*, 1937–39.)

1937. Pentreath, Edward Uther Haldane, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Derby County Mental Hospital, Mickleover, Derby.

1927. Perera, Clement Osmund, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Superintendent, Mental Hospital, Angoda, Ceylon.

1928. Perk, David, M.D.Leeds, D.P.M., "Aldington", 7, Poole Road, Bournemouth.

1929. Peters, Gordon Frank, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Claybury Hospital, Woodford Bridge, Essex.

1911. Petrie, Alfred Alexander Webster, M.D., B.S., F.R.C.P., M.D., F.R.C.S.Edin., D.P.M., Medical Superintendent, Banstead Hospital (L.C.C.), Sutton, Surrey; Lect. on Ment. Dis., Charing Cross Hosp. and West Lond. Hosp. (*Vice-Chairman Research and Clinical Committee, since* 1932; *Chairman, Educational Committee, since* 1933.)

1908. Phillips, John George Porter, M.D., B.S., F.R.C.P., M.P.C., Resident Physician-Superintendent, Bethlem Royal Hospital, Monk's Orchard, Beckenham, Kent; 19, Cavendish Square, London, W. 1. (*Secretary, Educational Committee*, 1913–20.)

1906. Phillips, Nathaniel Richard, M.D.Brux., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Monmouth County Mental Hospital, Abergavenny.
1905. Phillips, Norman Routh, M.D.Brux., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, St. Andrew's Hospital, Northampton. (*Acting Registrar*, 1937–38.)
1921. Phillips, Philip Gordon, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Bryn, The Avenue, Collingham, Leeds.
1924. Pickworth, Frederick Alfred, B.Sc., M.B., B.S., M.R.C.S., L.R.C.P., A.I.C.(exam.), Ph.C., Director, Joint Board of Research for Mental Diseases, City and University of Birmingham; Dept. of Mental Disease Research, Medical School, Hospitals Centre, Birmingham, 15.
1939. Pilkington, Francis Edward, M.A., M.B., B.Ch., M.R.C.P., M.R.C.P.I., D.P.M., Senior Assistant Medical Officer, Warwickshire Mental Hospital, Thistley Hill, Hill Farm Road, Hatton, nr. Warwick.
1935. Pinkerton, William Maurice, M.B., B.Ch., D.P.H., Assistant Medical Officer, Wilts County Mental Hospital, Devizes.
1934. Pool, Arthur, M.B., Ch.B., M.R.C.P., D.P.M., Medical Superintendent, The Retreat, York; Lecturer in Mental Disease, Sheffield University.
1921. Poynder, Ernest George Thornton, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Plymouth Mental Hospital, Blackadon, Ivybridge, Devon.
1931. Prentice, David, M.B., Ch.B., Glasg., D.P.M., Assistant Medical Officer, Royal Western Counties Institution, Starcross, Devon.
1936. Price, Annie Bapty, B.Sc., M.B., Ch.B., D.T.M.&H., The Lawn, Lincoln.
1918. Prideaux, Joseph Francis Engledue, M.R.C.S., L.R.C.P., D.C.M.S.; Ministry of Pensions, 1, Sanctuary Buildings, Great Smith Street, London, S.W. 1.
1928. Pullar Strecker, Herbert A. J., M.D.Würzb., L.R.C.P.&S.Edin., 73, Shepherd's Hill, London, N. 6.
1928. Quine, Margaret Annette, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Lancashire County Mental Hospital, Winwick, Warrington.
928. Raitt, William John, M.B., Ch.B.Aberd., Dipl. Psych., Senior Assistant Physician, Royal Mental Hospital, Aberdeen.
933. Rao, Bhaskara, M.R.C.S., L.R.C.P., Medical Officer, Government Hospital, Trivellore, Chingleput Dt., S. India.
1937. Rao, S. Venkata Subba, M.D., D.P.M., Superintendent, Government Mental Hospital, Kilpauk, Madras.
936. Ratcliffe, Tom Arundel, B.A., M.B., B.Chir.Cantab., M.R.C.S., L.R.C.P., D.P.M., D.C.H., Senior Assistant Medical Officer, Nottingham City Mental Hospital; Robin Wood, The Wells Road, Mapperley, Nottingham.
1889. Raw, Nathan, *C.M.G.*, M.D., B.S., M.R.C.P., F.R.C.S., F.R.S.Edin., L.S.Sc.Durh., M.P.C., 22, Ashworth Road, London, W. 9. (*Chairman, Parliamentary Committee since* 1926; PRESIDENT, 1929–30.)
1920. Read, Walter Woolfe, M.D.Brux., M.R.C.S., L.R.C.P., 14, West Cliff Terrace, St. Laurence Cliffs, Ramsgate Kent.
1927. Rees, Thomas Percy, B.Sc., M.D., B.Ch.Wales, M.R.C.P., M.R.C.S.Eng., D.P.M., Medical Superintendent, Warlingham Park Hospital, Upper Warlingham, Surrey.
1911. Reeve, Ernest Frederick, M.B., B.S., M.R.C.S., L.R.C.P., Medical Superintendent, Lancashire County Mental Hospital, Rainhill, near Liverpool; Lect. on Ment. Dis., Univ. of Liverp.
1931. Reid, Benjamin, M.D., Ch.B.Glasg., D.P.M., Medical Superintendent, East Sussex Mental Hospital, Hellingly.
1911. Reid, Daniel McKinley, M.D., Ch.B., F.R.F.P.S.Glasg., Medical Superintendent, City Mental Hospital, Exeter.
1910. Reid, William, M.A.St.And., M.B., Ch.B.Edin., Medical Superintendent, Stafford Mental Hospital, Burntwood, Lichfield.
1932. Reid, William Muirhead, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., D.P.H., Assistant Medical Officer, Kingseat Mental Hospital, Newmachar, Aberdeen.
1939. Reitmann, Francis, M.D.Budapest, M.D.Vienna, Arthington, Barton Road, Torquay.
1929. Rich, Gilbert J., A.B., A.M., Ph.D.Cornell, M.D.Chicago, D.N.B., Director, Milwaukee County Mental Hygiene Clinic, 515, Public Safety Bldg., Milwaukee, Wisconsin, U.S.A.
1937. Richards, Beresford Tom, M.R.C.S., L.R.C.P., D.P.M., L.D.S., Deputy Medical Officer, Erdington House, Birmingham.
1938. Richardson, John Dixon, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Friern Hospital; 39, The Ridgeway, Friern Barnet, N. 11.
1922. Riches, Reginald George, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, St. Bernard's Hospital, Southall, Middlesex.

1920. Rickman, John, M.A., M.D., B.Ch.Camb., Physician, London Clinic of Psycho-Analysis; 11, Kent Terrace, London, N.W. 1.
1938. Rizvi, Khwaja Nasir Husain, M.B., B.S.Lucknow, D.P.M., Medical Officer, Civil Hospital and Thomason Engineering Hospital, Roorkee, U.P., India.
1931. Roachsmith, C. E., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Napsbury Mental Hospital, St. Albans.
1911. Robarts, Henry Howard, M.D., Ch.B.Edin., D.P.H., Medical Officer, East Lothian Mental Hospital, Ennerdale, Haddington, Scotland.
1922. Robb, John Robert Beith, M.D.Durh., L.R.C.P.&S.Edin., F.R.F.P.S.Glasg., Medical Superintendent, Woodilee House, Lenzie, Glasgow.
1938. Roberts, Constance Dix, M.B., Ch.B.Glasg., Junior Medical Officer, City of Norwich Mental Hospital; "The Orchard", Lower Hellesdon, Norwich.
1921. Roberts, Edward Douglas Thomas, M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Superintendent, Herts County Mental Hospital, Hill End, St. Albans.
1938. Roberts, John Alexander Fraser, M.A., M.B., Ch.B., D.Sc., F.R.S.E., Principal Investigator to the Burden Mental Research Trust; Special Lecturer on Human Genetics, University of Bristol; Stoke Park Colony, Bristol.
1936. Roberts, John Herbert Owen, M.D., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, North Wales Counties Mental Hospital, Denbigh; Carn Ingli, Denbigh.
1903. Roberts, Norcliffe, *O.B.E.*, M.D., B.S.Durh., D.P.M., Medical Superintendent, West Park Hospital, Epsom.
1935. Roberts, Reginald F., M.B., Ch.B., Medical Officer, County Mental Hospital, Rainhill, St. Fillans, Elton Head Road, St. Helens, Lancs.
1927. Robertson, David, M.D., Ch.B.Glasg., Medical Superintendent, Bootham Park, York.
1908. Robertson, George Dunlop, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Dipl. Psych., 58, Kelvingrove Street, Glasgow, C. 3.
1934. Robertson, Guy Scott, M.B., Ch.B., Medical Superintendent, Calderstones, Whalley, near Blackburn.
1920. Robinson, William, M.D., Ch.B.Leeds, D.P.M., Medical Superintendent, City of London Mental Hospital, Stone, Dartford.
1937. Robson, James Smylie, M.B., B.Ch., B.A.O., Assistant Medical Officer, County Mental Hospital, Lancaster.
1936. Robson, Mary M., M.B., B.Ch., B.A.O.Belf., D.P.H., Assistant Medical Officer, Mental Hospital, Antrim, Ireland.
1922. Rodger, Kenneth Mann, M.B., Ch.B.Glasg., D.P.M., Medical Superintendent, Mental Hospital, Bulawayo, S. Rhodesia.
1914. Rodger, Murdoch Mann, M.D., Ch.B.Glasg., Dechmont, Helouan, Egypt.
1930. Rodger, Thomas Ferguson, B.Sc., M.B., Ch.B.Glasg., D.P.M., 30, Falkland Mansions, Glasgow, W. 2.
1908. Rodgers, Frederick Millar, *O.B.E.*, M.D., ChB.Vict., D.P.H., Clayton, Cooden Drive, Bexhill-on-Sea.
1934. Rohan, James Charles, M.B., B.Ch., B.A.O.N.U.I., D.P.M., Assistant Medical Officer, Coleshill Hall, Coleshill, near Birmingham.
1895. Rolleston, Lancelot William, *C.B.E.*, M.B., B.S.Durh., M.R.C.S., L.R.C.P., Queen Anne's Mansions, St. James's Park, London, S.W. 1.
1922. Rollins, Ernest Edward, B.A., M.B., B.Ch.Dubl., Resident Medical Superintendent, Brooke House, Upper Clapton. London, E. 5.
1931. Roper, William Francis, M.B., B.S.Lond., M.R.C.S., L.R.C.P., Medical Officer's House, Princetown, Devon.
1934. Rose, Douglas John, M.R.C.S., L.R.C.P., Deputy Medical Superintendent, Brockhall Certified Institution for Mental Defectives, Langho, near Blackburn, Lancs.
1935. Rose, Louis, M.R.C.S., L.R.C.P., Superintendent, Atkinson Morley Hospital, Copes Hill; 4, Arundel Court, Ipswich Grove, Norwich.
1935. Ross, Charles MacDonald, M.B., Ch.B.Edin., Deputy Physician-Superintendent, 151, Morningside Drive, Edinburgh, 10.
1938. Ross, David, M.B., Ch.B., F.R.F.P.S.G., Assistant Physician, Aberdeen Royal Mental Hospital, Aberdeen.
1910. Ross, Donald, M.B., Ch.B., M.R.C.P.Edin., M.P.C., *J.P.*, Medical Superintendent, Argyll and Bute Asylum; Tigh-na-Linne, Lochgilphead, Argyll. (*Vice-Chairman, Educational Committee*, 1927–33, and since 1937; *Chairman, Scottish Division*, 1936–38.)
1899. Rotherham, Arthur, M.A., M.B., B.Ch.Camb., Lord Chancellor's Visitor; "Hazards" Enton, Godalming, Surrey.
1922. Roy, John Allen Chisholm, M.B., Ch.B.Vict., Medical Superintendent, Royal Hospital, Cheadle, Cheshire.

1938. Roy, Jyotermay, M.B.Cal., D.P.M.Eng., Superintendent, Mental Hospital, Nagpur, India.
1924. Rudolf, Gerald de Montjoie, M.R.C.P., D.P.H., D.P.M., Physician, British Hospital for Functional Nervous Disorders; 5, Pembroke Road, Clifton, Bristol 8.
1929. Russell, David, M.D., Ch.B.Glasg., D.P.M., 24, Kempnough Hall Road, Worsley, near Manchester.
1923. Russell, John, M.B., Ch.B.Glasg., D.P.M., Medical Superintendent, Exeter City Mental Hospital, Exeter, Devon.
1912. Russell, John Ivison, M.D., Ch.B., F.R.F.P.S.Glasg., D.P.M., M.P.C., Medical Superintendent, North Riding Mental Hospital, Clifton, York. (*Secretary, N. and M. Division, since* 1929.)
1938. Russell, Leonard William, M.B., Ch.B.Leeds, D.P.M., Assistant Medical Officer, St. Bernard's Hospital, Southall, Middlesex.
1915. Russell, William, *M.C.*, M.D., Ch.B.Edin., Dip. Psych., D.T.M., Commissioner for Mental Hygiene, Union Buildings, Pretoria, South Africa.
1912. Rutherford, Cecil, B.A., M.B., B.Ch.Dubl., Assistant Medical Officer, Holloway Sanatorium, Virginia Water, Surrey.
1907. Rutherford, Henry Richard Charles, F.R.C.S., L.R.C.P.Irel., D.P.H., Medical Superintendent, Farnham House, Finglas, co. Dublin.
1896. Rutherford, James Mair, M.B., C.M., F.R.C.P.Edin., M.P.C., Brislington House, Bristol.

1908. Samuels, William Frederick, L.M., L.Ch.Dubl., "Etrusca", Berry Grove Lane, Aldenham, Herts.
1932. Sanders, Marjorie Elizabeth Frances, M.B., Ch.B.Edin., D.P.M., Assistant Medical Officer, Long Grove Hospital, Epsom.
1935. Sands, Dalton Eric, M.R.C.P., L.R.C.S.Edin., L.R.F.P.S.Glasg., D.P.M., Assistant Medical Officer, Claybury Hospital, Woodford Bridge, Essex.
1923. Sang, Janet Adeline Agnes, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., Long Acre, Station Road, Scholes, Leeds.
1939. Santyanand, David, M.B., B.S., Assistant Deputy Medical Superintendent, Punjab Mental Hospital, Lahore, India.
1938. Saville, James Edwin, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Deputy Medical Officer's House, H.M. Prison, Pentonville, London, N. 7.
1932. Schneider, Frank Edwin Ernest, M.D.Lond., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Rampton State Institution for Mental Defectives, Retford, Notts.
1928. Scholberg, Harold Alfred, M.B., M.R.C.S., L.R.C.P., D.P.H., Pathologist, Cardiff City Mental Hospital; 3, St. Andrew's Crescent, Cardiff.
1926. Scoresby-Jackson, Margaret, M.D., B.S.Durh., c/o Union Bank of Scotland, Ltd., 62, Cornhill, London, E.C. 3.
1925. Scott, Francis Leonard, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, City of Canterbury Mental Hospital, Canterbury, Kent.
1930. Scott, James, M.B., B.Ch., L.M., D.P.M., 8, Loraine Road, Holloway, London, N. 7.
1935. Scott, William Clifford Munroe, B.Sc., M.B., L.C.P.S.Ont., L.M.S.S.A., D.P.M., 18, Devonshire Street, London, W. 1.
1911. Scroope, Gervace Wm. Mavy, M.B., B.Ch.Dubl., Resident Medical Superintendent, Central Criminal Asylum, Dundrum, co. Dublin.
1925. Selkirk, Elizabeth Thompson, M.B., Ch.B.Edin., Deputy Medical Superintendent, Hollymoor Mental Hospital, Northfield, Birmingham.
1929. Selling, Lowell Sinn, B.A.Mich., M.A.Columbia, D.N.B., Sc.M.New York, M.D.Bellevue, Ph.D., Psychopathic Clinic, Recorder's Court, City of Detroit; 16196, Cherrylawn Avenue, Detroit, Mich., U.S.A.
1938. Senanayeke, Irving Aloysius, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Superintendent, Lunatic Asylum, Angoda, Ceylon; 63, Priory Road, West Hampstead, London, N.W. 6.
1939. Senneck, Beryl, M.B., B.S., D.P.M., Resident Medical Officer, Ivy Lodge, Coleshill Road, Marston Green, nr. Birmingham.
1912. Sergeant, John Noel, M.B., B.S., M.R.C.S., L.R.C.P., Medical Superintendent, Newlands House, Tooting Bec Common, London, S.W. 17. (*Secretary, South-Eastern Division*, 1913–35.)
1939. Shah, Mazhar Hussain, M.R.C.P., D.P.M., Captain, I.M.S., Civil Surgeon, New Delhi, India.
1925. Shand, George Ernest, M.D., Ch.B.Aberd., D.P.H., Villa Belga, Westbourne Avenue, Bagatelle, Jersey.
1938. Sharma, Ram Singh, M.B., B.S.Pb., D.T.M.Cal., Deputy Medical Superintendent, Punjab Mental Hospital; 37, Jail Road, Lahore, India.

1938. Sharman, Sydney, M.B., Ch.B.Glasg., Assistant Medical Officer, Mapperley Hospital, Nottingham.
1937. Sharp, William, M.B., Ch.B.Leeds, Assistant Medical Officer, Storthes Hall Mental Hospital, Kirkburton, nr. Huddersfield.
1930. Sharpe, John Smith, M.B., Ch.B.Glasg., Assistant Medical Officer (Biochemist), County Mental Hospital, Stafford.
1901. Shaw, Benjamin Henry, M.D., B.Ch.R.U.I., Lislee, St. Mawes, Cornwall. (*Chairman, N. and M. Division*, 1932–33; *Secretary, Research and Clinical Committee*, 1927–31.)
1936. Shaw, David, M.D.Lond., M.R.C.P., Assistant Medical Officer, Bexley Hospital (L.C.C.), Bexley, Kent.
1909. Shaw, William Samuel Jagoe, M.D.Belf., M.B., B.Ch.R.U.I., Lt.-Col. *I.M.S.* (ret.), Calcote House, Sandicotes Road, Parkstone, Dorset.
1920. Shearer, Christina Hamilton, M.B., Ch.B.Glasg., Senior Medical Officer, Cassel Hospital, Swaylands, Penshurst, Kent.
1928. Shepherd, Andrew, M.B., Ch.B.Glasg., D.P.M., Medical Superintendent, Worcester County Mental Hospital, Barnsley Hall, Bromsgrove.
1923. Shepherd, Charles Ernest Alan, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Kent County Mental Hospital, Chartham Down, near Canterbury.
1938. Shepley, William Hadfield, M.B., Ch.B., D.P.M.Vict., Deputy Medical Superintendent, Warlingham Park Hospital, Upper Warlingham, Surrey.
1927. Shera, Arthur Geoffrey, M.A., M.D., B.Ch.Camb., M.R.C.S., L.R.C.P., Pathologist, Eastbourne Hospitals and East Sussex County Mental Hospital, Hellingly; 10, Upperton Gardens, Eastbourne.
1928. Sheridan, Alfred, L.R.C.P.&S.Irel., Resident Medical Superintendent, Mayo County Mental Hospital, Castlebar, Ireland.
1914. Sherlock, Edward Birchall, B.Sc., M.D.Lond., D.P.H., Barrister-at-Law, 20, Beresford Avenue, Twickenham, Middlesex.
1923. Shore, George William, *O.B.E.*, M.D.Lond., D.P.H. D.P.M., Medical Superintendent, Middlesex County Mental Hospital, Shenley, Herts.
1938. Short, Francis, M.B, B.Ch., B.A.O., Assistant Medical Officer, St. Patrick's Hospital, Dublin.
1922. Shortt, Jane Elder, M.B., Ch.B.Glasg., Upton Grove, Slough, Bucks.
1928. Silverston, Joseph Denzil, M.B., B.S.Durh., Medical Superintendent, County Mental Hospital, Lancaster.
1928. Sinclair, Arthur Crawford, M.D.Belf., D.P.M., D.P.H., D.M.R.E., Deputy Medical Superintendent, County Mental Hospital, Dorchester.
1939. Singh, Mahabir, M.B., B.S., D.T.M.&H., D.P.M., Superintendent of Dispensaries, Lashkar, Gwalior State, India.
1921. Skene, Leslie Henderson, *M.C.*, M.B., Ch.B.Edin., Dipl. Psych., Medical Superintendent, Mental Hospital, Union Mills, Isle of Man.
1935. Skinner, Edward Fretson, M.A., M.B., B.Ch.Cantab., F.R.C.P., Physician, Sheffield Royal Hospital; 342, Glossop Road, Sheffield.
1925. Skottowe, James Stewart Ian, M.D.Glasg., D.P.M., Medical Superintendent, Bucks Mental Hospital, Stone, Aylesbury, Bucks.
1934. Slight, David, M.B., Ch.B.Edin., F.R.C.P., D.P.M., Professor of Psychiatry, University Clinics Division of Chicago, The University of Chicago, U.S.A.
1939. Small, Doris Kathleen, L.R.C.P.I.L.M.&L.R.C.S.I.L.M., Assistant Medical Officer, Heigham Hall, Norwich, Norfolk.
1933. Small, James Alexander, M.A., M.B., Resident Licensee, Heigham Hall, Norwich.
1928. Smith, Arthur Wallace Herbert, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, The Mental Hospital, New Amsterdam, British Guiana.
1934. Smith, Edward, M.B., B.S.Durh., Assistant Medical Officer, West Riding Mental Hospital, Menston, near Leeds.
1938. Smith, Edwin Charles Allan, M.R.C.P., L.R.C.S.Edin., L.R.F.P. & S.Glas., D.P.H., Superintendent, Central Hospital for Mental Diseases, Yeravda; River Prospect, Yeravda, Poona, India.
1905. Smith, George William, *O.B.E.*, M.B., Ch.B.Edin., Wyke House, Isleworth, Middlesex. (*Treasurer since* 1931.)
1933. Smith, Gilbert Mackay, B.A., M.B., B.Ch.Dubl., D.P.M., Assistant Medical Officer, City Mental Hospital, Mapperley Hill, Nottingham.
1936. Smith, Henry St.George, M.A., M.D., B.Ch., B.A.O.(Dub. Univ.), Resident Medical Superintendent, The Stewart Institution, Palmerstown, co. Dublin.
1923. Smith, Herbert, M.R.C.S., L.R.C.P., Deputy Medical Superintendent, City Mental Hospital, Fishponds, Bristol.
1934. Smith, James Morrison, M.B., Ch.B., Deputy Medical Superintendent, York City Mental Hospital, Fulford, York.

1899. Smith, John Grimmond, M.D., C.M.Edin., " Pine Grange ", Bath Road, Bournemouth.
1931. Smith, Robert Sydney Steele, L.M.S.S.A., Assistant Medical Officer, Caterham Hospital (L.C.C.), Caterham, Surrey.
1913. Smith, Thomas Cyril, M.B., Ch.B.Edin., Deputy Medical Superintendent, County Mental Hospital, Barnwood, Gloucester.
1926. Snell, Harvie Kennard, M.D., B.S., M.R.C.S., L.R.C.P., D.P.H., Medical Officer, H.M. Prison, Liverpool.
1938. Soddy, Kenneth, M.B., B.S., D.P.M., 3*a*, Highbury Quadrant, London, N. 5.
1923. Somerville, George, M.D., Ch.B.Edin., D.P.M., Deputy Medical Superintendent, West Ham Mental Hospital, Goodmayes, Ilford.
1906. Spark, Percy Charles, M.R.C.S., L.R.C.P., c/o Barclays Bank, Hanwell, London, W. 7.
1925. Speer, James Millar Craig, M.D., B.Ch.Belf., D.P.M., Deputy Medical Superintendent, Wilts County Mental Hospital, Devizes.
1929. Spence, David Sheridan, B.A., M.B., B.Ch., B.A.O.Dubl., Assistant Medical Officer, Somerset and Bath Mental Hospital, Wells, Somerset.
1922. Spence, Thomas Reginald Carwardine, *M.C.*, M.B., Ch.B.Edin., Dipl. Psych., Medical Superintendent, Royal Scottish National Institution; Westerpark, Larbert, Stirlingshire.
1938. Spiridion, Jan Tadeusz, M.A., M.B., Ch.B.Camb., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Springfield Hospital, London, S.W. 17.
1937. Stalker, Harry, M.B., Ch.B., Assistant Physician, Royal Edinburgh Hospital; West House, Morningside, Edinburgh.
1901. Starkey, William, M.B., B.Ch.R.U.I., Bryn-y-Neuadd, Llanfairfechan, N. Wales. (*Secretary, S.W. Division*, 1922–30.)
1936. Starr, Donald, M.B., Ch.B., Assistant Medical Officer, Chartham Mental Hospital, Canterbury, Kent.
1928. Statham, Hugh, M.B., B.C.Camb., M.R.C.S., L.R.C.P., Physician for Nervous Diseases, Royal Victoria and West Hants Hospital; 3, Elgin Road, Bournemouth.
1934. Steadman, Harry Hubert, M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Long Grove Hospital, Epsom, Surrey.
1927. Steel, John P., M.D., Ch.B.Edin., Medical Superintendent, Smithdown Road Hospital, Liverpool.
1925. Steel, Samuel Maxwell, M.B., Ch.B.Glasg., Deputy Medical Superintendent, Monyhull Colony, Kings Heath, Birmingham.
1907. Steele, Patrick, M.D., Ch.B., F.R.C.P.Edin., Medical Superintendent, Roxburgh District Mental Hospital; The Hermitage, Melrose.
1929. Stenhouse, Jack Fingland Martin, M.B., Ch.B.Glasg., D.P.M., Assistant Medical Officer, Banstead Hospital (L.C.C.), Sutton, Surrey.
1929. Stephen, Adrian Leslie, B.A., M.B., B.S.Lond., Barrister-at-Law, Physician, London Clinic of Psycho-Analysis; 50, Gordon Square, London, W.C. 1.
1914. Stephens, Harold Freize, M.R.C.S., L.R.C.P., Medical Superintendent, Birmingham Certified Institution, Coleshill Hall, Coleshill, near Birmingham.
1933. Stephenson, George Vaughan, M.B., B.Ch., D.P.M., Assistant Medical Officer, The Priory, Roehampton, London, S.W. 15.
1933. Stern, Edward Samuel, M.A., M.B., B.Ch.Cantab., M.R.C.P., D.P.M., Deputy Medical Superintendent, City Mental Hospital, Humberstone, Leicester.
1909. Steward, Sidney John, *D.S.O.*, M.D., B.Ch.Camb., M.R.C.S., L.R.C.P., D.P.H., Dapdune, Guildford, Surrey.
1922. Stewart, Francis Hugh, M.A., D.Sc.St.And., M.D., Ch.B.Edin., D.P.M., Major *I.M.S.* (retired), 12, Grange Court, Pinehurst, Cambridge.
1927. Stewart, Francis Melville, M.B., Ch.B.Edin., Deputy Medical Superintendent, County and City Mental Hospital, Littlemore, Oxford.
1938. Stewart, Richard Arthur, M.B., B.Ch., B.A.O.T.C.D., Medical Superintendent, Halliford House, Upper Halliford, Shepperton.
1931. Stewart, Ronald, M.B., Ch.B.Glasg., Deputy Medical Officer of Health for Mental Services, Corporation of Glasgow: 23, Montrose Street, Glasgow.
1887. Stewart, Rothsay Charles, L.S.A., M.R.C.S.Eng., " The Elms ", Oak End Waye, Gerrard's Cross, Bucks.
1914. Stewart, Roy MacKenzie, M.D., Ch.B., F.R.C.P.Edin., M.R.C.P., D.P.M., Medical Superintendent, Leavesden Hospital; Coles Farm, Leavesden, Watford, Herts. (*Chairman, South-Eastern Division*, 1937–38.)
1939. Still, Robert Merrick Lloyd, M.R.C.S., L.R.C.P., Major, I.M.S., Superintendent, Tadagale Mental Hospital, Rangoon, Burma.

1899. Stilwell, Reginald John, M.R.C.S., L.R.C.P., Moorcroft House, Hillingdon, Middlesex.
1938. Stirling, Pauline W. M. C., M.B., Ch.B., D.P.M., Assistant Medical Officer, Cane Hill Hospital, Coulsdon, Surrey.
1939. Stockings, George Tayleur, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Warlingham Park Hospital, upper Warlingham, Surrey.
1897. Stoddart, William Henry Butter, M.D., B.S.Lond., F.R.C.P., M.P.C., 57*a*, Wimpole Street, London, W. 1. (*Secretary, Educational Committee*, 1908–1912.)
1909. Stokes, Frederick Ernest, M.D., Ch.B.Glasg., D.P.H., " Glenmalure ", Portsmouth Road, Lee-on-the-Solent, Hants.
1937. Stoller, Allan, M.R.C.S., L.R.C.P., Assistant Medical Officer, Storthes Hall Mental Hospital, Kirkburton, nr. Huddersfield.
1885. Street, Charles Tidbury, M.R.C.S., L.R.C.P., Haydock Lodge, Newton-le-Willows, Lancs.
1929. Ström-Olsen, Rolf, M.D., B.Ch., B.Sc.Wales, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Runwell Hospital, near Wickford, Essex.
1909. Stuart, Frederick Joshua, *O.B.E.*, M.R.C.S., L.R.C.P., 55, Hillway, Highgate, London, N. 6.
1927. Stungo, Ellis, L.R.C.P.&S.Edin., L.R.F.P.S.Glasg., 1, Heath Drive, Hampstead, London, N.W. 3.
1886. Suffern, Alex. Canning, *O.B.E.*, M.D., M.Ch.R.U.I., Glan-y-Mor, Hill Head, Fareham.
1921. Suffern, Canning, M.A., M.B., B.Ch.Camb., M.R.C.S., L.R.C.P.Lond., Glan-y-Mor, Hill Head, Fareham.
1922. Sullivan, Patrick Daniel, F.R.C.S., L.R.C.P.Irel., Medical Superintendent, Verville Asylum, Clontarf, co. Dublin ; 44, Harrington Street, Dublin.
1918. Sutherland, Francis, M.B., Ch.B.Edin., D.P.H., Deputy Commissioner, General Board of Control ; 25, Palmerston Place, Edinburgh.
1939. Sutton, Isaac, B.Sc., M.B., Ch.B.Vict., M.R.C.S., L.R.C.P., D.P.M.Vict., Assistant Medical Officer, County Mental Hospital, Prestwich, Lancs.
1928. Sykes, Elizabeth Sarah Marples, M.B., Ch.B.Sheff., Assistant Medical Officer, South Yorks Mental Hospital, Wadsley, Sheffield.

1926. Talbot, Geoffrey, B.Sc., M.B., Ch.B.Manch., Assistant Medical Officer, Lancashire County Mental Hospital, Prestwich, Manchester.
1923. Tattersall, Stanley Roy, M.R.C.S., L.R.C.P., Deputy Medical Superintendent, Bucks County Mental Hospital, Stone, near Aylesbury, Bucks.
1931. Taylor, Arthur Leslie, M.D.Leeds, Ch.B., Hon. Pathologist, Bristol General Hospital ; Visiting Pathologist, Bristol Mental Hospital ; 83, Pembroke Road, Clifton, Bristol, 8.
1910. Taylor, Arthur Loudoun, B.Sc., M.B., Ch.B., F.R.C.P.Edin., Senior Assistant Medical Officer, Stafford County Mental Hospital, Burntwood, Lichfield.
1935. Taylor, Fred Hayden, M.D., B.S., B.Hy., M.R.C.S., L.R.C.P., D.P.H., Medical Officer, H.M. Prison, Wormwood Scrubs ; 156, Du Cane Road, Shepherd's Bush, London, W. 12.
1897. Taylor, Frederick Ryott Percival, M.D., B.S., M.R.C.S., L.R.C.P., 10, Carew Road, Eastbourne. (*Chairman, Educational Committee*, 1927–33 ; *Chairman, S.E. Division*, 1930–32.)
1935. Taylor, Moore, Major I.M.S., M.D., D.P.H., Medical Superintendent, Ranchi European Mental Hospital, P.O. Kanké, Bihar and Orissa, India.
1932. Taylor, Richard Hamilton, M.B., B.Ch., B.A.O., D.P.H.N.U.I., 119, Lower Baggot Street, Dublin.
1925. Taylor, Robert, L.R.C.P.&S.Irel., D.P.M., Senior Assistant Medical Officer, St. Patrick's Hospital, Dublin.
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1938. Thomas, David Howell Hugh, B.Sc., M.R.C.S., L.R.C.P., D.P.M., Medical Officer to Wilts County Council M.D. Institutions ; Manor House, Easton Royal, near Marlborough.
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1908. **Thomas, Joseph David, B.A., M.B., B.C.Camb., " Dan-y-Graig ", Cheyne Road, Stoke Bishop, Bristol.**

1911. Thomas, William Rees, M.D., B.S., F.R.C.P., M.R.C.S., D.P.M., M.P.C., Senior Commissioner, Board of Control; 34, Chartfield Avenue, Putney Hill, London, S.W. 15. (*Vice-Chairman, Mental Deficiency Committee, since* 1935.)

1925. Thompson, Robert, M.B., B.Ch.Belf., D.P.M., Medical Superintendent, County Mental Hospital, Armagh, N. Ireland. (*Secretary, Irish Division* 1929–37.)

1921. Thomson, Aidan Gordon Wemyss, M.B., Ch.B.Glasg., D.Psych., Commissioner, General Board of Control; 23, Eglinton Crescent, Edinburgh.

1920. Thomson, William George, M.A., M.B., Ch.B.Aberd., D.P.H., D.P.M., Deputy Medical Superintendent, Royal Hospital, Cheadle, Cheshire.

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1937. Thorley, Arnold Stanley, M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Friern Hospital New Southgate, London, N. 11.

1927. Thorpe, Frederick Thomas, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer and Pathologist, South Yorkshire Mental Hospital, Wadsley, Sheffield.

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1935. Torrance, Lionel Stanley, M.B., Ch.B., D.P.M., L.M., 97, King's Avenue, London, S.W. 4.

1938. Tooley, Patrick Hocart, M.B., B.S.Lond., M.R.C.S., L.R.C.P., Assistant Medical Officer, Claybury Hospital, Woodford Bridge, Essex.

1903. Tredgold, Alfred Frank, M.D.Durh., F.R.C.P., F.R.S.Edin., "St. Martin's", Guildford, Surrey; Lect. on Ment. Deficiency, London Univ.

1938. Tredgold, Roger Francis, M.B., B.Ch., L.R.C.P., M.R.C.S., Assistant Medical Officer, County Mental Hospital, Brentwood, Essex.

1906. Turnbull, Peter Mortimer, *M.C.*, M.B., B.Ch.Aberd., D.P.M., Medical Superintendent, Tooting Bec Hospital, London, S.W. 17.

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1933. Turner, Cyril Edward Hedgman, M.R.C.S., L.R.C.P., Senior Medical Officer, Storthes Hall Mental Hospital, Kirkburton, nr. Huddersfield, Yorks.

1906. Turner, Frank Douglas, M.B., M.R.C.S., L.R.C.P., Medical Superintendent, Royal Eastern Counties Institution, Colchester. (PRESIDENT, 1933–34; *Chairman, Mental Deficiency Committee, since* 1935.)

1922. Twomey, John Christopher, M.B., Ch.B.Liverp., D.P.H., Physician Superintendent, The Mental Hospital, Port Alfred, Cape Province, South Africa.

1934. Tyrrell, Thomas Anger Fereman, M.B., B.S.Lond., L.M.S.S.A., St. Mildred's, Milverton, Somerset.

1939. Uytman, John Douglas, M.B., Ch.B., Assistant Medical Officer, Scalebor Park, Burley-in-Wharfedale, Yorks.

1931. Valentine, James, M.B., Ch.B.Glasg., D.P.M., Medical Superintendent, Scalebor Park, Burley-in-Wharfdale.

1939. Van Dam, Lucie, M.B., Ch.B.Glasg., Assistant Physician, The Mental Hospital, Grahamstown, South Africa.

1938. Van Someren, Gerald Antony, M.R.C.S.Eng., L.R.C.P.Lond., Assistant Medical Officer, Carlton Hayes Hospital, Narborough, near Leicester.

1922. Viehoff, Herman Crowther, M.R.C.S., L.R.C.P., 48, Moor Lane, Great Crosby, Lancs.

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1923. Wadsworth, George Reginald, M.B., B.Ch.Belf., D.P.M., Assistant Medical Officer, Lancashire County Mental Hospital, Lancaster.

1928. Waldo, Henry Cecil, M.R.C.S., L.R.C.P., Barrister-at-Law, Medical Superintendent, Notts County Mental Hospital, Radcliffe-on-Trent, Notts.

1926. Walk, Alexander, M.D., B.S.Lond., D.P.M., Deputy Medical Superintendent, Horton Hospital, Epsom, Surrey. (*Assistant Editor*, 1928–31, *and Co-Editor of Journal since* 1931.)

1914. Walker, Robert Clive, M.D., Ch.B.Edin., Medical Superintendent, West Riding Mental Hospital, Menston, Leeds.

1908. Wallace, John Andrew Leslie, M.D., Ch.B.Edin., F.R.A.C.P., M.P.C., *J.P.*, Inspector-General of Mental Hospitals, New South Wales.

1912. Wallace, Vivian, L.R.C.P.&S.Irel., D.P.H., Ballinakill, Multyfarnham, co. Westmeath.

1932. Walsh, Fergus O'Connell, L.R.C.P.&S.Irel., Assistant Medical Officer, Portlaoighise (Maryborough) District Mental Hospital, Portlaoighise, co. Leix, Ireland.

1939. Walsh, John, M.B., B.Ch., D.P.M., Assistant Medical Officer, Plymouth Mental Hospital, Blackadon, Ivybridge, Devon.
1928. Walsh, Michael Anthony, L.R.C.P.&S.I., D.P.M., Assistant Medical Officer, Claybury Hospital, Woodford Bridge, Essex.
1889. Warnock, John, *C.M.G.*, B.Sc., M.D., C.M.Edin., M.R.C.S.Eng., 234, Kew Road, Kew, Surrey.
1922. Watson, Douglas Chalmers, M.D., F.R.C.P.Edin., Fenton Barns, Drem, East Lothian.
1924. Watson, John, *M.C.*, M.B., B.Ch.Edin., Resident Medical Superintendent, District Asylum, Londonderry.
1939. Watterson, Donald James, B.A., M.B., B.Ch., D.P.M., Assistant Medical Officer, L.C.C. Mental Service; Beech Lodge, Effingham, Surrey.
1911. Webber, Leonard Mortis, M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Surrey County Mental Hospital, Netherne, Coulsdon.
1929. Weber, Hilda Marion, B.Sc., M.D.Lond., D.P.M., Physician, The Institute of Medical Psychology; 72, New Cavendish Street, London, W. 1.
1922. Webster, William Leckie, M.B., Ch.B.Edin., M.P.C., Lt.-Col. *R.A.M.C.*, c/o Glyn, Mills & Co., Kirkland House, Whitehall, London, S.W. 1.
1936. Weir, Hugh, B.Sc., M.B., Ch.B., Assistant Physician, The House of Daviot, Pitcaple, Aberdeenshire.
1932. Weir, Thomas William Harold, M.D., B.Ch., B.A.O.Belf., D.P.H., D.P.M., Assistant Medical Officer, Joint Counties Mental Hospital, Carmarthen, Wales.
1919. Westrup, Joseph Perceval, M.R.C.S., L.R.C.P., c/o Lloyds Bank, Ltd., Salisbury.
1938. White, Alfred Arnold, M.B., B.Ch.Aberd., Assistant Medical Officer, Wilts County Mental Hospital, Devizes, Wiltshire.
1911. White, Edward Barton Cartwright, M.R.C.S., L.R.C.P., St. Merryn, Braunton, N. Devon. (*Chairman, S.W. Division*, 1930–33.)
1921. Whitelaw, William, M.B., B.Ch.Glasg., 58, Hazelwood Road, Acocks Green, Birmingham.
1937. Whittaker, Duncan, B.A.Cantab., M.R.C.S., L.R.C.P., Assistant Physician, Bethlem Royal Hospital, Monk's Orchard, Beckenham, Kent.
1913. Wilkins, William Douglas, M.B., Ch.B.Vict., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, Stafford County Mental Hospital, Cheddleton, Leek.
1920. Will, George Wishart, *O.B.E.*, M.B., Ch.B.N.Z., M.P.C., Major *R.A.M.C.*, British Military Hospital, Colaba, Bombay, India.
1925. Williams, Edward Lincoln, M.R.C.S., L.R.C.P., The Hall, Harrow Weald, Middlesex.
1922. Williamson, David Hardie, M.B., Ch.B.Edin., Assistant Medical Officer, Glasgow District Mental Hospital, Woodilee. Lenzie, Scotland.
1937. Williamson, Geoffrey, M.B., Ch.B.Manch., D.P.M., Assistant Medical Officer, County Mental Hospital, Rainhill, St. Helens, Lancs.
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1930. Wilson, Henry Leonard, M.D., B.Ch.Camb., M.R.C.P., D.P.M., Physician, The Tavistock Clinic; 142, Harley Street, London, W. 1.
1923. Wilson, Isabel Grace Hood, M.D., Ch.B.Edin., M.R.C.P., D.P.M., Commissioner, Board of Control, Hobart House, Grosvenor Place, London, S.W. 1.
1920. Wilson, James Leitch, M.B., Ch.B.Edin., D.P.M., 146, Harley Street, London, W. 1.
1937. Wilson, Robert Edward, M.B., Ch.B., Liverp., L.R.C.S., L.R.C.P., L.R.F.P.&S., Assistant Medical Officer, County Mental Hospital, Rainhill, Lancs.
1938. Wilson, Robert Scott, L.R.C.P., L.R.C.S.Edin., L.D.S., Assistant Medical Officer, Warwickshire and Coventry Mental Hospital, Hatton, near Warwick.
1937. Wilson, Thomas Muir, M.B., Ch.B., Senior Resident Medical Officer, Gartloch Mental Hospital, Gartcosh, Glasgow.
1937. Wishart, John William, B.A., M.B., B.S.Lond., M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Cheddleton Mental Hospital, Staffs.
1938. Woddis, Gideon Mordecai, M.R.C.S., L.R.C.P., Assistant Medical Officer, The Coppice, Nottingham.

1934. Wood, Alexander, M.B., Ch.B.Aberd., Deputy Medical Superintendent, County Mental Hospital, Newport, I. of Wight.
1912. Woods, James Cowan, B.A.R.U.I., M.D., B.S., M.R.C.S., L.R.C.P., 40, Harley Street, London, W. 1.; Lect. on Ment. Dis., London Hospital.
1885. Woods, John Francis, M.D.Durh., L.S.A., M.R.C.S., 7, Harley Street, London, W. 1.
1912. Wootton, John Charles, *M.C.*, M.R.C.S., L.R.C.P., Medical Superintendent, Haydock Lodge, Newton-le-Willows, Lancs.
1922. Wootton, Leonard Henry, *M.C.*, B.Sc., M.B., B.S., M.R.C.S., L.R.C.P., D.P.M., Medical Superintendent, St. Ebba's Hospital, Epsom.
1900. Worth Reginald, *O.B.E.*, M.B., B.S.Durh., M.R.C.S., L.R.C.P., Cedar Cottage, Hill Head, Hampshire. (*Hon. General Secretary*, 1919–36; PRESIDENT, 1935–36.)
1917. Wright, Maurice Beresford, *O.B.E.*, M.D., C.M.Edin., Physician, The Tavistock Clinic; 86, Brook Street, London, W. 1.
1938. Wright, William Robinson, M.B., B.Ch., B.A.O., Assistant Medical Superintendent, Mental Hospital, Armagh.
1933. Wyatt, Walter, M.B., Ch.B.Edin., D.P.M.Lond., 11, Western Terrace, Edinburgh, 12.
1929. Wyllie, Andrew McNae, B.Sc., M.B., Ch.B., Midpark South, Bankend Road, Dumfries.

1928. Yates, Arthur Gurney, M.A., M.D.Edin., F.R.C.P., Physician, Sheffield Royal Infirmary, 53, Wilkinson Street, Sheffield.
1934. Yates, Irene, M.D., B.S.Lond., M.R.C.P.Lond., D.P.M., 11, The Grange, Maitland Park Road, London, N.W. 3.
1921. Yellowlees, David, M.B., Ch.B.Glasg., 17, Lynedoch Crescent, Glasgow, C. 3.
1914. Yellowlees, Henry, *O.B.E.*, M.D., Ch.B., F.R.C.P.Edin., F.R.F.P.S.Glasg., F.R.C.P., D.P.M., Physician and Lect. on Psych. Med., St. Thomas's Hospital; 93A, Harley Street, London, W. 1.
1938. Young, George Campbell, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Hull City Mental Hospital, Willerby, Hull.

1938. Zscherpel, Harold Duncan, M.R.C.S., L.R.C.P., Superintendent, Central Prison, Peshawar; Medical Officer i/c Mental Hospital, Peshawar; 1A, North Circular Road, Peshawar, India.

OBITUARY.

Honorary Members.

1928. Bleuler, Eugen, Prof. Dr., Zollikerstrasse 98, Zollikon bei Zürich, Switzerland.
1930. Cushing, Harvey, *C.B.*, A.M., LL.D., Sc.D., Litt.D., M.D., M.Ch., F.R.C.S., Professor of Surgery, The Yale Medical School, New Haven, Connecticut, U.S.A.
1923. Ellis, Henry Havelock, L.S.A., Cherry Ground, Hintlesham, nr. Ipswich, Suffolk.
1936. Freud, Prof. Dr. Sigmund, 39, Elsworthy Road, London, N.W. 3.
1939. Potts, W. A., M.A.Camb., M.D., M.R.C.S., L.R.C.P., 231, Hagley Road, Edgbaston, Birmingham. (*Ordinary Member since* 1913.)

Ordinary Members.

1909. Bain, John, M.A., M.B., Ch.B.Glasg., Medical Superintendent, Derby Borough Mental Hospital, Rowditch.
1934. Boyd, Arthur Ross, M.B., B.Ch., B.A.O.R.U.I., Resident Medical Superintendent, County Mental Hospital, Antrim.
1938. Crook, Hugh Walter Dover, M.R.C.S., L.R.C.P., D.P.M., Assistant Medical Officer, Knowle Mental Hospital, Fareham, Hants.
1879. Dodds, William John, D.Sc., M.D., C.M.Edin., 19, Marina Road, Prestwick, Ayrshire.
1924. Hayes, Henry Douglas, M.D., Ch.B.Edin., D.P.M., Medical Superintendent, The Mental Hospital, Seacliff, Otago, New Zealand.
1929. Muthiah, Asainayagam Richard, L.M.S.Singapore, Assistant Physician, Central Mental Hospital, Tanjong Rambutan, Perak, Federated Malay States.
1905. Shaw, Charles John, M.D., Ch.B., M.R.C.P.Edin., *J.P.*, Medical Superintendent, Royal Asylum, Montrose. (*Chairman, Scottish Division*, 1933–34.)
1900. Wilkinson, Harry Bacon, M.R.C.S., L.R.C.P., "Dalestorth", Lynton Drive, Hillside, Southport, Lancs.

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Part I.—Original Articles.

A REVIEW OF GESTALT PSYCHOLOGY.

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1. INTRODUCTION.

THE prevailing type of psychology in the first decade of the present century was a combination of associationistic philosophy with analytical introspections. The introspections, which provided the units of sensation, images and ideas, were of an esoteric brand ; they were bereft of what was called the "experience error", and made to correspond with physiological impressions. Thus if a subject in some experiment observed a penny lying on a table top he, if he had not been trained in this type of introspection, would see it as a round object from whatever angle he might look at it. Yet the physiological impression on his retina would only be round if he were observing the penny from directly above ; in all other cases the image would be more or less ovoid, according to the angle from which he viewed it. To say that the penny was round when it was being viewed from an angle was, therefore, to be guilty of the "~~experience~~ stimulus error", and since the experience of different subjects would be likely to be different, their introspections could not be regarded as equivalent. By a process of long training, therefore ("three years' hard introspecting"), one had to learn to correlate one's sensations with one's physiological impressions, so that as one altered one's angle of view one actually saw the penny change in shape. Only then, it was thought, could different sensations be regarded as truly equivalent and comparable units, for only then would they all be

devoid of the varying effects of experience. What was true of the observation of the penny held for other types of observation also. Such " pure sensations ", which formed the units of the science of psychology at that time, were bound together in different ways by the association of one with another as a result of different experiences. The more frequently and the more recently any one of these units was associated with any other, the more likely were they to occur together on subsequent occasions. In this way the more complex mental processes were supposed to be developed out of simpler units.

By 1910, however, this type of psychology, which has been variously called Structuralism, Elementarism and Introspectionism—and which is associated in particular with the name of Titchener (1), following Wundt—was rapidly losing contact with current psychological interests, and within a few years two widely different schools had started on their careers. One of these, behaviourism, rebelled against the subjectivity of the introspectionist school. Its background was the objectivity of the American practical man. It wanted concrete facts readily acquired rather than obscure intangibilities obtainable only after several years of hard effort. It therefore threw on one side as unreliable all subjective phenomena, such as introspections, images, feelings and ideas, and concentrated on observable behavioural facts. For their units the behaviourists took simple reflex actions, and, while retaining the associationistic side of their predecessors' psychology, explained complex types of behaviour in terms of the association of a number of simple reflex arcs with one another (2). Thus they felt that complex behavioural phenomena could be analysed into their constituent simple reflexes, and they left the impression that such an analysis would explain the behaviour in question.

The other revolt against structuralism had the German philosophical tradition as its background. Its main criticism, therefore, was directed against the analytical aspects of the current psychology. The fundamental principle of this, the Gestalt school was, in the words of its founder Wertheimer, " Es gibt Zusammenhänge, bei denen nicht, was im Ganzen geschieht, sich daraus herleitet, wie die einzelne Stücke sind und sich zusammensetzen, sondern umgekehrt, wo—im prägnanten Fall—sich *das, was an einem Teil dieses Ganzen geschieht, bestimmt von inneren Strukturgesetzen dieses seines Ganzen*" (3). (There exist relations in which the behaviour of wholes is not determined by that of their elements, but, on the contrary, the parts are determined by the nature of the wholes.)

It therefore followed from this view that, in the opinion of the Gestalt psychologists, much more valuable psychological material could be obtained by considering behaviour as it is actually experienced in all its complexity as the primary datum, and to start further investigation from this point, rather than to begin with unreal and hypothetical elements, and try to build up the complexities of behaviour out of them. It is on this basis that their experimental work has been founded.

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2. Experiments on Perception.

The experiment that is regarded as the first to start the Gestalt psychologists on their crusade was on a phenomenon that is a familiar feature of present day life, encountered most frequently in the cinema—the phenomenon of apparent motion. In watching a cinema film one knows—if one cares to think about it—that one is seeing a series of still photographs presented in quick succession. But one does not experience anything that corresponds with this type of physical stimulation; one experiences the perception of movement. In this phenomenon, therefore, as with the perception of the penny on the table, the experience radically differs from the physical impression. In Wertheimer's experiment (4) the subject was seated in a darkened room, and two points of light, separated from each other by a short distance were successively exposed. When the most favourable distance of separation and the most favourable interval between the exposures of the two points had been discovered, the subject's experience was of the motion of a single point of light from one point to the other. Although there was no actual movement the property of the whole situation was such that the subject thought that movement had taken place. This phenomenon was given the name of the " phi phenomenon " by Wertheimer in the hope that a neutral name would encourage a further unprejudiced examination of its origin and properties.

In extending the experiment a stage further it was observed that the subject's experience was the same both when the experiment was conducted in the manner already described, and also when a single point of light was used and actually made to travel from one position to the other. Subjectively the experience was the same in the two cases (provided, of course, that the speed of movement in the second case had been adjusted to correspond to the interval between the appearance of the points of light in the first), yet objectively the conditions were very different, for in the first case there was no stimulation of the intervening points on the retina, whereas in the second case there was. The same experience was obtained under two very different conditions of physical stimulation, and the Gestalt psychologists therefore put forward the explanation that the experience depended on certain properties of the whole situation rather than on the properties of point stimulation.

The same point was emphasized even more strongly in Köhler's " Figure 4 " diagram (5), for in this case it could be demonstrated that an appeal to the effects of experience to explain the phenomenon was totally inadequate. Between the two big figures in the diagram (Fig. 1) there is a figure 4. It is difficult to see it because the two vertical strokes form part of the two big figures, and the horizontal stroke forms a part of the long horizontal line. The unity of the figure 4, therefore, is broken by the properties of the whole diagram, and it disappears from view because its parts are used to finish off or close

more dominant figures. The explanation is not simply due to the unfam
of the diagram, to the fact that we have never before seen a figure 4
position, and that we overlook its presence in consequence; for a c

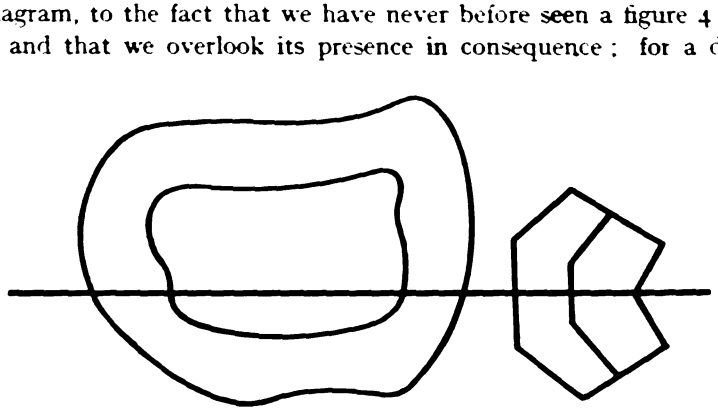

FIG. 1.—From Köhler, W., *Gestalt Psychology*, p. 155.

quite as unfamiliar may be constructed, such as that in Fig. 2, in wh
can be no hesitation in recognizing the presence of the figure 4. On
the properties of the whole diagram will determine the properti
component parts.

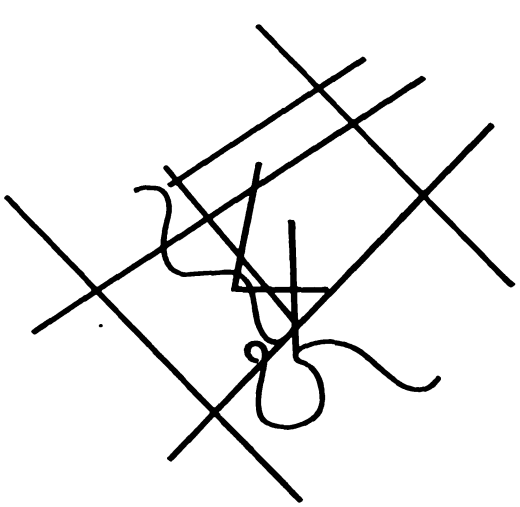

FIG. 2.—From Köhler, W., *Gestalt Psychology*, p. 162.

On this basis the Gestalt psychologists have analysed some of t
in the structure of objects which will influence their organizati
way they are perceived (6).

(a) *Grouping*.—One of the most important of the features dete
organization of objects in perception is grouping. In any percept

more dominant figures. The explanation is to be simply due to the unfamiliar of the diagram, to the fact that we have never before seen a figure in that position, and that we therefore do not recognize it. But a figure

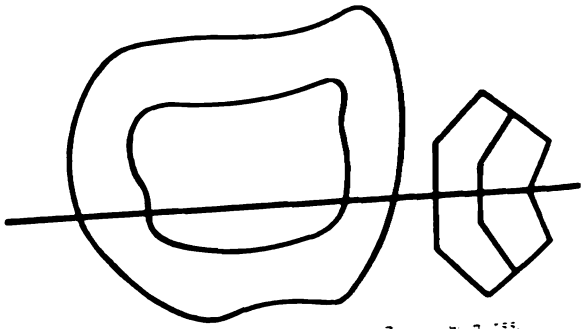

FIG. 1.—From Köhler, W., *Gestalt Psychology*, p. 155.

quite as unfamiliar may be constructed such as that in Fig. 2, in which there can be no hesitation in recognizing the presence of the figure 4. Once again the properties of the whole diagram will determine the properties of its component parts.

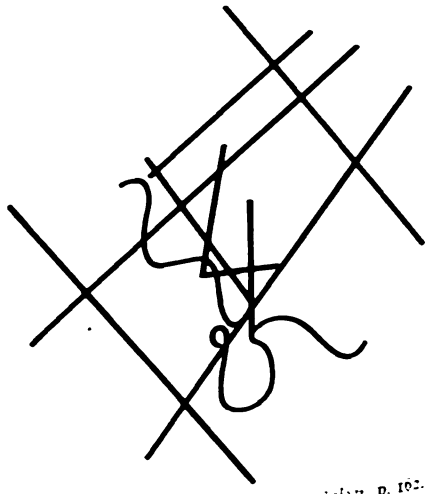

FIG. 2.—From Köhler, W., *Gestalt Psychology*, p. 162.

On this basis the Gestalt psychologists have analysed some of the factors in the structure of objects which will influence their organization and the way they are perceived (6).

(a) *Grouping.*—One of the most important of the features determining the organization of objects in perception is grouping. In any perceptual situation

certain things are grouped together and differentiated from others. This one of the difficulties of performing experiments on what is called the "span attention". If it is desired to know how many objects an individual c correctly perceive at a single glance, the simplest thing would appear to be present him with a series of cards on which are drawn an increasing number objects, until he fails to name the correct number. This is, in fact, what t early experimenters did, and when experiments of this kind have been p formed it has been found that the largest number of discrete objects that c be correctly estimated is about seven. But one of the difficulties in experimer of this kind is to arrange the objects in such a way that they do not fo

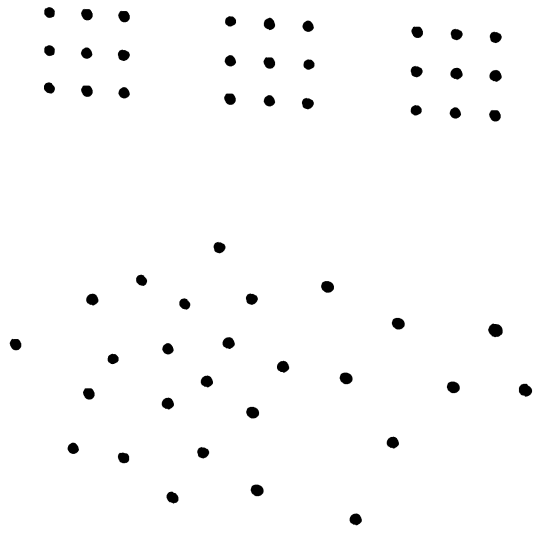

FIG. 3.

groups. If a large number of objects can be grouped together easily it is mu easier to estimate correctly the number present than when they form discre and ungroupable entities. It is, for example, much easier to perceive the fi arrangement of dots in Fig. 3 as 27 than it is to perceive the second arrangeme as the same number. This tendency towards grouping appears in almo every case, and even the second arrangement, if looked at for a sufficie length of time, will tend to form itself into a few groups of a few dots each.

(b) *Nearness.*—The same tendency to group objects together is shown Köhler's example (7) illustrated in Fig. 4. This is seen as two groups of thr blots each, not as three groups of two nor as six separate patches. In th case the relative nearness of some of the patches to one another compared wi their distance from others is probably the reason for the particular type organization that ensues. In other cases, however, other factors may shown to be stronger than nearness.

[illegible] *Similarity.*—In the example given in Fig. 5, for example, the [illegible] nearer to the circles than they are to the another [illegible] yet the first [illegible] seen as horizontal rows rather than as vertical columns, while the [illegible] seen as vertical columns rather than as horizontal rows.

[illegible] *Symmetry.*—A fourth factor making grouping is symmetry. [illegible] presented the figures shown in Fig. 6 to sixty-four people. The [illegible]

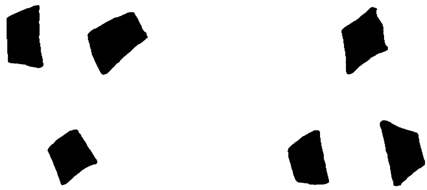

FIG. 6.—From [illegible]

seen as black symmetrical or white unsymmetrical stripes [illegible] white symmetrical or black unsymmetrical stripes. He found th[illegible] of the cases the symmetrical stripes were reported, and in only one c[illegible] unsymmetrical reported. The other cases were unstable and ambi[illegible]

[illegible] *Closure.*—Another factor is closure. The six equidistan[illegible] Fig. 7 tend at first sight to be seen as six discrete units. There is n[illegible] tendency to rearrange them in groups in any special way. If [illegible] small horizontal line is added at the top and bottom of each the re[illegible]

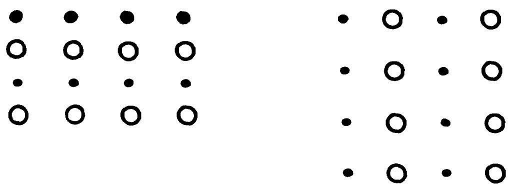

FIG. 5.

different, and, as can be seen in Fig. 8, they at once form the[illegible] three groups composed of two vertical lines each. The effect [illegible] horizontal lines is to close the figures, and it is of such strength tha[illegible] Fig. 7 the lines *a*, *b*, *c*, *d*, *e* and *f* looked equidistant, yet in Fig. [illegible] looks nearer to *a* than to *c*, and similarly with the remaining lines[illegible]

The Gestalt psychologists suggest that the factor of closure m[illegible] the explanation of the Müller-Lyer illusion. Although the lines [illegible] Fig. 9 are equal, the arrow-heads in the first figure cause a part[illegible] that figure, with the result that the distance *ab* looks shorter th[illegible] is. With *cd*, however, there is no tendency to closure.

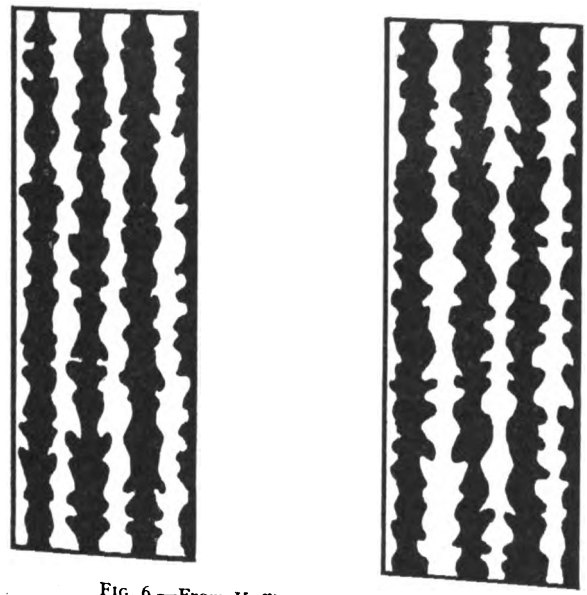

FIG. 6.—From Koffka, after Bahnsen.

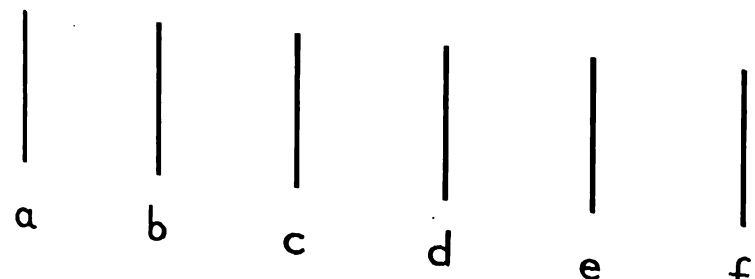

FIG. 7.

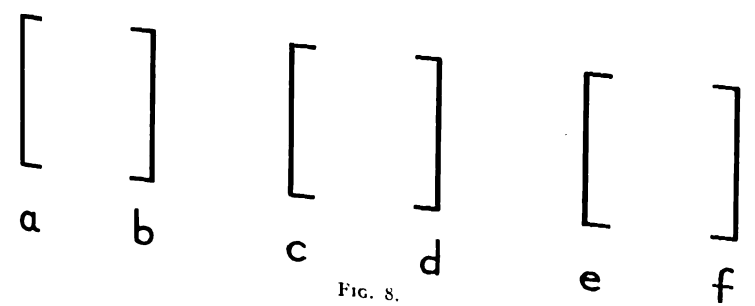

FIG. 8.

f *Good continuation.*—The factor of closure is closely related t
known as good continuation. This has been illustrated in K
diagram, and there are many other examples as well. It is easier, f

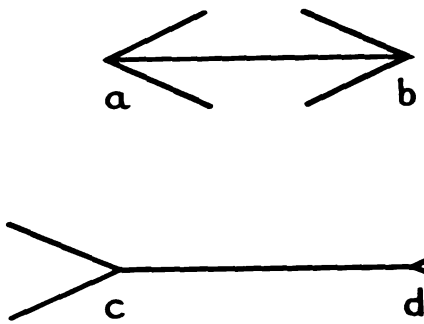

FIG. 9.—The Muller-Lyer illusion.

to see Fig. 10 as made out of a straight line and an "S" curve t
out of the hook and crook designs of Fig. 11. The crook on the
10 appears to be an essential part of the curve on its left; it form
it, and it loses its continuation with the straight line. This
camouflage: first to break up the unity of a particular object, and

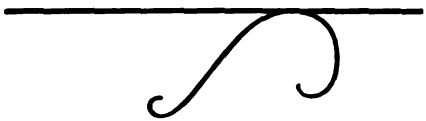

FIG. 10.

FIG. 1

its parts form essential portions of some other object. Thus it
lose its identity. This is also the art of the puzzle-picture devis
reason for the effectiveness of protective coloration in anim
being assimilated into its background and apparently form
part of it.

(g) *The "figure-ground" phenomenon.*—Such considerat
the Gestalt psychologists in developing their theory and th

(f) *Good continuation.*—The factor of closure is closely related to the well-known as good continuation. This has been illustrated in Koffka's [illegible] diagram, and there are many other examples as well. It is easier to realize

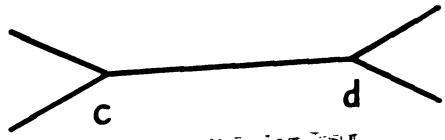

FIG. 9.—The Müller-Lyer illusion.

to see Fig. 10 as made out of a straight line and an "S" curve than as [illegible] out of the hook and crook designs of Fig. 11. The crook on the right in Fig. 10 appears to be an essential part of the curve on its left: it forms a unity with it, and it loses its continuation with the straight line. This is the art of camouflage: first to break up the unity of a particular object and then to make

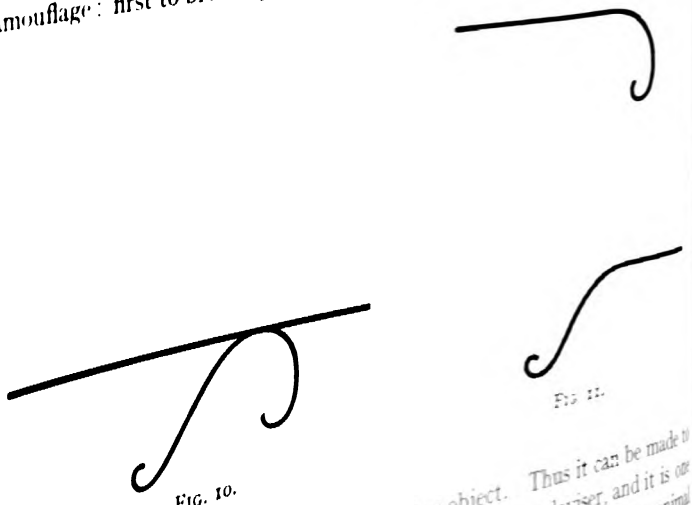

FIG. 10.

FIG. 11.

its parts form essential portions of some other object. Thus it can be made to lose its identity. This is also the art of the puzzle-picture deviser, and it is one reason for the effectiveness of protective coloration in animals, the animal being assimilated into its background and apparently forming an essential [illegible] "figure-ground" phenomenon.—Such considerations influenced [illegible] in developing their theory and their experimental

work on the basis of the "figure-ground" phenomenon expounded by Rubin (9). In Fig. 12 one sees a small square standing out from a background of enclosing white space. But if the size of the square is increased beyond a

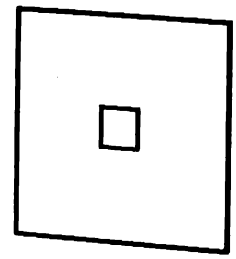

FIG. 12.

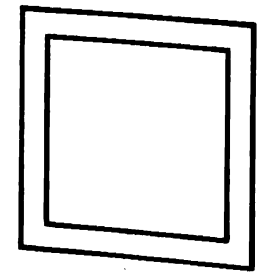

FIG. 13.

certain point the character of the perception changes and one sees, as in Fig. 13, a double square standing out as the figure with the enclosed white space as background. The enclosed white space was figure and is now ground, and instead of standing out in front of the background it now appears to lie behind the figure. In general the same phenomenon is encountered: figures appear to stand out in front of grounds, and grounds appear to lie behind figures. As in

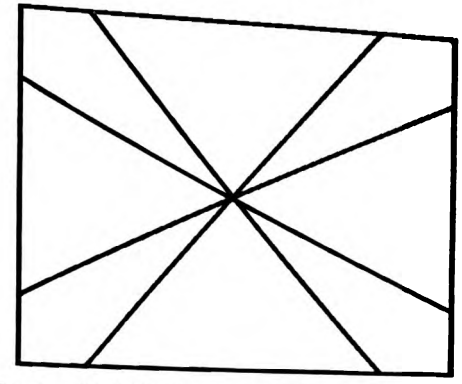

FIG. 14.—The Maltese-cross-propeller reversible figure.

the Müller-Lyer illusion, the structure of the whole alters the apparent relationships of the parts.

(h) *Reversible figures.*—The shifting relationships of figure and ground are seen, too, in reversible figures, e. g., the propeller-Maltese-cross phenomenon illustrated in Fig. 14. Sometimes the propeller is seen as figure, sometimes the Maltese cross. When the propeller is seen as figure it stands out and the

remainder recedes into the background. When the Maltese cros
figure the rest recedes. The whole appearance alters as perception
This again shows, according to the Gestalt psychologists, that perc
must depend on the organization of the whole. The actual p
retina being stimulated are the same in both cases, yet the subjectiv
is quite different. The perception must depend, therefore, not
stimulation of particular points of the retina, but also on the organi
whole and the relationship between its component parts. This or
sometimes subjective, as when one alternates the perceptions in
figure at will, but at other times it depends on the inherent prop
figure itself. Thus Kopfermann (10) has shown that even para
overcome, and an actual tridimensional object seen as a plane
certain forms which favour bi-dimensional organization are use

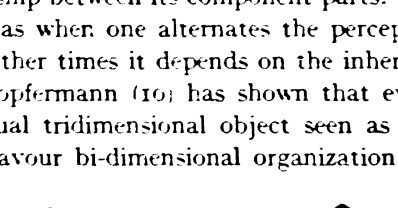

FIG. 15.

illustration of this is in the three diagrams shown in Fig. 15. No
seen as a plane figure, No. 3 as a tri-dimensional cube, and No
plane or as a tri-dimensional figure.

Auditory Perception.

The predominance of the whole over its parts is also de
auditory perception. A particular melody may be heard at
played on a piano, whistled in the street by an errand-boy, p
whistle, or played by a full orchestra in a concert hall. In eac
have heard it in a different key with different overtones and diffe
notes. Yet it is recognizable as the same melody. Perhaps, too
boy whistled it in the street the sound of a motor horn intrud
point. Yet when we hum the melody over to ourselves afterw
of the motor horn—though it may be remembered—does not
the melody. The point stimulation—the individual character
therefore is of minor importance compared with the charac
whole melody, and it is the organization of the whole, influencin
relationship between its component parts, which enables us t
melody as the same even when it is presented under very diffe

remainder recedes into the background. When the Maltese cross is seen as figure the rest recedes. The whole appearance alters as perception changes. This again shows, according to the Gestalt psychologists, that perception does not must depend on the organization of the whole. The actual points of the retina being stimulated are the same in both cases, yet the subjective experience is quite different. The perception must depend therefore not only on the stimulation of particular points of the retina, but also on the organization of the whole and the relationship between its component parts. This organization is sometimes subjective, as when one alternates the perceptions in a reversible figure at will, but at other times it depends on the inherent properties of the figure itself. Thus Kopfermann (10) has shown that even perfect symmetry may be overcome, and an actual tridimensional object seen as a plane figure with certain forms which favour bi-dimensional organization are used. A simple

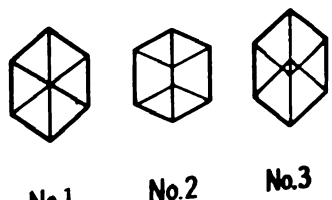

FIG. 15.

illustration of this is in the three diagrams shown in Fig. 15. No. 1 tends to be seen as a plane figure, No. 3 as a tri-dimensional cube, and No. 2 as either a plane or as a tri-dimensional figure.

Auditory Perception.

The predominance of the whole over its parts is also demonstrated in auditory perception. A particular melody may be heard at different times played on a piano, whistled in the street by an errand-boy, played on a full orchestra in a concert hall. In each case we may whistle, or played by a full orchestra in a concert hall. In each case we may have heard it in a different key with different overtones and different individual notes. Yet it is recognizable as the same melody. Perhaps, too, as the errand-boy whistled it in the street the sound of a motor horn intruded at a certain point. Yet when we hum the melody over to ourselves afterwards the sound of the motor horn—though it may be remembered—does not form a part of the melody. The point stimulation—the individual character of each note—is therefore of minor importance compared with the characteristics of the melody, and it is the organization of the whole, influencing as it does the [illegible] its component parts, which enables us to recognize the [illegible] when it is presented under very different conditions.

3. PHYSICAL GESTALTEN.

Having demonstrated in their experiments on perception that the properties of the whole determined the relationship between its parts rather than the reverse, the Gestalt psychologists proceeded to turn the tables on the behaviourists, and to show that the same thing was generally true in the physical world as well.

The behaviourists regarded the physical world somewhat mechanistically. They were impressed by the quantitative aspects of physics and chemistry, and, consciously or otherwise, it was their aim to make psychology as like their conception of the other sciences as possible. It appeared to them to be a reasonable assumption that if in the physical world complex phenomena were no more than the additive functions of elementary processes, the same should be true in psychology also. Their position is expressed by Watson (11):

"We use the term *stimulus* in psychology as it is used in physiology. Only in psychology we have to extend somewhat the usage of the term. In the psychological laboratory, when we are dealing with relatively simple factors, such as the effect of ether waves of different lengths, the effect of sound-waves, etc., and are attempting to isolate their effects upon the adjustment of men, we speak of stimuli. On the other hand, when factors leading to reactions are more complex, as, for example, in the social world, we speak of *situations*. A situation is, of course, upon final analysis, resolvable into a complex group of stimuli. As examples of stimuli we may name such things as rays of light of different wave-lengths; sound-waves differing in amplitude, length, phase and combination; gaseous particles given off in such small diameters that they affect the membrane of the nose; solutions which contain particles of matter of such size that the taste buds are thrown into action; solid objects which affect the skin and mucous membrane; radiant stimuli which call out temperature response; noxious stimuli, such as cutting, pricking, and those injuring tissue generally. Finally, movements of the muscles and activity in the glands themselves serve as stimuli by acting upon the afferent nerve-endings in the moving muscles."

The Gestalt psychologists, however, approached the problem from the other end. Being first of all impressed by the predominance of the whole situation over its parts, illustrated in their experiments on perception, they then proceeded to look about the physical world to see whether the same phenomenon was observed there. And they came to the conclusion that it was:

"Let us take the simplest example we can find: water is explained by the atomic theory as a compound of two elements, hydrogen and oxygen, in such a way that it consists of molecules, each of which is composed of three atoms, two of hydrogen and one of oxygen. Moreover, hydrogen occurs in nature in a form in which it is not composed of hydrogen atoms, but of hydrogen

molecules, each composed of two hydrogen atoms. Thus we H_2O. This sounds like a straight molecular theory, but it is no the kind. For H, H_2, and H_2O have all different properties wh derived by *adding* properties of H's and O's." (12).

The predominance of the whole over the parts is also illustrate systems of the reversible reaction type in chemistry :

" When it is heated to a high temperature phosphorus penta up into the trichloride and chlorine. At the same temperature substances also combine to form the pentachloride. At any gi perature there is a certain percentage of the pentachloride left at any moment. At 200° 51·5% of the pentachloride is left, having split up. At 250° these proportions are 20% and 80 But this does not mean that at these temperatures 51·5% of th molecules are permanently united. The whole system is in a at any moment, for example, an individual atom of chlorin while at the next moment it may form part of a pentachloride at any given temperature there are always in the aggregate ap many trichloride molecules and so on. Thus a specific numbe cules at a given temperature will exhibit a constancy which esse change of individual elements, but which is nevertheless non Let us say that such a chemical system is, in an elementary wa that there will always be present in the average a certain spe pentachloride molecules. This conserved group will be compo molecules from time to time ; but there will always be preser as long as the system persists." (13)

Another example is the buffer solution also cited by Hump

" ' We take a solution of 1 kg. of sodium bicarbonate in 1 and allow it to attain equilibrium with an unlimited atmos one gramme of carbon dioxide per litre. Let hydrochloric a small portions at a time, constantly shaking the solution so always be equilibrium with the carbon dioxide in the gas When this is done a characteristic thing happens. The h reacts with the sodium bicarbonate, with the formation of and the liberation of carbon dioxide. This cannot be retaine for the carbon dioxide there is already in equilibrium with th sphere '. Consequently the newly liberated carbon dioxide liquid, and the acidity remains what it was before, the or diminished concentration of the alkaline salt. When, howe bonate is neutralized, this ' buffer ' effect ceases to operat the addition of two grammes of hydrochloric acid ' causes n in acidity as the previous 318 grammes had done, or about t the rise caused by a hundred times the amount at the first st ment'. . . . Considering the system comprising the atmosphere it may be said to be so constituted that by mean systemic changes a certain constancy is preserved in spite ditions such as would, without special organization, greatl In respect of alkalinity or acidity the system is, within self-preserving."

molecules, each composed of two hydrogen atoms. Thus we have H, H
H_2O. This sounds like a straight molecular theory, but it is not anything
the kind. For H, H_2, and H_2O have all different properties which cannot
derived by *adding* properties of H's and O's." (12).

The predominance of the whole over the parts is also illustrated by statistic
systems of the reversible reaction type in chemistry :

" When it is heated to a high temperature phosphorus pentachloride spl
up into the trichloride and chlorine. At the same temperature the latter
substances also combine to form the pentachloride. At any given high te
perature there is a certain percentage of the pentachloride left undissociat
at any moment. At 200° 51·5% of the pentachloride is left, the remain
having split up. At 250° these proportions are 20% and 80%, and so
But this does not mean that at these temperatures 51·5% of the pentachlor
molecules are permanently united. The whole system is in a state of flu
at any moment, for example, an individual atom of chlorine may be fr
while at the next moment it may form part of a pentachloride molecule. B
at any given temperature there are always in the aggregate approximately
many trichloride molecules and so on. Thus a specific number of such m
cules at a given temperature will exhibit a constancy which essentially involv
change of individual elements, but which is nevertheless none the less re
Let us say that such a chemical system is, in an elementary way, so organiz
that there will always be present in the average a certain specific number
pentachloride molecules. This conserved group will be composed of differ
molecules from time to time ; but there will always be present such a gro
as long as the system persists." (13)

Another example is the buffer solution also cited by Humphrey (14) :

" ' We take a solution of 1 kg. of sodium bicarbonate in 100 litres of wat
and allow it to attain equilibrium with an unlimited atmosphere contain
one gramme of carbon dioxide per litre. Let hydrochloric acid be added
small portions at a time, constantly shaking the solution so that there
always be equilibrium with the carbon dioxide in the gas phase.' . .
When this is done a characteristic thing happens. The hydrochloric a
reacts with the sodium bicarbonate, with the formation of sodium chlor
and the liberation of carbon dioxide. This cannot be retained in the solut
for the carbon dioxide there is already in equilibrium with that in the ' atm
sphere '. Consequently the newly liberated carbon dioxide escapes from th
liquid, and the acidity remains what it was before, the only effect being
diminished concentration of the alkaline salt. When, however, all the bica
bonate is neutralized, this ' buffer ' effect ceases to operate. At this sta
the addition of two grammes of hydrochloric acid ' causes nearly as much
in acidity as the previous 318 grammes had done, or about two hundred time
the rise caused by a hundred times the amount at the first stage of the exp
ment '. . . . Considering the system comprising the solution and
atmosphere it may be said to be so constituted that by means of compensat
systemic changes a certain constancy is preserved in spite of change of co
such as would, without special organization, greatly alter conditions
alkalinity or acidity the system is, within limits, relative

A dynamic system such as a pendulum also possesses properties depending on the whole system. It is the organization of the individual molecular forces into a whole in the pendular system that gives the system its peculiar properties, and these properties were discovered quite independently of the knowledge of its atomic or molecular properties, of which we have still only hazy ideas, though we know with considerable exactitude the properties of the pendulum itself.

Köhler discusses the properties of physical Gestalten at considerable length and detail in his book (15). In one example he shows that a charge of static electricity will distribute itself as a whole over the surface of a spherical conductor. If, then, the charge of electricity is increased or diminished at any one point the charge in the system as a whole will be affected, not merely the charge at that point.

Such processes have certain maximum-minimum properties, that is to say, " a given parameter of these processes has not just any magnitude but the smallest or the greatest possible " (16). Thus a soap-bubble adopts a spherical shape because a sphere has the greatest possible volume for a given surface— or the smallest possible surface for a given volume. Similarly, too, if one pricks the inside of a loop of thread of irregular shape thrown onto a soap film, that part of the soap film disappears and the thread immediately adopts a circular shape. Here again the region enclosed by the thread will have the largest possible area and the remaining film will have the smallest possible area.

In simple conditions, therefore, stationary systems tend to possess the greatest possible regularity, symmetry and simplicity. But when the conditions are more complex they lose some of this simplicity. Thus if a drop of water is suspended in a medium of equal density it will become a perfect sphere ; if it lies on a table-top it becomes slightly flattened ; if it falls from the table through the air it becomes pear-shaped. Here again, however, it follows maximum-minimum principles, for it will offer the least possible resistance in its new shape to the air through which it is falling.

The observation that physical systems tend to adopt the most favourable form to meet the surrounding circumstances was at once applied to psychological systems. This *Law of Prägnanz*, formulated by Wertheimer, was that psychological organization is always as " good " as the prevailing conditions allow. The term " good " was undefined, but it included such properties as regularity, symmetry, simplicity, and others already mentioned in the preceding section on perception.

The importance of this contribution was that it implied a correspondence between physical and psychological processes, and this idea was developed into what the Gestalt psychologists call the "*Principle of Isomorphism*"—that the properties of physical processes are the same as those of the conscious processes which they are supposed to underlie. In Köhler's words, "Any actual

consciousness is in every case not only blindly coupled to its correspon physical processes, but is akin to it in essential structural prop one thing is experienced as being " between " two others, this is a by a functional " between " in the concrete dynamic context o physiological events. If one thing is experienced as " belonging t there corresponds a dynamical unit or whole in the underlying processes.

The Gestalt psychologists attach much importance to this di thesis. If true, it provides them with a unity between organic a processes which the behaviourists had assumed. But it is a un different order.

4. Experiments on Learning.

The associationistic theory of the nature of learning, whicl psychologists set out to refute, had a twofold basis. In the firs were the conditioned reflex experiments of Pavlov (17). As a r there had been developed a theory of the fine localization of r cortex:

" It becomes obvious . . . that through the medium o cortex a great number of environmental changes establish now negative conditioned reflexes and determine in this manner effector activities of the animal organism, and its everyday b these conditioned reflexes must have definite representation i cortex in one or another definite group of cells. One such grou be connected with one definite activity of the organism, anotl another activity ; one group may determine a positive activity may inhibit an activity. The cerebral cortex can accordingly as an exceedingly rich mosaic, or as an extremely complicated However, in spite of its extreme complexity as a switchboard tl large spaces reserved for the development of new connections. M which are already involved in a definite conditioned activity fre their physiological role and become connected with some other animal " (18).

It fell to a behaviourist, however, to refute this position performed a series of experiments in which rats were taught mazes and puzzle boxes. He compared groups of normal rats rats which had had different amounts of their cortexes destro cautery. His main findings showed that the capacity to depended on the *amount* of cortex that the animal possessed. learn decreased proportionately with the amount of destructio and *independently of the locus of the destruction.* He found habit formed before operation was disturbed by operations to cortex, and the amount of reduction of efficiency of performa tional to the extent of the injury and independent of the loc experiments he concluded (1) that the learning and retention o

consciousness is in every case not only blindly coupled to its corresponding psycho-physical processes, but is akin to it in essential structural properties". If one thing is experienced as being "between" two others, this is accompanied by a functional "between" in the concrete dynamic context of concurrent physiological events. If one thing is experienced as "belonging to" another there corresponds a dynamical unit or whole in the underlying physiological processes.

The Gestalt psychologists attach much importance to this difficult hypothesis. If true, it provides them with a unity between organic and inorganic processes which the behaviourists had assumed. But it is a unity of a very different order.

4. Experiments on Learning.

The associationistic theory of the nature of learning, which the Gestalt psychologists set out to refute, had a twofold basis. In the first place there were the conditioned reflex experiments of Pavlov (17). As a result of these there had been developed a theory of the fine localization of reflexes in the cortex:

"It becomes obvious . . . that through the medium of the cerebral cortex a great number of environmental changes establish now positive, now negative conditioned reflexes and determine in this manner the differentiated effector activities of the animal organism, and its everyday behaviour. All these conditioned reflexes must have definite representation in the cerebral cortex in one or another definite group of cells. One such group of cells may be connected with one definite activity of the organism, another group with another activity; one group may determine a positive activity while another may inhibit an activity. The cerebral cortex can accordingly be represented as an exceedingly rich mosaic, or as an extremely complicated 'switchboard'. However, in spite of its extreme complexity as a switchboard there are always large spaces reserved for the development of new connections. Moreover points which are already involved in a definite conditioned activity frequently change their physiological role and become connected with some other activity of the animal" (18).

It fell to a behaviourist, however, to refute this position. Lashley performed a series of experiments in which rats were taught and re-taught mazes and puzzle boxes. He compared groups of normal rats with groups of rats which had had different amounts of their cortexes destroyed by thermocautery. His main findings showed that the capacity to learn the mazes depended on the *amount* of cortex that the animal possessed. The ability to learn decreased proportionately with the amount of destruction of the cortex and *independently of the locus of the destruction*. He found that the maze habit formed before operation was disturbed by operations to *any* part of the cortex, and the amount of reduction of efficiency of performance was proportional to the extent of the injury and independent of the locus. From these experiments he concluded (1) that the learning and retention of the habits were

not dependent on finely localized structures, and (2) that the contribution of different parts of a specialized area, or of the whole cortex in the cases of non-localized functions, was qualitatively the same. His conclusions therefore argue against a fine localization of behaviour patterns in the cortex.

Furthermore, the conditioned reflex experiments were performed under highly artificial conditions, all extraneous sounds, sights and smells being excluded by means of a sound-proof room, and the dog being fixed in an uncomfortable position on a table for long periods of time. There is no obvious justification, therefore, for applying any results obtained in such circumstances to the complex conditions of ordinary life. And even when the technique of the conditioned reflex experiments has been repeated, a different type of learning from that described by Pavlov may sometimes be shown to occur (20).

The other line of support for the associationistic theory came from what is known as "trial and error" learning. It is on this branch that the Gestalt psychologists have directed most of their fire. As a result of his experiments on animals in puzzle boxes, Thorndike (21) formulated two associationistic laws which he thought would be sufficient to explain the phenomena of learning. These two laws are known as the "Law of Exercise (or Frequency)" and the "Law of Effect".

The law of frequency is that "any response to a situation will, other things being equal, be more strongly connected with the situation in proportion to the number of times it has been connected with that situation and to the average vigour and duration of the connections".

The law of effect is that "of several responses made to the same situation those which are accompanied or closely followed by satisfaction to the animal will, other things being equal, be more firmly connected with the situation so that when it recurs they will be more likely to recur", and that those which are accompanied or closely followed by dissatisfaction to the animal will tend to be dropped out. Thorndike has recently reviewed his opinion in regard to dissatisfaction. He now holds that dissatisfaction may have a strengthening effect (22).

The Gestalt psychologists, however, are not satisfied that the phenomena of learning can be adequately explained by these laws (23). They criticize the law of effect on many grounds, e.g., (1) that an animal does not make exactly the same movements every time it releases the catch of the puzzle box to obtain food; sometimes it may open it with its paw, sometimes with its nose, sometimes with its teeth, and so on. There is no single response, therefore, to be stamped in in association with the pleasurable after-effects. (2) An animal may make many movements between the act which releases the catch and the act which gets it the food. On a strict interpretation of the associationistic theory these acts should be stamped in just as strongly as the act of releasing the catch. Yet what the animal learns is to release the catch, not to perform the other movements which were more closely followed by the reward. This

is most clearly illustrated in the fact that the animal gets its satisfaction from chewing the food. Yet when put in the puzzle-b on a subsequent occasion it does not sit still and make chewing m releases the catch.

Many criticisms have been levelled, too, against the law o They are based on the fact that the frequent occurrence of a part a given situation does not necessarily imply that the act will occu the same situation recurs. A simple example is when an anima elementary T-shaped maze in which there is only one choice, a right, say, which is correct and leads to food, and a choice to the incorrect and leads only to a blind alley. In such a maze a make the right choice only *once* in any given trial, for as soon a the right choice it gets the reward and the trial is at an end. make the wrong choice a number of times in any one trial: it left, find the blind alley, return to the starting-point, return to turn again to the left, and so on. In any series of trials the prob the wrong choice will be made more frequently than the right the animal eventually learns the problem and makes no fur The same argument may be used with greater validity where many blind alleys.

The law of frequency has been further examined from a point of view, and has been found to be an insufficient expla takes place in learning (24). It has even been shown (25) tha response has been very frequently performed by a subject wh wrong response, the effect is to stamp out that response rathe it in.

The associationistic theory proving an insufficient explana that learning takes place, the Gestalt psychologists approac from their usual viewpoint. Again it was their object to empl importance of the properties of the whole situation rather t individual stimuli within it. Thus when Hertz (26) hid food number of similar flower-pots, the jay which observed thi able to fly straight to the correct pot when it was arranged in stand out from the others. If the pots were arranged in the f a straight line with the correct pot outside or inside the circ of the straight line (see Fig. 16), the bird chose the correct tation. When, however, the correct pot formed part of the line itself (as shown in Fig. 17), the bird made a number before finally reaching the correct pot. When, that is to was segregated from the others in some way the bird could but when it merely formed one of a homogeneous series of correct choice became a matter of chance, with the odds l bird.

is most clearly illustrated in the fact that the animal gets its immediate satisfaction from chewing the food. Yet when put in the puzzle-box situation on a subsequent occasion it does not sit still and make chewing movements, it releases the catch.

Many criticisms have been levelled, too, against the law of frequency. They are based on the fact that the frequent occurrence of a particular act in a given situation does not necessarily imply that the act will occur again when the same situation recurs. A simple example is when an animal is in a very elementary T-shaped maze in which there is only one choice, a choice to the right, say, which is correct and leads to food, and a choice to the left which is incorrect and leads only to a blind alley. In such a maze an animal can make the right choice only *once* in any given trial, for as soon as it has made the right choice it gets the reward and the trial is at an end. But it may make the wrong choice a number of times in any one trial: it may go to the left, find the blind alley, return to the starting-point, return to the junction, turn again to the left, and so on. In any series of trials the probability is that the wrong choice will be made more frequently than the right one, and yet the animal eventually learns the problem and makes no further mistakes. The same argument may be used with greater validity where the maze has many blind alleys.

The law of frequency has been further examined from an experimental point of view, and has been found to be an insufficient explanation of what takes place in learning (24). It has even been shown (25) that when a wrong response has been very frequently performed by a subject who knows it is a wrong response, the effect is to stamp out that response rather than to stamp it in.

The associationistic theory proving an insufficient explanation of the way that learning takes place, the Gestalt psychologists approached the matter from their usual viewpoint. Again it was their object to emphasize the greater importance of the properties of the whole situation rather than those of the individual stimuli within it. Thus when Hertz (26) hid food under one of a number of similar flower-pots, the jay which observed this procedure was able to fly straight to the correct pot when it was arranged in such a way as to stand out from the others. If the pots were arranged in the form of a circle, a straight line with the correct pot outside or inside the circle, or to one side of the straight line (see Fig. 16), the bird chose the correct one without hesitation. When, however, the correct pot formed part of the circle or straight line itself (as shown in Fig. 17), the bird made a number of wrong choices before finally reaching the correct pot. When, that is to say, the right pot was segregated from the others in some way the bird could choose correctly, but when it merely formed one of a homogeneous series of identical objects correct choice became a matter of chance, with the odds heavily against the bird.

The importance of the relationship between the stimuli over the absolute stimulus itself was further emphasized in Köhler's experiments with hens. The hens were offered two stimuli, a medium and a dark grey, and they were

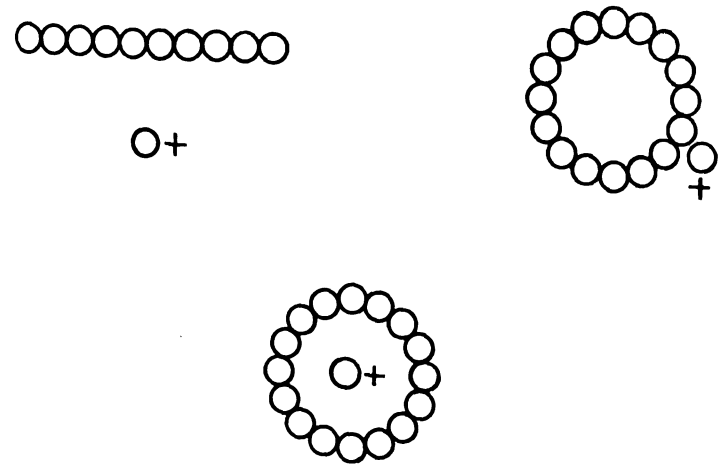

FIG. 16.

trained to choose the medium grey and to avoid the dark. The use of the dark stimulus was then abandoned and in its place was used a still lighter grey—one which bore a similar relationship to the medium grey as the medium grey had to the dark grey in the first part of the experiment. Now if the hens

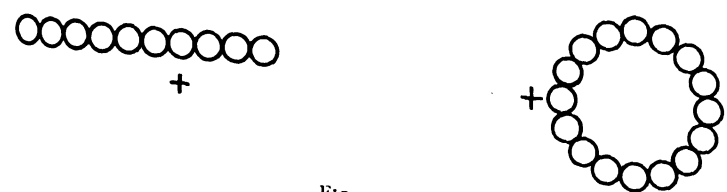

FIG. 17.

had learnt to react to an absolute stimulus, they would continue to react positively to the medium grey in the second part of the experiment. If, however, they had learnt to react to the relationship between the stimuli and to choose the lighter of the two greys, they would choose the light grey in the second part of the experiment. In the actual experiment it was found that the hens chose the light grey rather than the medium grey. The learning,

therefore, was a function more of the relationship between the sti
the absolute stimuli.

In more complex experiments the importance of the whole
even more clearly observable. In an experiment by Maier (27)
obtain food which could not be reached directly. This is shown

Point *A* was the starting-point, and *F* the position of the f
separated from *A* by a wire cage. *b*, *c*, *d* and *e* were points on th
led from the table to the food. *g*, *h*, *i*, *j* and *k* were any points
except *b*. The rat was first allowed to become familiar with a
except those lying on the maze. Consequently *b* was no more f
any of the other points *g*, *h*, *i*, *j* or *k*. The rat was then taugh

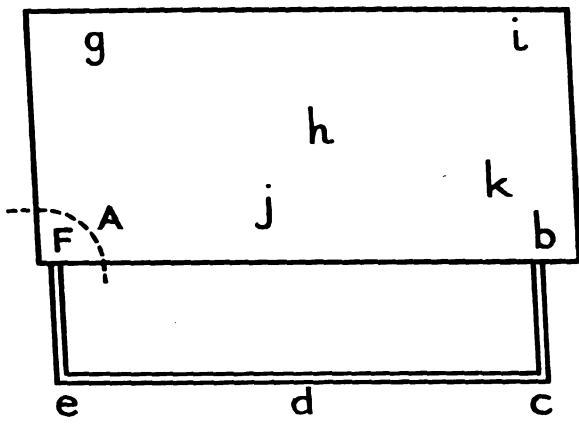

FIG. 18.

b to *F*. In the test which followed the rat was placed at *A*
food he had to follow the path *A*–*b*–*F*. He had, therefore, t
A–*b*. This could be done either by using the experience gain
learn *b*–*F*, that is to say by selecting the relation *A*–*b* rathe
or any other, or by wandering away from *A* until by chance he
a chain of associations would be set off, which would lead him
would be an intelligent type of solution, the second a solutio
error type, and if the second were used in learning the pr
untrained on the pathway *b*–*F* would be expected to go to t
soon as rats which knew the path. Maier's results, however,
was not so. For rats not familiar with *b*–*F* there was at firs
before leaving the starting-point, and the total time taken b
the point *b* was 103, 180 and 135 seconds. Rats which ha
trained on the *b*–*F* pathway, however, took only 25 and 15

therefore, was a function more of the relationship between the stimuli than of the absolute stimuli.

In more complex experiments the importance of the whole situation is even more clearly observable. In an experiment by Maier (27) rats had to obtain food which could not be reached directly. This is shown in Fig. 18.

Point *A* was the starting-point, and *F* the position of the food. *F* was separated from *A* by a wire cage. *b*, *c*, *d* and *e* were points on the maze which led from the table to the food. *g*, *h*, *i*, *j* and *k* were any points on the table except *b*. The rat was first allowed to become familiar with all the points except those lying on the maze. Consequently *b* was no more favoured than any of the other points *g*, *h*, *i*, *j* or *k*. The rat was then taught to go from

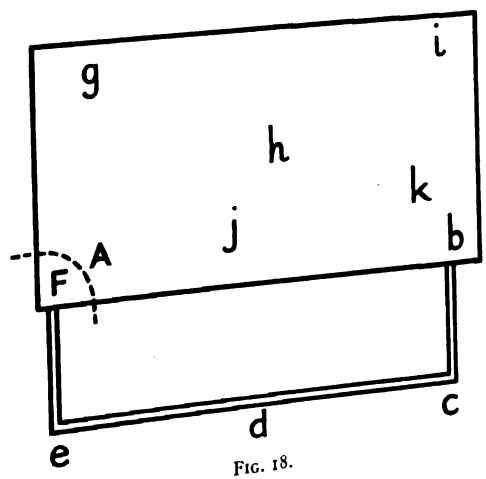

FIG. 18.

b to *F*. In the test which followed the rat was placed at *A*, and to get the food he had to follow the path *A*–*b*–*F*. He had, therefore, to fill in the gap *A*–*b*. This could be done either by using the experience gained previously to learn *b*–*F*, that is to say by selecting the relation *A*–*b* rather than *A*–*g*, *A*–*i* or any other, or by wandering away from *A* until by chance he came to *b*, when a chain of associations would be set off, which would lead him to *F*. The first would be an intelligent type of solution, the second a solution of the trial and error type, and if the second were used in learning the problem, then rats untrained on the pathway *b*–*F* would be expected to go to the point *b* just as soon as rats which knew the path. Maier's results, however, showed that this was not so. For rats not familiar with *b*–*F* there was at first great hesitancy before leaving the starting-point, and the total time taken before they reached the point *b* was 103, 180 and 135 seconds. Rats which had been previously trained on the *b*–*F* pathway, however, took only 25 and 15 seconds to reach

the point *b*. From this experiment, therefore, he concluded that the organization of the whole situation was the important thing in learning, and that point stimulation was of minor importance.

Probably the best known of the Gestalt experiments on learning were performed by Köhler on chimpanzees (28). Köhler showed that the solutions to problems tended to take place as a single, continuous occurrence, and not as a series of trial and error actions leading by chance to the correct result. When, for example, food was suspended out of the chimpanzees' reach, they did not rush about here and there until they finally hit upon the correct solution by chance; they tended to integrate their actions towards the final end of piling boxes on top of one another until they had made a structure of sufficient height for them to reach the food. All their behaviour was not, of course, always perfect in these circumstances: sometimes a box which wobbled slightly was not climbed upon though it formed a stable structure; sometimes one which hung over the edge of another was climbed upon, though it fell as soon as the chimpanzees' weight was on it; sometimes the most unstable structures were prevented from collapsing only by the agility of the chimpanzees in balancing; sometimes the chimpanzees tried to increase the height of the structure by turning one of the boxes on to its corner, and so on.

In another experiment food was placed outside the chimpanzees' cage and out of their reach. They were provided with two sticks, neither of which was long enough to reach the food, but if fitted together a sufficiently long tool was obtained. The solution to this problem came by what Köhler called "insight". The chimpanzee seemed suddenly to appreciate the relationship between joining the sticks together and getting food. Köhler therefore defined "insight" as "the appearance of a complete solution with reference to the whole lay-out of the field".

5. Experiments on Thinking.

When associationistic principles are applied to the processes of thinking, a "determining tendency" has to be assumed to explain why one association rather than another is selected. Thus, for instance, if one is presented with a card on which there is a figure 7 with a figure 3 below it, the most usual associations that have existed in the past will lead one to give as the answer 10, or 4, or 21. The "determining tendency" determines which of these associations will be strongest, and which answer will be given. Thus, if an individual has been given instructions to add, the determining tendency to add will strengthen the adding association relatively to the subtracting or multiplying association, so that the answer 10 will be given. If he has been given instructions to subtract, this determining tendency will strengthen the subtracting association relatively to the others, and the answer 4 will be given. One of the neatest demonstrations was that in which a subject was hypnotized and then given the suggestion that after he had woken up he would give the sum of the two digits

on the first card he would be shown and the difference between t
the second. He was then wakened up and shown a card on whi
digits 6/2, to which he immediately said " 8 " ; then he was sh
containing the digits 4/2 and he said " 2 ". He did not remember
tion, and it did not occur to him that 8 was the sum of 6 and 2, o
the difference between 4 and 2.

The concept of determining tendency, therefore, seemed to c
factory explanation of the processes of thinking on an associati
But the Gestalt psychologists criticize it on the ground that it offers
tion of solutions to *new* problems. Even if it exists as a factor in
selection of a particular association out of several that already
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arise in a new problem, for in a new problem there are no alr
associations in the subject's mind waiting to be appropriately s
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to determine.

The Gestalt experimenters, therefore, approached the prob
characteristic way. They concentrated on the organization of
as a whole. In one such experiment Maier (29) concerned him
appearance of the solution to a problem. The subjects were pre
problem to which there were several solutions, all but one of whi
obvious. When one was found the subject was asked to find a
experiment was carried out in a large room which contained
such as poles, ringstands, clamps, pliers, extension cords, tabl
Two cords were hung from the ceiling and were of such len
reached the floor. One hung near the wall and the other in the
room. The subject was told, " Your problem is to tie the end
strings together ". The subject soon learnt that if he held eith
hand he could not reach the other. He was then told he co
anything he wished in order to get the two cords tied together.

The different types of solution were (1) one cord was anchore
object, such as a chair, placed part of the way between the c
other cord was brought near it ; (2) one of the cords was len
the extension cord, for example—and the other was reached v
(3) while holding one cord, the other was pulled in with a pole
was tied to the cord hung from the centre of the room and
motion, thus making a pendulum ; the other cord was then br
centre, and the swinging cord caught as it approached the middl
the two cords.

If after ten minutes the subject had not found solution
suggestions were given : (*a*) The experimenter walked about th
passing the cord which hung from the centre of the room he
motion a few times. This was done without the subject k

on the first card he would be shown and the difference between the digits on the second. He was then wakened up and shown a card on which were the digits 6 2, to which he immediately said "8"; then he was shown a card containing the digits 4 2 and he said "2". He did not remember the suggestion, and it did not occur to him that 8 was the sum of 6 and 2, or that 2 was the difference between 4 and 2.

The concept of determining tendency, therefore, seemed to offer a satisfactory explanation of the processes of thinking on an associationistic basis. But the Gestalt psychologists criticize it on the ground that it offers no explanation of solutions to *new* problems. Even if it exists as a factor influencing the selection of a particular association out of several that already exist simultaneously in the subject's mind, it cannot enable a correct association to arise in a new problem, for in a new problem there are no already existing associations in the subject's mind waiting to be appropriately selected by a determining tendency. There is, in fact, nothing for the determining tendency to determine.

The Gestalt experimenters, therefore, approached the problem in their characteristic way. They concentrated on the organization of the problem as a whole. In one such experiment Maier (29) concerned himself with the appearance of the solution to a problem. The subjects were presented with a problem to which there were several solutions, all but one of which were quite obvious. When one was found the subject was asked to find another. The experiment was carried out in a large room which contained many objects such as poles, ringstands, clamps, pliers, extension cords, tables and chairs. Two cords were hung from the ceiling and were of such length that they reached the floor. One hung near the wall and the other in the centre of the room. The subject was told, "Your problem is to tie the ends of those two strings together". The subject soon learnt that if he held either cord in his hand he could not reach the other. He was then told he could use or do anything he wished in order to get the two cords tied together.

The different types of solution were (1) one cord was anchored with a large object, such as a chair, placed part of the way between the cords, while the other cord was brought near it; (2) one of the cords was lengthened—with the extension cord, for example—and the other was reached with the hand; (3) while holding one cord, the other was pulled in with a pole; (4) a weight was tied to the cord hung from the centre of the room and then put into motion, thus making a pendulum; the other cord was then brought near the centre, and the swinging cord caught as it approached the middle point between the two cords.

If after ten minutes the subject had not found solution 4, the following suggestions were given: (*a*) The experimenter walked about the room, and in passing the cord which hung from the centre of the room he put it in slight motion a few times. This was done without the subject knowing that a

suggestion was being given. (*b*) In case the first hint failed to bring about a solution within a few minutes, the subject was handed a pair of pliers and told, "With the aid of this and no other object there is another way of solving the problem".

If the second hint failed the first was repeated, and if this failed the subject was shown the solution.

Of the 61 subjects,

24 (39·3%) solved the problem without the aid of helps.
23 (37·7%) solved the problem after helps had been given.
14 (23%) failed to find the solution.

The second group is the only group considered here. It was found that the number of seconds which elapsed between the time that the effective hint was given and the appearance of the solution was very short, averaging 42 seconds. In 16 cases the solution appeared as a whole, that is to say, the idea of making a pendulum occurred to the subject; in 7 cases the idea of swinging the cord and the idea of attaching a weight appeared separately. But the interesting thing was that only one of the 16 subjects reported that the first hint had brought about the solution. The other 15 subjects did not mention the swaying of the cord, and four of them insisted that their solution did not depend on its swaying; in fact they denied having seen it.

After checking alternative hypotheses by further experiments Maier concluded that the first hint was not experienced because the sudden experience of the solution to the problem dominated consciousness and drove everything else out. This was also supported by the subjects' introspections. They said that when they experienced the knowledge of the solution there was a sudden change in the organization and in the meaning of the problem. The perception of the solution was rather like the sudden perception of a hidden figure in a puzzle picture. In both (*a*) the perception is sudden, (*b*) there is no conscious intermediate stage, and (*c*) the relationships of the elements in the final perceptions are different from those in the preceding stages.

In Harrower's experiments with jokes (30) the organization occurring in higher mental processes was also demonstrated. Harrower selected jokes as convenient entities because they stand out as units with unmistakable and characteristic boundaries. No one who has been told two jokes successively is likely to regard half of one joke as one unit and the other half of the same joke together with the whole of the second as another unit.

In the first place Harrower showed that jokes could be diagrammatized. She selected four jokes, for each of which she drew an approximate diagram, and then put this diagram with three arbitrary diagrams on to a card. The subjects were told the joke, shown the appropriate card, and then asked to select the drawing which seemed to them to approximate to this joke. There were ten subjects in this experiment, and by pure chance each diagram would be selected 2·5 times. The actual number of times that the intended diagram

was selected was always higher than this. This is shown in th
table :

Joke.	Chance.	Actual number of times selected.
1	2·5	3
2	2·5	4
3	2·5	7·5
4	2·5	7

To illustrate the method joke 4 is given below, together with t
which were shown to the subjects.

Joke 4.

The Employer: So you want a job, eh ? Do you ever tell lie
Sambo: No sir, but I kin learn.

The diagram intended to represent this joke was the followin

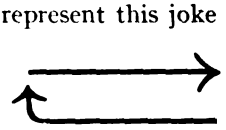

Fig. 19.

The card on which this diagram, together with three arbitr
was shown is given in Fig. 20.

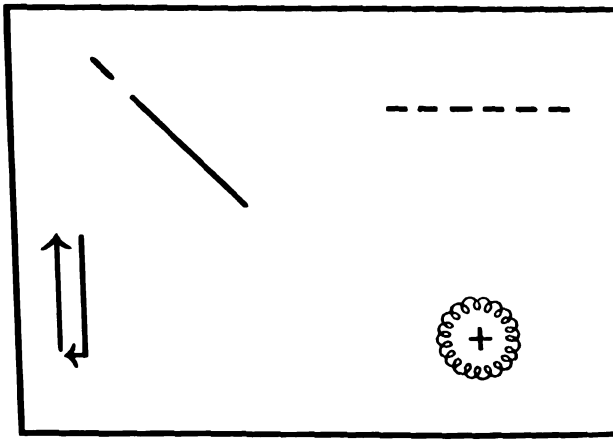

Fig. 20.

Having shown that joke structures could be diagramma
maintained that these joke structures possessed properties

2. Experiments on Perception.

The experiment that is regarded as the first to start the Gestalt psychologists on their crusade was on a phenomenon that is a familiar feature of present-day life, encountered most frequently in the cinema—the phenomenon of apparent motion. In watching a cinema film one knows—if one cares to think about it—that one is seeing a series of still photographs presented in quick succession. But one does not experience anything that corresponds with this type of physical stimulation; one experiences the perception of movement. In this phenomenon, therefore, as with the perception of the penny on the table, the experience radically differs from the physical impression. In Wertheimer's experiment (4) the subject was seated in a darkened room, and two points of light, separated from each other by a short distance, were successively exposed. When the most favourable distance of separation and the most favourable interval between the exposures of the two points had been discovered, the subject's experience was of the motion of a single point of light from one point to the other. Although there was no actual movement, the property of the whole situation was such that the subject thought that movement had taken place. This phenomenon was given the name of the "phi phenomenon" by Wertheimer in the hope that a neutral name would encourage a further unprejudiced examination of its origin and properties.

In extending the experiment a stage further it was observed that the subject's experience was the same both when the experiment was conducted in the manner already described, and also when a single point of light was used and actually made to travel from one position to the other. Subjectively the experience was the same in the two cases (provided, of course, that the speed of movement in the second case had been adjusted to correspond to the interval between the appearance of the points of light in the first), yet objectively the conditions were very different, for in the first case there was no stimulation of the intervening points on the retina, whereas in the second case there was. The same experience was obtained under two very different conditions of physical stimulation, and the Gestalt psychologists therefore put forward the explanation that the experience depended on certain properties of the whole situation rather than on the properties of point stimulation.

The same point was emphasized even more strongly in Köhler's "Figure 4" diagram (5), for in this case it could be demonstrated that an appeal to the effects of experience to explain the phenomenon was totally inadequate. Between the two big figures in the diagram (Fig. 1) there is a figure 4. It is difficult to see it because the two vertical strokes form part of the two big figures, and the horizontal stroke forms a part of the long horizontal line. The unity of the figure 4, therefore, is broken by the properties of the whole diagram, and it disappears from view because its parts are used to finish off or close

more dominant figures. The explanation is not simply due to the unfamiliarity of the diagram, to the fact that we have never before seen a figure 4 in that position, and that we overlook its presence in consequence; for a diagram

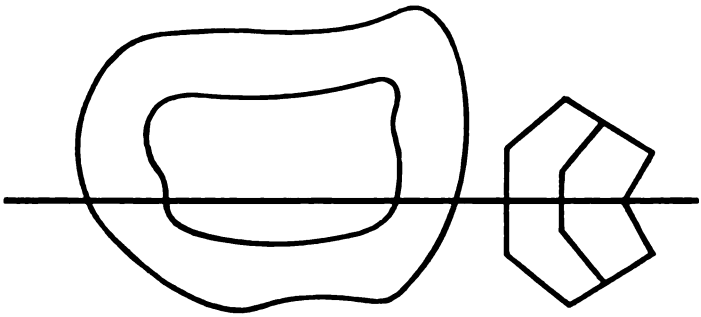

FIG. 1.—From Köhler, W., *Gestalt Psychology*, p. 155.

quite as unfamiliar may be constructed, such as that in Fig. 2, in which there can be no hesitation in recognizing the presence of the figure 4. Once again the properties of the whole diagram will determine the properties of its component parts.

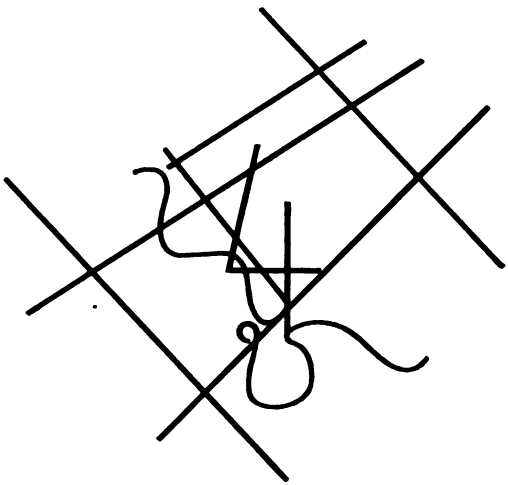

FIG. 2.—From Köhler, W., *Gestalt Psychology*, p. 162.

On this basis the Gestalt psychologists have analysed some of the features in the structure of objects which will influence their organization and the way they are perceived (6).

(a) *Grouping*.—One of the most important of the features determining the organization of objects in perception is grouping. In any perceptual situation

certain things are grouped together and differentiated from others. This is one of the difficulties of performing experiments on what is called the " span of attention ". If it is desired to know how many objects an individual can correctly perceive at a single glance, the simplest thing would appear to be to present him with a series of cards on which are drawn an increasing number of objects, until he fails to name the correct number. This is, in fact, what the early experimenters did, and when experiments of this kind have been performed it has been found that the largest number of discrete objects that can be correctly estimated is about seven. But one of the difficulties in experiments of this kind is to arrange the objects in such a way that they do not form

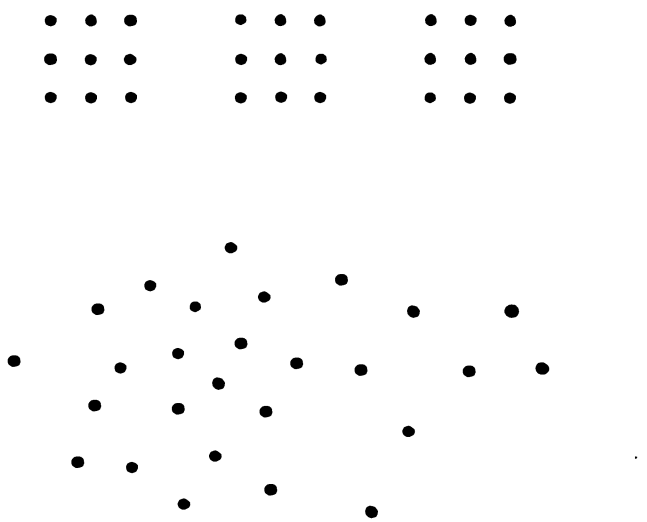

FIG. 3.

groups. If a large number of objects can be grouped together easily it is much easier to estimate correctly the number present than when they form discrete and ungroupable entities. It is, for example, much easier to perceive the first arrangement of dots in Fig. 3 as 27 than it is to perceive the second arrangement as the same number. This tendency towards grouping appears in almost every case, and even the second arrangement, if looked at for a sufficient length of time, will tend to form itself into a few groups of a few dots each.

(b) *Nearness.*—The same tendency to group objects together is shown in Köhler's example (7) illustrated in Fig. 4. This is seen as two groups of three blots each, not as three groups of two nor as six separate patches. In this case the relative nearness of some of the patches to one another compared with their distance from others is probably the reason for the particular type of organization that ensues. In other cases, however, other factors may be shown to be stronger than nearness.

(c) *Similarity.*—In the example given in Fig. 5, for example, the dots are nearer to the circles than they are to one another; yet the first pattern is seen as horizontal rows rather than as vertical columns, while the second is seen as vertical columns rather than as horizontal rows.

(d) *Symmetry.*—A fourth factor causing grouping is symmetry. Bahnsen (8) exposed the figures shown in Fig. 6 to sixty-four people. The first can be

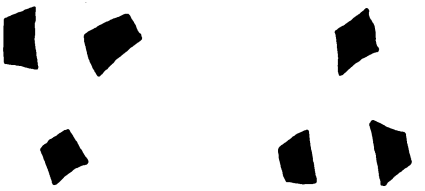

FIG. 4.—From Köhler, W., *Gestalt Psychology*, p. 118.

seen as black symmetrical or white unsymmetrical stripes; the second as white symmetrical or black unsymmetrical stripes. He found that in 89% of the cases the symmetrical stripes were reported, and in only one case was the unsymmetrical reported. The other cases were unstable and ambiguous.

(e) *Closure.*—Another factor is closure. The six equidistant lines in Fig. 7 tend at first sight to be seen as six discrete units. There is no immediate tendency to rearrange them in groups in any special way. If, however, a small horizontal line is added at the top and bottom of each the result is quite

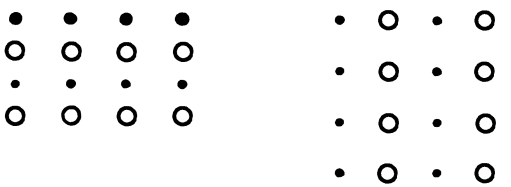

FIG. 5.

different, and, as can be seen in Fig. 8, they at once form themselves into three groups composed of two vertical lines each. The effect of the small horizontal lines is to close the figures, and it is of such strength that whereas in Fig. 7 the lines *a*, *b*, *c*, *d*, *e* and *f* looked equidistant, yet in Fig. 8 the line *b* looks nearer to *a* than to *c*, and similarly with the remaining lines.

The Gestalt psychologists suggest that the factor of closure may be part of the explanation of the Müller-Lyer illusion. Although the lines *ab* and *cd* in Fig. 9 are equal, the arrow-heads in the first figure cause a partial closure of that figure, with the result that the distance *ab* looks shorter than it actually is. With *cd*, however, there is no tendency to closure.

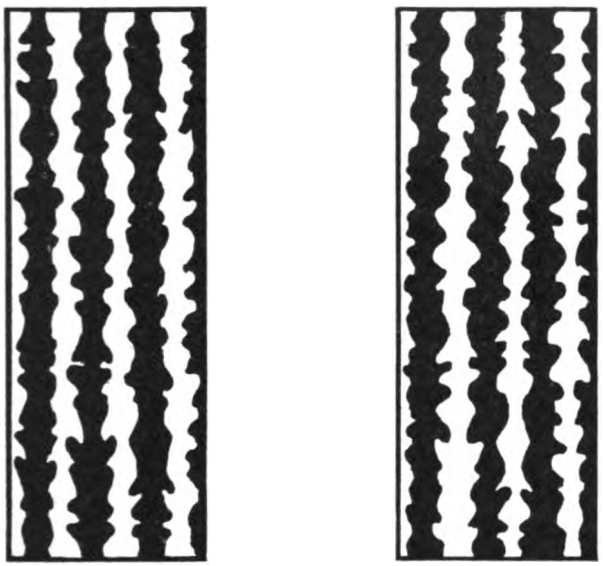

FIG. 6.—From Koffka, after Bahnsen.

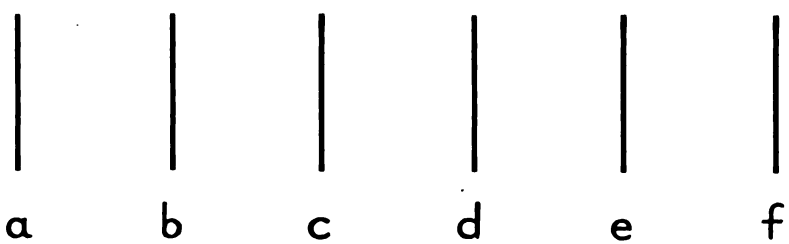

FIG. 7.

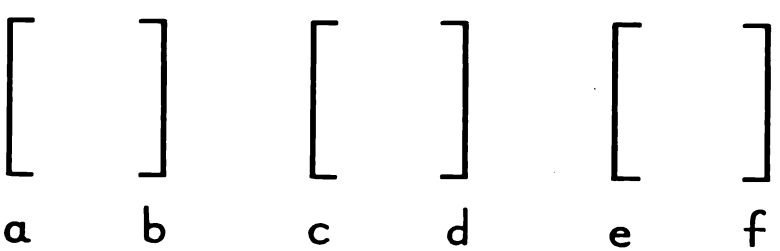

FIG. 8.

(f) *Good continuation.*—The factor of closure is closely related to the factor known as good continuation. This has been illustrated in Köhler's fig. 4 diagram, and there are many other examples as well. It is easier, for example,

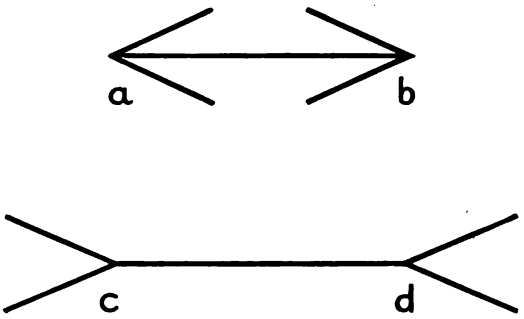

FIG. 9.—The Müller-Lyer illusion.

to see Fig. 10 as made out of a straight line and an "S" curve than as made out of the hook and crook designs of Fig. 11. The crook on the right in Fig. 10 appears to be an essential part of the curve on its left; it forms a unity with it, and it loses its continuation with the straight line. This is the art of camouflage: first to break up the unity of a particular object, and then to make

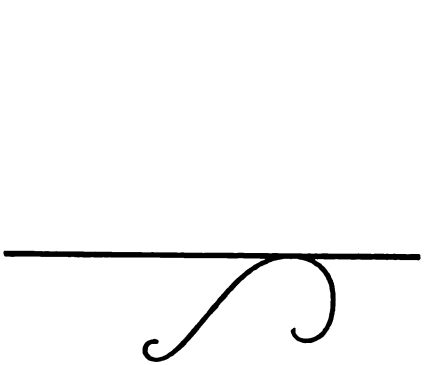

FIG. 10.

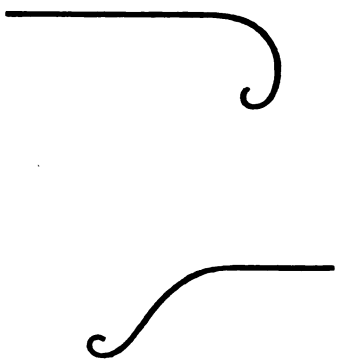

FIG. 11.

its parts form essential portions of some other object. Thus it can be made to lose its identity. This is also the art of the puzzle-picture deviser, and it is one reason for the effectiveness of protective coloration in animals, the animal being assimilated into its background and apparently forming an essential part of it.

(g) *The "figure-ground" phenomenon.*—Such considerations influenced the Gestalt psychologists in developing their theory and their experimental

work on the basis of the " figure-ground " phenomenon expounded by Rubin (9). In Fig. 12 one sees a small square standing out from a background of enclosing white space. But if the size of the square is increased beyond a

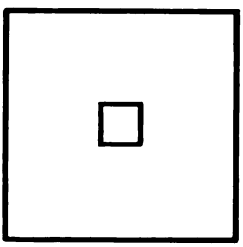

FIG. 12.

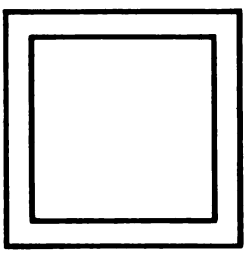

FIG. 13.

certain point the character of the perception changes and one sees, as in Fig. 13, a double square standing out as the figure with the enclosed white space as background. The enclosed white space was figure and is now ground, and instead of standing out in front of the background it now appears to lie behind the figure. In general the same phenomenon is encountered : figures appear to stand out in front of grounds, and grounds appear to lie behind figures. As in

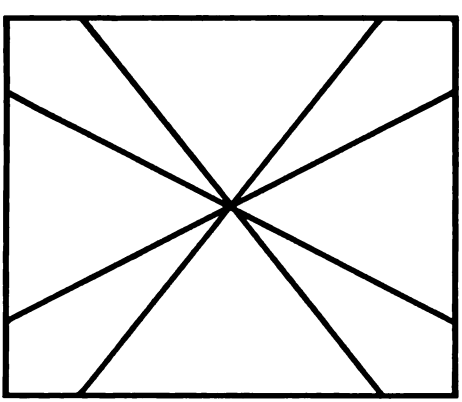

FIG. 14.—The Maltese-cross-propeller reversible figure.

the Müller-Lyer illusion, the structure of the whole alters the apparent relationships of the parts.

(h) *Reversible figures.*—The shifting relationships of figure and ground are seen, too, in reversible figures, e. g., the propeller-Maltese-cross phenomenon illustrated in Fig. 14. Sometimes the propeller is seen as figure, sometimes the Maltese cross. When the propeller is seen as figure it stands out and the

remainder recedes into the background. When the Maltese cross is seen as figure the rest recedes. The whole appearance alters as perception alternates. This again shows, according to the Gestalt psychologists, that perception itself must depend on the organization of the whole. The actual points on the retina being stimulated are the same in both cases, yet the subjective experience is quite different. The perception must depend, therefore, not only on the stimulation of particular points of the retina, but also on the organization of the whole and the relationship between its component parts. This organization is sometimes subjective, as when one alternates the perceptions in a reversible figure at will, but at other times it depends on the inherent properties of the figure itself. Thus Kopfermann (10) has shown that even parallax may be overcome, and an actual tridimensional object seen as a plane figure when certain forms which favour bi-dimensional organization are used. A simple

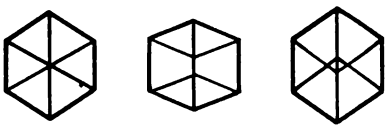

FIG. 15.

illustration of this is in the three diagrams shown in Fig. 15. No. 1 tends to be seen as a plane figure, No. 3 as a tri-dimensional cube, and No. 2 as either a plane or as a tri-dimensional figure.

Auditory Perception.

The predominance of the whole over its parts is also demonstrated in auditory perception. A particular melody may be heard at different times played on a piano, whistled in the street by an errand-boy, played on a tin whistle, or played by a full orchestra in a concert hall. In each case we may have heard it in a different key with different overtones and different individual notes. Yet it is recognizable as the same melody. Perhaps, too, as the errand-boy whistled it in the street the sound of a motor horn intruded at a certain point. Yet when we hum the melody over to ourselves afterwards the sound of the motor horn—though it may be remembered—does not form a part of the melody. The point stimulation—the individual character of each note—therefore is of minor importance compared with the characteristics of the whole melody, and it is the organization of the whole, influencing as it does the relationship between its component parts, which enables us to recognize the melody as the same even when it is presented under very different conditions.

3. Physical Gestalten.

Having demonstrated in their experiments on perception that the properties of the whole determined the relationship between its parts rather than the reverse, the Gestalt psychologists proceeded to turn the tables on the behaviourists, and to show that the same thing was generally true in the physical world as well.

The behaviourists regarded the physical world somewhat mechanistically. They were impressed by the quantitative aspects of physics and chemistry, and, consciously or otherwise, it was their aim to make psychology as like their conception of the other sciences as possible. It appeared to them to be a reasonable assumption that if in the physical world complex phenomena were no more than the additive functions of elementary processes, the same should be true in psychology also. Their position is expressed by Watson (11):

"We use the term *stimulus* in psychology as it is used in physiology. Only in psychology we have to extend somewhat the usage of the term. In the psychological laboratory, when we are dealing with relatively simple factors, such as the effect of ether waves of different lengths, the effect of sound-waves, etc., and are attempting to isolate their effects upon the adjustment of men, we speak of stimuli. On the other hand, when factors leading to reactions are more complex, as, for example, in the social world, we speak of *situations*. A situation is, of course, upon final analysis, resolvable into a complex group of stimuli. As examples of stimuli we may name such things as rays of light of different wave-lengths; sound-waves differing in amplitude, length, phase and combination; gaseous particles given off in such small diameters that they affect the membrane of the nose; solutions which contain particles of matter of such size that the taste buds are thrown into action; solid objects which affect the skin and mucous membrane; radiant stimuli which call out temperature response; noxious stimuli, such as cutting, pricking, and those injuring tissue generally. Finally, movements of the muscles and activity in the glands themselves serve as stimuli by acting upon the afferent nerve-endings in the moving muscles."

The Gestalt psychologists, however, approached the problem from the other end. Being first of all impressed by the predominance of the whole situation over its parts, illustrated in their experiments on perception, they then proceeded to look about the physical world to see whether the same phenomenon was observed there. And they came to the conclusion that it was:

"Let us take the simplest example we can find: water is explained by the atomic theory as a compound of two elements, hydrogen and oxygen, in such a way that it consists of molecules, each of which is composed of three atoms, two of hydrogen and one of oxygen. Moreover, hydrogen occurs in nature in a form in which it is not composed of hydrogen atoms, but of hydrogen

molecules, each composed of two hydrogen atoms. Thus we have H, H_2, H_2O. This sounds like a straight molecular theory, but it is not anything of the kind. For H, H_2, and H_2O have all different properties which cannot be derived by *adding* properties of H's and O's." (12).

The predominance of the whole over the parts is also illustrated by statistical systems of the reversible reaction type in chemistry :

" When it is heated to a high temperature phosphorus pentachloride splits up into the trichloride and chlorine. At the same temperature the latter two substances also combine to form the pentachloride. At any given high temperature there is a certain percentage of the pentachloride left undissociated at any moment. At 200° 51·5% of the pentachloride is left, the remainder having split up. At 250° these proportions are 20% and 80%, and so on. But this does not mean that at these temperatures 51·5% of the pentachloride molecules are permanently united. The whole system is in a state of flux; at any moment, for example, an individual atom of chlorine may be free, while at the next moment it may form part of a pentachloride molecule. But at any given temperature there are always in the aggregate approximately so many trichloride molecules and so on. Thus a specific number of such molecules at a given temperature will exhibit a constancy which essentially involves change of individual elements, but which is nevertheless none the less real. Let us say that such a chemical system is, in an elementary way, so organized that there will always be present in the average a certain specific number of pentachloride molecules. This conserved group will be composed of different molecules from time to time ; but there will always be present such a group, as long as the system persists." (13)

Another example is the buffer solution also cited by Humphrey (14) :

" ' We take a solution of 1 kg. of sodium bicarbonate in 100 litres of water and allow it to attain equilibrium with an unlimited atmosphere containing one gramme of carbon dioxide per litre. Let hydrochloric acid be added in small portions at a time, constantly shaking the solution so that there shall always be equilibrium with the carbon dioxide in the gas phase.' . . . When this is done a characteristic thing happens. The hydrochloric acid reacts with the sodium bicarbonate, with the formation of sodium chloride and the liberation of carbon dioxide. This cannot be retained in the solution, for the carbon dioxide there is already in equilibrium with that in the ' atmosphere '. Consequently the newly liberated carbon dioxide escapes from the liquid, and the acidity remains what it was before, the only effect being a diminished concentration of the alkaline salt. When, however, all the bicarbonate is neutralized, this ' buffer ' effect ceases to operate. At this stage the addition of two grammes of hydrochloric acid ' causes nearly as much rise in acidity as the previous 318 grammes had done, or about two hundred times the rise caused by a hundred times the amount at the first stage of the experiment'. . . . Considering the system comprising the solution and the atmosphere it may be said to be so constituted that by means of compensatory systemic changes a certain constancy is preserved in spite of change of conditions such as would, without special organization, greatly alter conditions. In respect of alkalinity or acidity the system is, within limits, relatively self-preserving."

A dynamic system such as a pendulum also possesses properties depending on the whole system. It is the organization of the individual molecular forces into a whole in the pendular system that gives the system its peculiar properties, and these properties were discovered quite independently of the knowledge of its atomic or molecular properties, of which we have still only hazy ideas, though we know with considerable exactitude the properties of the pendulum itself.

Köhler discusses the properties of physical Gestalten at considerable length and detail in his book (15). In one example he shows that a charge of static electricity will distribute itself as a whole over the surface of a spherical conductor. If, then, the charge of electricity is increased or diminished at any one point the charge in the system as a whole will be affected, not merely the charge at that point.

Such processes have certain maximum-minimum properties, that is to say, "a given parameter of these processes has not just any magnitude but the smallest or the greatest possible" (16). Thus a soap-bubble adopts a spherical shape because a sphere has the greatest possible volume for a given surface—or the smallest possible surface for a given volume. Similarly, too, if one pricks the inside of a loop of thread of irregular shape thrown onto a soap film, that part of the soap film disappears and the thread immediately adopts a circular shape. Here again the region enclosed by the thread will have the largest possible area and the remaining film will have the smallest possible area.

In simple conditions, therefore, stationary systems tend to possess the greatest possible regularity, symmetry and simplicity. But when the conditions are more complex they lose some of this simplicity. Thus if a drop of water is suspended in a medium of equal density it will become a perfect sphere; if it lies on a table-top it becomes slightly flattened; if it falls from the table through the air it becomes pear-shaped. Here again, however, it follows maximum-minimum principles, for it will offer the least possible resistance in its new shape to the air through which it is falling.

The observation that physical systems tend to adopt the most favourable form to meet the surrounding circumstances was at once applied to psychological systems. This *Law of Prägnanz*, formulated by Wertheimer, was that psychological organization is always as "good" as the prevailing conditions allow. The term "good" was undefined, but it included such properties as regularity, symmetry, simplicity, and others already mentioned in the preceding section on perception.

The importance of this contribution was that it implied a correspondence between physical and psychological processes, and this idea was developed into what the Gestalt psychologists call the "*Principle of Isomorphism*"—that the properties of physical processes are the same as those of the conscious processes which they are supposed to underlie. In Köhler's words, "Any actual

consciousness is in every case not only blindly coupled to its corresponding psycho-physical processes, but is akin to it in essential structural properties". If one thing is experienced as being "between" two others, this is accompanied by a functional "between" in the concrete dynamic context of concurrent physiological events. If one thing is experienced as "belonging to" another, there corresponds a dynamical unit or whole in the underlying physiological processes.

The Gestalt psychologists attach much importance to this difficult hypothesis. If true, it provides them with a unity between organic and inorganic processes which the behaviourists had assumed. But it is a unity of a very different order.

4. Experiments on Learning.

The associationistic theory of the nature of learning, which the Gestalt psychologists set out to refute, had a twofold basis. In the first place there were the conditioned reflex experiments of Pavlov (17). As a result of these there had been developed a theory of the fine localization of reflexes in the cortex:

"It becomes obvious . . . that through the medium of the cerebral cortex a great number of environmental changes establish now positive, now negative conditioned reflexes and determine in this manner the different effector activities of the animal organism, and its everyday behaviour. All these conditioned reflexes must have definite representation in the cerebral cortex in one or another definite group of cells. One such group of cells must be connected with one definite activity of the organism, another group with another activity; one group may determine a positive activity while another may inhibit an activity. The cerebral cortex can accordingly be represented as an exceedingly rich mosaic, or as an extremely complicated 'switchboard'. However, in spite of its extreme complexity as a switchboard there are always large spaces reserved for the development of new connections. Moreover points which are already involved in a definite conditioned activity frequently change their physiological role and become connected with some other activity of the animal" (18).

It fell to a behaviourist, however, to refute this position. Lashley (19) performed a series of experiments in which rats were taught and re-taught mazes and puzzle boxes. He compared groups of normal rats with groups of rats which had had different amounts of their cortexes destroyed by thermo-cautery. His main findings showed that the capacity to learn the maze depended on the *amount* of cortex that the animal possessed. The ability to learn decreased proportionately with the amount of destruction of the cortex, and *independently of the locus of the destruction.* He found that the maze habit formed before operation was disturbed by operations to *any* part of the cortex, and the amount of reduction of efficiency of performance was proportional to the extent of the injury and independent of the locus. From these experiments he concluded (1) that the learning and retention of the habits were

not dependent on finely localized structures, and (2) that the contribution of different parts of a specialized area, or of the whole cortex in the cases of non-localized functions, was qualitatively the same. His conclusions therefore argue against a fine localization of behaviour patterns in the cortex.

Furthermore, the conditioned reflex experiments were performed under highly artificial conditions, all extraneous sounds, sights and smells being excluded by means of a sound-proof room, and the dog being fixed in an uncomfortable position on a table for long periods of time. There is no obvious justification, therefore, for applying any results obtained in such circumstances to the complex conditions of ordinary life. And even when the technique of the conditioned reflex experiments has been repeated, a different type of learning from that described by Pavlov may sometimes be shown to occur (20).

The other line of support for the associationistic theory came from what is known as " trial and error " learning. It is on this branch that the Gestalt psychologists have directed most of their fire. As a result of his experiments on animals in puzzle boxes, Thorndike (21) formulated two associationistic laws which he thought would be sufficient to explain the phenomena of learning. These two laws are known as the " Law of Exercise (or Frequency) " and the " Law of Effect ".

The law of frequency is that " any response to a situation will, other things being equal, be more strongly connected with the situation in proportion to the number of times it has been connected with that situation and to the average vigour and duration of the connections ".

The law of effect is that " of several responses made to the same situation those which are accompanied or closely followed by satisfaction to the animal will, other things being equal, be more firmly connected with the situation so that when it recurs they will be more likely to recur ", and that those which are accompanied or closely followed by dissatisfaction to the animal will tend to be dropped out. Thorndike has recently reviewed his opinion in regard to dissatisfaction. He now holds that dissatisfaction may have a strengthening effect (22).

The Gestalt psychologists, however, are not satisfied that the phenomena of learning can be adequately explained by these laws (23). They criticize the law of effect on many grounds, e.g., (1) that an animal does not make exactly the same movements every time it releases the catch of the puzzle box to obtain food; sometimes it may open it with its paw, sometimes with its nose, sometimes with its teeth, and so on. There is no single response, therefore, to be stamped in in association with the pleasurable after-effects. (2) An animal may make many movements between the act which releases the catch and the act which gets it the food. On a strict interpretation of the associationistic theory these acts should be stamped in just as strongly as the act of releasing the catch. Yet what the animal learns is to release the catch, not to perform the other movements which were more closely followed by the reward. This

is most clearly illustrated in the fact that the animal gets its immediate satisfaction from chewing the food. Yet when put in the puzzle-box situation on a subsequent occasion it does not sit still and make chewing movements, it releases the catch.

Many criticisms have been levelled, too, against the law of frequency. They are based on the fact that the frequent occurrence of a particular act in a given situation does not necessarily imply that the act will occur again when the same situation recurs. A simple example is when an animal is in a very elementary T-shaped maze in which there is only one choice, a choice to the right, say, which is correct and leads to food, and a choice to the left which is incorrect and leads only to a blind alley. In such a maze an animal can make the right choice only *once* in any given trial, for as soon as it has made the right choice it gets the reward and the trial is at an end. But it may make the wrong choice a number of times in any one trial: it may go to the left, find the blind alley, return to the starting-point, return to the junction, turn again to the left, and so on. In any series of trials the probability is that the wrong choice will be made more frequently than the right one, and yet the animal eventually learns the problem and makes no further mistakes. The same argument may be used with greater validity where the maze has many blind alleys.

The law of frequency has been further examined from an experimental point of view, and has been found to be an insufficient explanation of what takes place in learning (24). It has even been shown (25) that when a wrong response has been very frequently performed by a subject who knows it is a wrong response, the effect is to stamp out that response rather than to stamp it in.

The associationistic theory proving an insufficient explanation of the way that learning takes place, the Gestalt psychologists approached the matter from their usual viewpoint. Again it was their object to emphasize the greater importance of the properties of the whole situation rather than those of the individual stimuli within it. Thus when Hertz (26) hid food under one of a number of similar flower-pots, the jay which observed this procedure was able to fly straight to the correct pot when it was arranged in such a way as to stand out from the others. If the pots were arranged in the form of a circle or a straight line with the correct pot outside or inside the circle, or to one side of the straight line (see Fig. 16), the bird chose the correct one without hesitation. When, however, the correct pot formed part of the circle or straight line itself (as shown in Fig. 17), the bird made a number of wrong choices before finally reaching the correct pot. When, that is to say, the right pot was segregated from the others in some way the bird could choose correctly, but when it merely formed one of a homogeneous series of identical objects a correct choice became a matter of chance, with the odds heavily against the bird.

The importance of the relationship between the stimuli over the absolute stimulus itself was further emphasized in Köhler's experiments with hens. The hens were offered two stimuli, a medium and a dark grey, and they were

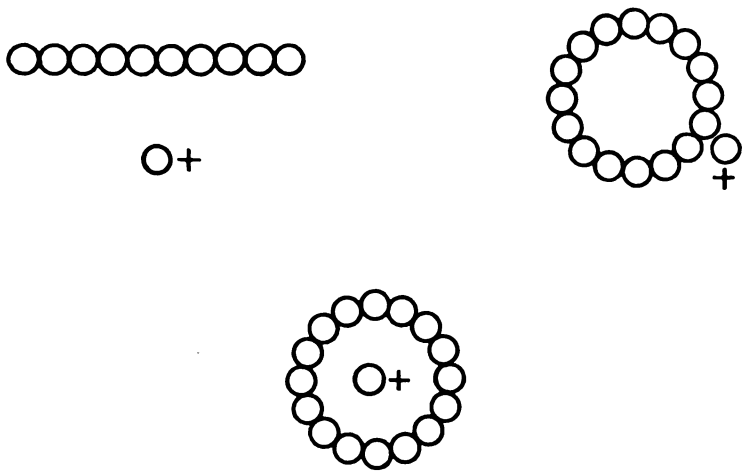

Fig. 16.

trained to choose the medium grey and to avoid the dark. The use of the dark stimulus was then abandoned and in its place was used a still lighter grey—one which bore a similar relationship to the medium grey as the medium grey had to the dark grey in the first part of the experiment. Now if the hens

Fig. 17.

had learnt to react to an absolute stimulus, they would continue to react positively to the medium grey in the second part of the experiment. If, however, they had learnt to react to the relationship between the stimuli and to choose the lighter of the two greys, they would choose the light grey in the second part of the experiment. In the actual experiment it was found that the hens chose the light grey rather than the medium grey. The learning,

therefore, was a function more of the relationship between the stimuli than of the absolute stimuli.

In more complex experiments the importance of the whole situation is even more clearly observable. In an experiment by Maier (27) rats had to obtain food which could not be reached directly. This is shown in Fig. 18.

Point *A* was the starting-point, and *F* the position of the food. *F* was separated from *A* by a wire cage. *b*, *c*, *d* and *e* were points on the maze which led from the table to the food. *g*, *h*, *i*, *j* and *k* were any points on the table except *b*. The rat was first allowed to become familiar with all the points except those lying on the maze. Consequently *b* was no more favoured than any of the other points *g*, *h*, *i*, *j* or *k*. The rat was then taught to go from

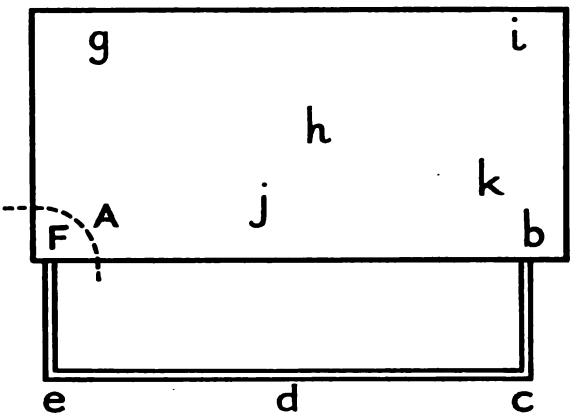

FIG. 18.

b to *F*. In the test which followed the rat was placed at *A*, and to get the food he had to follow the path *A*–*b*–*F*. He had, therefore, to fill in the gap *A*–*b*. This could be done either by using the experience gained previously to learn *b*–*F*, that is to say by selecting the relation *A*–*b* rather than *A*–*g*, *A*–*h* or any other, or by wandering away from *A* until by chance he came to *b*, where a chain of associations would be set off, which would lead him to *F*. The first would be an intelligent type of solution, the second a solution of the trial and error type, and if the second were used in learning the problem, then rats untrained on the pathway *b*–*F* would be expected to go to the point *b* just as soon as rats which knew the path. Maier's results, however, showed that this was not so. For rats not familiar with *b*–*F* there was at first great hesitancy before leaving the starting-point, and the total time taken before they reached the point *b* was 103, 180 and 135 seconds. Rats which had been previously trained on the *b*–*F* pathway, however, took only 25 and 15 seconds to reach

the point *b*. From this experiment, therefore, he concluded that the organization of the whole situation was the important thing in learning, and that point stimulation was of minor importance.

Probably the best known of the Gestalt experiments on learning were performed by Köhler on chimpanzees (28). Köhler showed that the solutions to problems tended to take place as a single, continuous occurrence, and not as a series of trial and error actions leading by chance to the correct result. When, for example, food was suspended out of the chimpanzees' reach, they did not rush about here and there until they finally hit upon the correct solution by chance; they tended to integrate their actions towards the final end of piling boxes on top of one another until they had made a structure of sufficient height for them to reach the food. All their behaviour was not, of course, always perfect in these circumstances: sometimes a box which wobbled slightly was not climbed upon though it formed a stable structure; sometimes one which hung over the edge of another was climbed upon, though it fell as soon as the chimpanzees' weight was on it; sometimes the most unstable structures were prevented from collapsing only by the agility of the chimpanzees in balancing; sometimes the chimpanzees tried to increase the height of the structure by turning one of the boxes on to its corner, and so on.

In another experiment food was placed outside the chimpanzees' cage and out of their reach. They were provided with two sticks, neither of which was long enough to reach the food, but if fitted together a sufficiently long tool was obtained. The solution to this problem came by what Köhler called "insight". The chimpanzee seemed suddenly to appreciate the relationship between joining the sticks together and getting food. Köhler therefore defined "insight" as "the appearance of a complete solution with reference to the whole lay-out of the field".

5. Experiments on Thinking.

When associationistic principles are applied to the processes of thinking, a "determining tendency" has to be assumed to explain why one association rather than another is selected. Thus, for instance, if one is presented with a card on which there is a figure 7 with a figure 3 below it, the most usual associations that have existed in the past will lead one to give as the answer 10, or 4, or 21. The "determining tendency" determines which of these associations will be strongest, and which answer will be given. Thus, if an individual has been given instructions to add, the determining tendency to add will strengthen the adding association relatively to the subtracting or multiplying association, so that the answer 10 will be given. If he has been given instructions to subtract, this determining tendency will strengthen the subtracting association relatively to the others, and the answer 4 will be given. One of the neatest demonstrations was that in which a subject was hypnotized and then given the suggestion that after he had woken up he would give the sum of the two digits

on the first card he would be shown and the difference between the digits on the second. He was then wakened up and shown a card on which were the digits 6/2, to which he immediately said "8"; then he was shown a card containing the digits 4/2 and he said "2". He did not remember the suggestion, and it did not occur to him that 8 was the sum of 6 and 2, or that 2 was the difference between 4 and 2.

The concept of determining tendency, therefore, seemed to offer a satisfactory explanation of the processes of thinking on an associationistic basis. But the Gestalt psychologists criticize it on the ground that it offers no explanation of solutions to *new* problems. Even if it exists as a factor influencing the selection of a particular association out of several that already exist simultaneously in the subject's mind, it cannot enable a correct association to arise in a new problem, for in a new problem there are no already existing associations in the subject's mind waiting to be appropriately selected by a determining tendency. There is, in fact, nothing for the determining tendency to determine.

The Gestalt experimenters, therefore, approached the problem in their characteristic way. They concentrated on the organization of the problem as a whole. In one such experiment Maier (29) concerned himself with the appearance of the solution to a problem. The subjects were presented with a problem to which there were several solutions, all but one of which were quite obvious. When one was found the subject was asked to find another. The experiment was carried out in a large room which contained many objects, such as poles, ringstands, clamps, pliers, extension cords, tables and chairs. Two cords were hung from the ceiling and were of such length that they reached the floor. One hung near the wall and the other in the centre of the room. The subject was told, "Your problem is to tie the ends of those two strings together". The subject soon learnt that if he held either cord in his hand he could not reach the other. He was then told he could use or do anything he wished in order to get the two cords tied together.

The different types of solution were (1) one cord was anchored with a large object, such as a chair, placed part of the way between the cords, while the other cord was brought near it; (2) one of the cords was lengthened—with the extension cord, for example—and the other was reached with the hand; (3) while holding one cord, the other was pulled in with a pole; (4) a weight was tied to the cord hung from the centre of the room and then put into motion, thus making a pendulum; the other cord was then brought near the centre, and the swinging cord caught as it approached the middle point between the two cords.

If after ten minutes the subject had not found solution 4, the following suggestions were given: (*a*) The experimenter walked about the room, and in passing the cord which hung from the centre of the room he put it in slight motion a few times. This was done without the subject knowing that a

suggestion was being given. (*b*) In case the first hint failed to bring about a solution within a few minutes, the subject was handed a pair of pliers and told, " With the aid of this and no other object there is another way of solving the problem ".

If the second hint failed the first was repeated, and if this failed the subject was shown the solution.

Of the 61 subjects,

24 (39·3%) solved the problem without the aid of helps.
23 (37·7%) solved the problem after helps had been given.
14 (23%) failed to find the solution.

The second group is the only group considered here. It was found that the number of seconds which elapsed between the time that the effective hint was given and the appearance of the solution was very short, averaging 42 seconds. In 16 cases the solution appeared as a whole, that is to say, the idea of making a pendulum occurred to the subject ; in 7 cases the idea of swinging the cord and the idea of attaching a weight appeared separately. But the interesting thing was that only one of the 16 subjects reported that the first hint had brought about the solution. The other 15 subjects did not mention the swaying of the cord, and four of them insisted that their solution did not depend on its swaying ; in fact they denied having seen it.

After checking alternative hypotheses by further experiments Maier concluded that the first hint was not experienced because the sudden experience of the solution to the problem dominated consciousness and drove everything else out. This was also supported by the subjects' introspections. They said that when they experienced the knowledge of the solution there was a sudden change in the organization and in the meaning of the problem. The perception of the solution was rather like the sudden perception of a hidden figure in a puzzle picture. In both (*a*) the perception is sudden, (*b*) there is no conscious intermediate stage, and (*c*) the relationships of the elements in the final perceptions are different from those in the preceding stages.

In Harrower's experiments with jokes (30) the organization occurring in higher mental processes was also demonstrated. Harrower selected jokes as convenient entities because they stand out as units with unmistakable and characteristic boundaries. No one who has been told two jokes successively is likely to regard half of one joke as one unit and the other half of the same joke together with the whole of the second as another unit.

In the first place Harrower showed that jokes could be diagrammatized. She selected four jokes, for each of which she drew an approximate diagram, and then put this diagram with three arbitrary diagrams on to a card. The subjects were told the joke, shown the appropriate card, and then asked to select the drawing which seemed to them to approximate to this joke. There were ten subjects in this experiment, and by pure chance each diagram would be selected 2·5 times. The actual number of times that the intended diagram

was selected was always higher than this. This is shown in the following table :

Joke.	Chance.	Actual number of times selected.
1	2·5	3
2	2·5	4
3	2·5	7·5
4	2·5	7

To illustrate the method joke 4 is given below, together with the diagrams which were shown to the subjects.

Joke 4.

The Employer: So you want a job, eh ? Do you ever tell lies ?
Sambo: No sir, but I kin learn.

The diagram intended to represent this joke was the following :

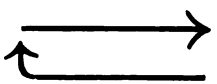

FIG. 19.

The card on which this diagram, together with three arbitrary diagrams, was shown is given in Fig. 20.

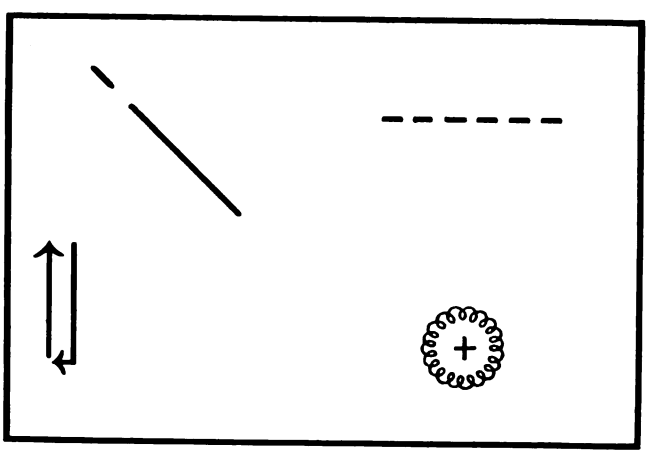

FIG. 20.

Having shown that joke structures could be diagrammatized, Harrower maintained that these joke structures possessed properties similar to those

found in perception. For example, they possessed a tendency to closure—a closure which was very seldom arbitrary. The type of closure seemed to depend on the intrinsic properties of the structure itself. This was demonstrated by presenting unfinished jokes to a group of subjects and asking them to finish them. Some types of jokes tend to be completed by all subjects in a uniform way, and this is held to indicate that the joke structure possesses tensions or stresses which determine this particular type of closure. The structure of other jokes, however, may be closed by selecting either one of two completions of exactly opposite meaning. For example:

The prisoner in court: But, your worship, I wasn't going 50 miles an hour, nor 40, nor even 30 . . .

The judge: . . .

One type of answer continued the prisoner's statement to an absurd point, e. g., "You'll be going backwards soon"; the other type jumped in the opposite direction, e. g., "No, you were going faster".

Where there was more than one type of completion Harrower showed that it was possible to control the type of completion that the subject gave. By reading over a series of jokes to her subjects and then asking them to finish the "judge" joke she showed that when the judge joke was immediately preceded by a joke which was given a positive completion, the judge joke was invariably given a positive completion too; when it was immediately preceded by a joke given a negative completion it was invariably given a negative completion; and when it was presented under neutral conditions the positive and negative completions were equally likely.

6. General Behaviour and Emotion.

Finally the Gestalt approach has been applied to questions of action and behaviour in general (31). Once again instead of searching for elementary units into which complex types of behaviour may be analysed, they consider the complex types of behaviour themselves. The actions of individuals are regarded as the resultant of stresses, tensions, or valencies which exist in the total situation, and any particular action is regarded as a means by which such stresses may be relieved. For instance, if we feel the need to write a letter we set up a system of stresses which are not relieved until the letter has been written. Usually such tensions are relieved after we have found pen and ink and paper and actually written the letter, but it is sometimes possible also to relieve them by writing the letter in our heads—that is to say without overt action. At all events the tensions are relieved when the *appropriate* organization has been found. Then the individual returns to adjustment with the environment.

For the most part individuals seem to exist in a constant flux of stresses and tensions which arise for lack of organization and complete adjustment.

The uncompleted organizations which give rise to these tensions are constantly changing in kind, extent and direction. They originate in the inherent properties of objects to be attractive or repulsive. To say that an object is attractive is merely another way of saying that tensions exist which tend to shorten the distance between that object and the individual: when an object is repulsive there are tensions which serve to lengthen the distance. Thus a handle invites turning, a mountain invites climbing, chocolate invites eating and so on. Objects may be grouped according to the kind of uncompleted organization that they are likely to give rise to. A letter-box, in the first place, is an example of an object which attracts only spasmodically. If we have a letter in our hand which we want to post, the letter-box has a "positive demand character", but it loses this as soon as we have posted the letter. The property of being attractive exists, so far as the letter-box is concerned, simply as a means of relieving a tension when the uncompleted organization "letter to be posted" exists. But when the letter has been posted the tension is relieved and the organization is completed, and the letter-box then temporarily loses its power of attracting attention.

Another type of object may be illustrated by food. This differs from the last in that the tensions are likely to recur in a more regular sequence, but it has this similarity, that food, like letter-boxes, sometimes has an attractive quality, sometimes an indifferent, and sometimes even a repulsive quality.

A third type of object which leads to the relief of tensions through action is that which possesses certain strong and persistent characteristics. An example of this is a telephone bell which seems to insist on a reply and to speed up the actions of anyone hearing it.

So far the discussion has been theoretical; but steps towards establishing the theory on an experimental basis have been provided by work done under Lewin's direction. In the first place there is Zeigarnik's ingenious experiment of comparing a subject's memory for completed and uncompleted tasks (32). The subjects were given 22 tasks, allowed to finish half of them, but stopped in the middle of the rest and told to continue with the next. They did not know beforehand that they would not be allowed to complete some of the tasks, and they had no idea that the effect of the interruption was the purpose of the experiment. When the 22 tasks were done they were asked to tell the experimenter what tasks they had been doing, and it was found that they could remember about twice as many of the uncompleted as of the completed tasks. This was not due to the emotional shock of the interruption itself, for in another experiment the interrupted tasks were given again later for completion and they were no better remembered than the tasks completed straight away. The explanation suggested by the Gestalt psychologists is that all tasks when begun set up uncompleted organizations and tensions which are only relieved when the tasks are completed. Therefore when tasks are interrupted before completion they are better remembered than completed

tasks, for in the latter the organization is completed and the tensions removed. The urgency of the desire for completion was further illustrated by some children who took part in the experiment. For some days after the experiment was over they asked to be allowed to finish the uncompleted tasks. They never asked for the repetition of a completed task, however interesting it might have been at the time.

The Gestalt psychologists suggest that the slight malaise which was evidently experienced by the subjects who were unable to complete their tasks may bear similarities to the more active emotional behaviour exhibited by subjects when conflicting impulses in a situation are much stronger. Dembo, for example, confronted her subjects with an *impossible* task and insisted on a completion of it (33). The subjects, who of course did not know that the task was impossible, soon exhibited very genuine emotional behaviour. They swore and they threatened and they smashed things up; they rushed out of the room and burst into tears. In all cases the situation presented them with a conflict between their wish to abandon the task and their desire to continue because they had volunteered to do the experiment—to say nothing of their vanity and prestige. Such conflicting tendencies regularly gave rise to vacillation and alternation of behaviour. Every time they exhibited anger they tended to be a little ashamed, and so to increase the tension that was already there. Had they known that the task was impossible their behaviour would have been quite different. Though they might have taken reprisals on the body of the experimenter, there would have been no conflict or tension in their attitude to the task.

In Karsten's experiment, too, similar conflicts arose (34). The subjects had to make strokes on pieces of paper, and to go on doing it as long as they could. Very soon the task became unpleasant, but the subject went on doing it for much the same reasons as in Dembo's experiment. Thus a conflict would arise which often led to overt emotional behaviour. That the conflict arose out of the subject's relationship to the situation was illustrated by the fact that on one occasion a subject refused to continue making strokes on the sheet of paper after he had done it for eighty minutes; but on the next occasion he went on quite happily for two-and-a-half hours without showing any deterioration in the quality of his work; it was the experimenter who eventually brought the session to a close. The reason was that on the second occasion the subject was trying to see how long he could go on without having to stop. Therefore the more he continued, the nearer he approached his goal of going on indefinitely, whereas on the first occasion he was no nearer to his goal at the end of an hour than he had been at the beginning. The energy he expended in the first case served only to increase the undesirability of the task, whereas on the second occasion it brought him nearer to his goal. Similarly, when several unemployed people were paid to do the task they went on almost indefinitely. One subject continued for four hours without

showing any deterioration in his work. Here again the longer the task continued the more the subject was paid, and therefore the greater the incentive to continue.

The expression of emotion, therefore, depends on the existence of a conflict within a situation. The kind of situation in which conflicting stresses are likely to arise is when, for one reason or another, the subject is unable to organize the elements within it properly. Such situations are likely to arise when, for example, an individual is in an unfamiliar situation, when a sudden change takes place for which he is unprepared, when a prolonged response is necessary, or when his ordinary response is obstructed. If the situation is a familiar one, one in which he has often been before, he knows what responses to make, he feels himself master of such a situation and he is well adjusted to it. Consequently no conflict of tensions arises and he feels unemotional in it.

7. Conclusion.

In the preceding sections an attempt has been made to present some of the most important contributions of the Gestalt school of psychologists. In doing this within a limited space much selection as well as condensation has, of course, been necessary—Koffka's *Principles of Gestalt Psychology* amounts to a quarter of a million words—and many of their contributions, such as the experimental work on constancy phenomena, Koffka's trace theory of memory, and Lewin's recent development of behavioural phenomena on a mathematical basis, have unfortunately been omitted altogether.

The main purpose of this review, however, is to give an indication of the consistency of the Gestalt point of view after they branched out from the problems of perception, with which they were first concerned, to the other manifold activities of human beings. Such consistency entails its own disadvantages, for in emphasizing the importance of their own approach over the molecular, associationistic approach of their rivals, they have sometimes spoken as if the effects of experience on present behaviour could be entirely overlooked. In showing that experience is insufficient to explain present behaviour, they occasionally seem to be saying that it can be ignored altogether and in every case.

It is also sometimes said that the concept of Gestalt itself is far too vague a concept to have any definite meaning, and that consequently entirely different things are frequently included under the single name of "Gestalt". The Gestalt psychologists admit that different things are included in the same heading, but they deny that this invalidates their theories. It is true that the only Gestalt which is uninfluenced by external conditions is the Gestalt of the universe as a whole. All other Gestalten are strictly speaking partial Gestalten. But even so this does not prevent these other Gestalten from having a degree

of internal coherence and organization sufficient to isolate them from other Gestalten. This, they consider, is the important thing.

Another criticism levelled against them is that there is really nothing new in what they have to say, and that it has all been said by their predecessors We are all familiar with stroboscopic movement, with insight, and so on ; the much vaunted characteristics of organization in, for example, auditory perception were mentioned by von Ehrenfels in 1890, and the protest against elementarism is as old as the Greeks. This line of criticism, however, is somewhat barren. The Gestalt psychologists, like all other schools, owe much to their predecessors, and they are the first to admit it. Their contribution, however, lies in the sifting and organizing of pre-existing material, the focusing of attention on to a problem which their predecessors often mentioned only incidentally in passing, and still more important, in their insistence on the experimental verification of all their contributions and theories. Above all else the Gestalt psychologists are experimentalists, and it has been their constant aim to check each new contribution with experimental evidence as soon as it may possibly be done. Anyone need only glance at the papers for which they have been responsible to realize the fact that their foremost concern has been with problems that are capable of experimental verification.

Within recent years the men who will always be associated with the Gestalt school, Wertheimer, Koffka, Köhler and Lewin, have been uprooted from Germany and scattered throughout different universities in America. The quality of joint effort, so characteristic of their earlier work when they were building up their system, has, through force of circumstances, largely disappeared. It is fortunate that while the moulding process was proceeding they were in constant contact with one another, and able, through the interchange of ideas about theories and experiments, to present the world with work characteristic not only of a single individual but also of the school as a whole.

Whatever the final fate of the school as a school may be, there is no doubt that it has played an essential part at a very important time in recasting ideas in psychology. Without the force and virility of their contributions there would have been little rallying-point for those who wished to resist the persuasive doctrines of behaviourism. Nowadays both behaviourism and Gestalt have lost some of the force of their earlier years. Both have made their contributions and their mark, and thanks to the wealth of material they have left behind them, psychologists are now faced with an easier task in presenting what they know of the facts of human behaviour.

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A CLINICAL STUDY OF THE MESCALINE PSYCHOSIS, WITH SPECIAL REFERENCE TO THE MECHANISM OF THE GENESIS OF SCHIZOPHRENIC AND OTHER PSYCHOTIC STATES.*

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THE experimental reproduction of psychotic phenomena in the normal person is a subject which has attracted much attention in recent years from psychiatrists, and which has added remarkable and interesting facts to our clinical knowledge.

The discovery of mescaline by Lewin at the end of the last century has marked a great advance in this particular branch of clinical experiment, in that it has placed in our hands a substance which has the property of reproducing in a normal individual all those phenomena which are met with in psychotic patients, without risk to the individual.

From the time of its discovery up to the present day, numerous experiments have been performed by investigators, and the literature contains many detailed accounts of the phenomena which the drug produces. It is the purpose of the writer to set forth in this paper the results of a series of experiments performed with the drug upon himself and upon a group of normal subjects, and to effect a comparison and correlation of the psychotic phenomena studied with those which are found in the naturally-occurring psychoses such as schizophrenia, confusional insanity, and the manic-depressive and delusional states.

Since many excellent and detailed descriptions of the mescaline psychosis already exist, only a brief description of the actual psychotic phenomena will be given, and the greater part of this paper will be devoted to an analysis of the more striking mental changes produced, and a comparison of them with those of the psychoses, with finally an evaluation of the results obtained in the experiments.

Mescaline is one of the four active alkaloids found in the cactus *Anhalonium Lewinii*, which grows in Mexico and Central America. It has been used from ancient times by the Indian tribes for producing a state of pleasant intoxication accompanied by visions in their religious ceremonies. The active principle is found in the flowering tops of the plant, which are roasted and eaten for

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this purpose. It can also be prepared synthetically, and the preparation used in the experiments referred to was a synthetic preparation of pure mescaline sulphate.

Chemically, mescaline is a well-defined organic compound, 3–4–5 trimethoxy-phenyl-ethyl-amine. It is a white crystalline powder, moderately soluble in water, and with a bitter metallic taste. The doses used in the writer's experiments varied from 0·2–0·5 grm. by mouth.

The actual experiments were performed by the writer upon himself, and upon a group of normal adults of ages from twenty to thirty years.

The pharmacological properties of the drug are, briefly, that it can reproduce in the normal subject striking psychopathological phenomena without clouding of consciousness or risk of harmful effects or habit-formation. It is a true cerebral stimulant, and has no narcotic properties. The mental changes produced are of an almost exactly similar nature to those found in psychotic patients—namely, hallucinations of all senses, delusions, transformation of personality, thought-disorders, abnormalities of conduct, affect changes, and disorders of temporal and spatial perception.

Of the exact mechanism of its action, little is known. The seat of action is undoubtedly the higher centres of the brain, particularly the auditory and visual perception-centres. The action is supposed to be on the neuron and upon its synapses. Quastel states that it depresses the normal oxidation processes and glucose-metabolism of the brain, and Henderson and Gillespie have pointed out the resemblance of its effects in this respect to those of certain toxic amines found in the intestinal tract. It is destroyed in the body by a process of oxidation in the liver. It has been found to abolish the α-waves of the electro-encephalogram.

Physical Signs.

Before proceeding to an account of the psychotic symptoms produced, a brief account of the physical signs observed in a subject under mescaline will first be given, as these are of considerable interest.

The most striking feature in the physical appearance of the subject is the close resemblance to a patient suffering from an acute toxic confusional psychosis or acute schizophrenic episode. The lips and tongue become dry, dirty and coated with sordes; the skin is flushed at first, and later becomes dry and harsh with an earthy pallor; the conjunctivæ are injected, and the eyes appear unnaturally bright. The urine is scanty and highly coloured, and there is absolute insomnia, anorexia, and in the later stages, restlessness.

In the central nervous system the changes found are marked dilatation of the pupils and increase of all the deep reflexes, with a mild degree of tremor and inco-ordination of movement. There is no muscular weakness or rigidity. The catatonic signs will be described later under disorders of conduct. On

the sensory side there is marked dulling of the pain sense, loss or perversion of the senses of weight and thermal appreciation, and complete loss of spatial discrimination and of the sense of orientation of the body.

The drug is a powerful stimulant of the medullary centres, producing hyperpnœa, and in the later stages, Cheyne-Stokes respiration, and there is always nausea and occasionally vomiting in the early stages.

The retinal cells appear to be specially sensitive to the action of the drug, as seen by the early exaggeration and prolongation of the after-images and the early appearance of Liepmann's sign.

In the cardiovascular system there is a small rise of blood-pressure, with increased force of the heart-beat and acceleration of the heart-rate in the early stages, followed later by cardiac slowing.

The action of the drug commences within half an hour of ingestion, and lasts approximately 10 to 12 hours.

Psychotic Phenomena.

The various psychotic phenomena will now be described in turn and their mechanism, and similarities to those of psychotic patients indicated. It is important to realize that, unless the dose has been very large, that is, above 0·4 grm., the mental changes take place in a state of clear consciousness and without weakness of the intellectual faculties ; this clearness of consciousness is all the more remarkable in view of the profound disorders of personality and thinking with which it is co-existent.

Hallucination.

In the sphere of perception the hallucinations are the outstanding feature. The most common are the visual, auditory, and somatic ; hallucinations of smell and taste are rare.

The visual hallucinations take the form of complex and fantastically beautiful kaleidoscopic patterns of every shape and colour, brilliantly coloured birds, dragon-like monsters, gigantic human figures in fantastic apparel, and scenes of fantastic gardens with wonderfully beautiful flowers. They are constantly changing, and their chief qualities are their wonderful beauty and variety, their stupendous and gigantic qualities, their arrangement in characteristic geometrical forms, and the fact that they are always incomplete or with parts missing. Sometimes sensible film-like scenes appear, but very often the visions consist of scenes quite indescribable in ordinary language, and bearing a close resemblance to the paintings and sculptures of the surrealistic school. These last are apparently almost unrecognizable condensations and symbolizations of past mental impressions.

These hallucinations have similar characteristics to those found in the psychotic states. Thus, their content is always in line with the subject's past mental experience. They are wish-fulfilling fantasies, and in them the fantasies of childhood can at once be recognized.

Thus, to give examples, one of my subjects, a schizothymic whose principal interest in his boyhood had been the study of ancient mythologies and archæology, saw the mythical personages and monsters of his childhood fantasies; these apocalyptic types of hallucinations are found especially in toxic deliria. Another, an extrovert type, who was an air-pilot, and whose interests were chiefly mechanical, saw visions of futuristic cities with fantastic machinery and engines.

The hallucinations also blot out all normal perceptions in their neighbourhood, as pointed out by Stoddart; like those of psychotics, they are favoured by silence, solitude and self-absorption, and mitigated or abolished by simple occupation—a fact noted in several of the subjects. They represent a reversion to an archaic type of thinking, as pointed out by Hesnard.

The mechanism of their production appears to be as follows: The principal factor in their genesis is an enormous increase in the power of mental imagery and vividness of thought—a true hypertrophy of the imagination; thus, they commence as vivid fantasy, seen on the mind's eye, as it were, not as external objects are seen; at a later stage, when the process of mental dissociation is complete, the imaginalized thought becomes entirely split off from the rest of the psychic processes, and the fully-formed hallucination, appearing as a real object outside the subject, is thus produced. All the various stages between thought, vivid fantasy (pseudo-hallucination) and fully-formed hallucination can thus be seen and studied in the mescaline subject.

Their genesis is also undoubtedly favoured by the characteristic disorder of thinking, the alteration of, and turning away from, reality and the preoccupation of the subject with the novel inner life of his psychosis.

These hallucinations are not influenced by external suggestion, thus differing from the type found in delirium tremens and allied states; the same applies to the auditory hallucinations.

It has been commonly stated by several authors that these latter are rare as compared with the visual hallucinations in mescaline psychosis. This has not been found to be the case in the writer's experience. In every case studied they were found to be relatively common. They appear to be of two types, one with an entirely novel content, apparently due to the specific action of the drug on the auditory centres; these take the form of indescribably beautiful musical sounds and of voices speaking in a strange language; the other type are really part of the disorder of thinking, and are experienced as a feeling of the subject that his thoughts have become separated from him, and are talking back to him as "voices". This last form is the most interesting, as it shows the mechanism of dissociation and projection well, and is probably

identical with that found in schizophrenia. The writer has obtained descriptions of this form from several schizophrenic patients.

The last type of hallucination, the somatic, takes the form of indescribable bodily sensations, such as, for example, that the limbs have changed size and shape independently of the rest of the body; that the subject has become gigantic and possessed of superhuman strength, or that parts of his body have been removed or substituted; a common feeling is that the whole body has been completely transformed into a lifeless rubbery substance, leading to absurd and nihilistic delusions of bodily change, such as that the patient's body has been turned into rubber, or that he has no heart or bowels—in fact, delusions of a typical schizophrenic or depressive type. A common sensation is that of tingling or "electricity", which, combined with the other strange paræsthesias, may lead to delusions of persecution or interference—a process which will be described further under the subject of delusions.

The remarkable similarity between these experiences and the type of hallucinations experienced by psychotics will at once be noted. A further remarkable fact is the extraordinary resemblance of the visual hallucinations to the strange symbolic drawings of schizophrenic patients, and to the fantastic and garish designs in painting and weaving produced by psychotic patients in the occupation-departments of mental hospitals—a point which will be referred to again later.

Closely connected with the hallucinations is the other form of visual and auditory disturbance, namely, the extraordinary change which appears to take place in the outer world.

Taking first the visual component of this change, we find that this takes the form of a remarkable alteration in appearance of the outer world. It appears to the subject as if, as it were, a veil of unreality had been laid over everything. This feeling of unreality of the outside world must, of course, be distinguished from the feeling of unreality of self, which will be described later. The remarkable feature of this change is that objects appear more or less unchanged as regards colour and shape, and yet they are completely different—the subject is now living in a world of his own.

This phenomenon of unreality is, of course, a well-known one found in psychopathological states, especially schizophrenia.

Superimposed upon this are a number of remarkable visual illusions. Thus, at the commencement of the intoxication, objects appear to become much more vivid to the subject, and their colours to have become richer and more pronounced. Often they seem to stand out at him, as it were, as if they have some special reference for him; when this coincides with the depressive stage the effect may be extraordinarily sinister and nightmarish to the subject, and so lead to outbursts of panic and impulsive action.

Another change commonly found is that of simple patterns upon objects, appearing to become more elaborate, and finally weaving themselves into

most complex patterns of figures; thus, for instance, a comparatively simple pattern of wavy lines on wallpaper may finally appear to evolve itself into a complex pattern of fantastic figures showing the geometrical arrangement, continuous movement, variety and majestic qualities of the true mescaline hallucination. Naturally, this gives an air of extraordinary beauty to the subject's surroundings; though sometimes the quality of the surroundings was found to be unbearably ghostly and sinister, and the subjects complained frequently of "everything looking awful".

Another remarkable feature observed was the change in the faces of other persons. The features appeared to become intensely vivid, and all the peculiarities of their physiognomy to be greatly exaggerated; at a later stage the faces appeared monstrously distorted, with huge eyes, enormous foreheads, and grim and menacing expressions. This illusion often leads to ideas on the part of the subject that faces are being made at him, that others are mocking him, or that he is being hypnotized or influenced in similar ways. The writer has obtained descriptions of exactly similar experiences from schizophrenic patients under sodium amytal narcosis. This phenomenon is apparently the principal exciting cause of the impulsive attacks on others which frequently occur in these conditions.

Another remarkable illusion is that of the room becoming filled with a strange and unearthly light, and of strange lights being flashed on the subject. These illusions, or hallucinations, of lights being played on the subject are frequently complaints found in the schizophrenic or delusional patient.

In the sphere of auditory perception, the most remarkable phenomenon is the strange new qualities which ordinary commonplace sounds appear to acquire. This symptom will be described now under the subject of delusions, since it appears to be an important part of the mechanism underlying their production.

Delusions.

Coming now to this important subject, it is found that one of the characteristic actions of mescaline intoxication is that it is always accompanied by the presence of morbid suspiciousness and often of fully-developed delusions and ideas of reference, the mechanism of which can be shown in a remarkable way by means of the experimental mescaline psychosis. The delusionary ideas of the mescaline subject are of the same type as those found in psychotic patients, namely, ideas of grandeur, persecution, and bodily change. A description of the mechanism of these as elucidated in these experiments will now be given, and their points of similarity to those of psychotic patients pointed out.

The basic factor in the genesis of the delusions appears to be a qualitative alteration of the functions of the higher cortical receptive centres, with resulting

distortion of their functions, and consequent misinterpretation of external stimuli. The delusions are thus dependent primarily on a disorder of the central perception organs, especially the auditory centres.

Taking first the delusions of persecution, we find that one of the characteristic actions of mescaline is that of sensitization of the auditory centres. Sounds appear to be either unnaturally loud, or distorted, and to have acquired strange qualities. They appear to the subject to rush upon him in an extraordinarily purposive and deliberate way, and to have a reference for him which they would not have in the normal state. Thus, to quote actual examples, seen in the writer's experiments, the sound of a typewriter being used in the next room seemed to vibrate and reverberate through the walls and into the subject's body; thus, the typewriter became an infernal machine persecuting him with rays of electricity; in another case a group of people talking in the next room becomes a gang of enemies plotting against him or interfering with him. Similarly, the announcer's voice is sending messages over the wireless specially meant for him.

In the visual sphere, the strange distorted appearance of people's faces, their movements and conversation all seem to be directed against him, so that he feels as if he was being watched, spied upon or otherwise interfered with.

Similarly, the strange bodily paræsthesiæ readily produce ideas of influence, electrical interference, or bodily changes produced by the machinations of other persons.

This delusionary state may vary from morbid suspiciousness to fully-developed ideas of persecution, according to the stage of intoxication and the surroundings of the subject. It is apparent that persecutory delusions require some stimulus, in the form of an auditory or visual perception, for their production.

Grandiose delusions may arise in two ways. One is from the somatic paræsthesiæ. One of the commonest of these is a feeling of having grown extremely tall and handsome, and of being possessed of superhuman strength. Appreciation of the weights of objects is always disordered, and common objects may seem extremely heavy to the subject; in this way he imagines, for instance, that in raising a chair he is lifting an enormous weight. The hallucinations of supernatural figures and voices similarly give rise to ideas of communion with God, and of being divinely inspired.

In these last types of delusions, the disorder of thinking and of association and lack of insight are important contributory factors in their production.

The striking similarity of the delusional states thus described to those found in schizophrenic and delusional cases will at once be observed. The phenomenon of exaggeration and distortion of ordinary sounds has been observed in paraphrenic and schizophrenic patients, from whom the writer has obtained descriptions on several occasions.

Depersonalization.

The study of the delusions leads us to the subject of the basic and fundamental symptom of the mescaline psychosis—that of the alteration of the personality. Mescaline intoxication is indeed a true "schizophrenia" if we use the word in its literal sense of "split mind", for the characteristic effect of mescaline is a molecular fragmentation of the entire personality, exactly similar to that found in schizophrenic patients. It is well-shown by the projection of parts of the mental content as hallucinations and delusions.

The state of depersonalization—an alteration in the personality of the subject, in which he feels that something has been taken away from his personality and something strange and foreign substituted, is characteristic. The change consists of a radical alteration of the mind and body. Thus, the subject may feel that he is being several different persons at once—a symptom sometimes found in schizophrenia. More characteristic still is the feeling that he is divided into two separate beings—one a purely intellectual and emotionless creature, the other a fantastic being of delusion and fantasy, the first being able to observe the other in an extraordinarily detached and unemotional fashion. This change, as Guttmann has pointed out in his paper on the mescaline psychosis, is of great value in the extraordinary faculty for self-observation and introspection which it confers on the subject, which he does not possess in his normal state.

The feeling of unreality, both as regards the self and the external world, so often found in schizophrenics, is one of the typical features of the mescaline psychosis. One of the most common descriptions given to the writer by his subjects of their feelings was that of living in a world of one's own. "I am living in a private world," and "Other people cannot understand me, because I am living in a different world from them", were actual descriptions obtained in these experiments.

Precisely similar descriptions were obtained from recovered schizophrenic patients studied by the writer who were asked to give, as far as they were able, a description of their experiences during the period of their acute illness. In both cases, those of the schizophrenic and the mescaline subject, the impossibility of putting their feelings and experiences during the acute stage of the psychosis into ordinary language was a striking feature.

Even more remarkable are the self-descriptions of their mental experiences by schizophrenic patients under sodium amytal. As is well known, this drug, when administered intravenously, has the property of temporarily producing a lucid interval in a psychotic subject previously inaccessible and incoherent. Under this drug, the writer has obtained from schizophrenic patients accounts of their mental experiences which bear a remarkable resemblance to those of mescaline intoxication. For instance, the bizarre hallucinations of colour and distorted appearance of external objects and of other persons

have been described by patients given sodium amytal by the author. The resemblance to the mescaline psychosis is even closer in the case of the confusional states, especially as regards the visual hallucinations.

A further feature of the personality changes must be mentioned before leaving this subject, namely, the symptom of transformation of the personality —that is, the belief that the patient has been changed into someone else. Thus the subject of the mescaline psychosis may believe that he has become transformed into some great personage, such as a god or a legendary character, or a being from another world. This is a well-known symptom found in states such as paraphrenia and paranoia. As found in the mescaline psychosis, it appears to be due partly to the abnormal bodily feelings referred to in the discussion of delusions of grandeur. Another mechanism, observed by the writer as occurring in his own case, was a process of identification of the subject's self with the stupendous beings of the mescaline fantasies. This process, in which the subject sometimes appears to lose the power of being able to distinguish between the self and the outside world, is strikingly reminiscent of the introjection processes of childhood.

Disturbances of Thought.

We now come to the subject of the peculiar disorder of thinking which is characteristic of the mescaline psychosis, and which is intimately bound up with the disorders of personality described above. As has already been stated, the drug produces no intellectual weakness or clouding of consciousness, except with very large doses, that is, of over 0·4 grm.

The characteristic symptom is a peculiar slowness and difficulty of thinking, a divorcement of the intellectual functions from the rest of the cerebration, with, simultaneously, a greatly increased output of spontaneous fantasy and imagery. Incoherence and thought-blocking are well shown, and give rise to the peculiar disorders of language presently to be described. Flight of ideas, as in the manic states, may occur as a principal feature, or in combination with blocking of thought on the intellectual side. The subject may complain of strange and foreign thoughts being put into his mind, or that each thought is simultaneously repeated as either an auditory or visual perception—the phenomenon of "double thought" so well exemplified in schizophrenic states. The feelings of passivity, of thoughts foreign to the subject being put into his mind from outside and ideas of influence are also well-known schizophrenic symptoms. Inability to hold a train of thought and follow it up to its logical conclusion, and perseveration and ideational inertia with disorders of association, are also found. A characteristic symptom is that there are several different simultaneous trains of thought running parallel in the mind of the subject. The thought-content is dominated by the subject's particular complexes, as in schizophrenic states. The peculiar scattered type of thinking

and volitional disorders are at once strongly reminiscent of schizophrenic phenomena, while the psychomotor retardation and flight of ideas bear a striking resemblance to the symptoms found in the depressive and manic psychoses respectively.

It was found that syndromes of flight of ideas, blocking of intellectual as distinguished from spontaneous fantastic thought could occur simultaneously, or alternate with one another in the same subject at different phases of the psychosis.

These disorders of the thought processes result, as would naturally be supposed, in a number of characteristic disorders of language. Thus, the psychomotor retardation was found, in the writer's cases, to lead to slowness and diminution in the flow of speech, the flight of ideas to garrulity and loquacity of hypomanic type, and the disorders of association to speech of the "word-salad" type and incoherence so commonly found in schizophrenic patients. Characteristic is a peculiar pompousness of utterance, with evident difficulty in choosing and expressing the words desired, a symptom the writer has observed frequently in many schizophrenics. Fatuous and irrelevant remarks suddenly made apropos of nothing were also commonly observed, and made the resemblance to schizophrenic language even more striking. The speech of the subject is often found to bear little or no relation to the thought-content.

Neologisms were noted in a few cases. These resulted from the subject's inability to express the indescribable mental experiences of his psychosis in ordinary language, especially the visuo-auditory synæsthesias, for which neologisms, which are usually condensations of two or more ordinary words, are invented.

Motor Disturbances.

On the motor side characteristic syndromes are observed. The most striking are the catatonic states. The writer was able to observe in himself the catatonic state, which is a most remarkable experience. The feeling is that of a delightful laziness and disinclination for active movement, resulting partly from extreme self-absorption and preoccupation with fantasy and indifference to the outer world—two characteristic symptoms of the intoxication. There is a peculiar inability to make up one's mind to a course of action, with wavering between two alternative courses of action. The fundamental disorder appears to be a block between the higher centres which are responsible for the initiation of a train of motor activity, and the parts of the motor cortex which are responsible for the performance of voluntary movement, although no actual loss of motor power is present. It has been shown by De Jongh that mescaline produces identical catatonic signs in animals.

Alternating with this state are impulsive outbursts of meaningless motor activity, sometimes resembling those of schizophrenic patients, and in

other subjects resembling the pressure of activity of the hypomanic. Peculiar grimacing and mannerisms are also encountered; these are usually secondary to the bizarre somatic paræsthesias. Attitudes of religious ecstasy, similar to those found in some acute schizophrenic cases, may be assumed as a result of vivid hallucinations with a religious content. Suicidal impulses, secondary to the terrifying feelings of unreality experienced in the early stages of the intoxication, and homicidal impulses, secondary to the ideas of reference and persecution, are also found. Extreme recklessness of conduct with disregard for all conventions and shamelessness are also seen, these being secondary to the thought-disorder and qualitative alteration of reality and emotional decontrol.

All these phenomena are closely dependent in their occurrence on the constitutional type of the subject, as will presently be more fully described.

The motor disorders of schizophrenic type are dependent on the condition of removal from reality, with complete indifference to the outside world, and preoccupation with internal fantasy. Thus it was found that in subjects who had passed into the state of catatonic stupor, painful stimuli, such as pricking with a pin, were often completely disregarded, although pain was still felt.

Negativism, with an attitude of hostility and stubbornness, and refusal of food with neglect of the ordinary bodily functions, were encountered in nearly all the subjects studied. The refusal of food and drink during the acute stage was partly due to the ideas that such food might be poisoned, and partly to the specific action which the drug possesses of abolishing thirst and hunger, in which its action resembles that of some of the habit-forming narcotics, such as morphine and cocaine.

Intellectual Disturbances.

As regards disorders of the intellectual functions, it has already been stated that mescaline produces no intellectual weakness, unlike alcohol and other narcotic drugs. The characteristic change appears to be the peculiar divorcing of the intellectual part of the personality from the rest of the psyche, with disturbance of association, blocking of voluntary intellectual thought, and extreme distractability. These factors, combined with the morbid suspiciousness and non-co-operativeness of the subject, render any proper assessment of the state of the intellectual functions extremely difficult. It is known that the mental efficiency, as measured by psychological tests, shows a great falling-off in performance. The subject can only perform the simplest tests and remember the most elementary facts from his past store of knowledge. The time taken for the performance of any test is increased, and the number of mistakes is also greatly increased.

As regards orientation in space and time, these are not impaired unless a very large dose has been taken. If the dose has been more than 0·4 grm., true clouding of consciousness with disorientation occurs, and the clinical picture becomes that of an acute confusional psychosis.

At this point will be mentioned the characteristic disorders of temporal and spatial perception which mescaline produces.

The characteristic disorder of time-perception is that time seems much longer than it actually is, in which respect the action of the drug is similar to that of such agents as cannabis indica, morphine and cocaine. With a small dose, i.e., 0·2 grm., this lengthening of time is the only change. With the larger doses, 0·3 to 0·4 grm., at which dosage full mental dissociation occurs, extraordinary illusions of time are also experienced. Thus the subject may feel as if time were reversing upon itself, or as if he were travelling backwards and forwards alternately in time, in addition to feeling that in the course of a single afternoon he has lived through thousands of years. Extraordinary "fourth-dimensional" effects are thus produced. The mechanism of this disorder of time-sense appears to depend upon two factors. The first is the enormous speed of the fantastic thoughts, which gives the impression that the subject has got through far more thinking processes in a given space of time than he would in his normal state. The second is the curious memory-disorder which the drug produces, in which there is defective memory for the immediately past mental experiences of his psychosis.

At this point the memory-disorder must be mentioned in greater detail. The subject's comprehension of, and memory for, the actual events taking place in the outside world during the period of his intoxication is good; but upon return to normality there is almost complete amnesia for the mental experiences, with the exception of one or two of the more striking hallucinatory scenes. The auditory hallucinations are always much better remembered than the visual. This amnesia for the mental experiences of the psychosis, with a good memory for the actual events in the world of reality, was a striking finding in many schizophrenic cases observed by the writer. These disorders of memory and temporal perception are probably the basis for the disorientation found in toxic confusional cases, and of the delusions of having lived to a great age found in some schizophrenic and delusional psychotics.

The characteristic disorder of space-perception is that space is greatly extended, and infinite in extent. Thus, rooms appear as huge fantastic chambers, or endless corridors, and the walls and floor appear to have changed their shape. Macropsia and micropsia are also observed.

Under the heading of "intellectual disturbances" we may mention the question of insight. It goes without saying that the subject of mescaline psychosis is entirely lacking in insight; one of the best demonstrations of this occurs in the early stage of the drug's action, when the subject repeatedly asserts that there is nothing wrong with him, and persists in believing that no toxic

drug has been given him, although he may show simultaneously gross thought and conduct disorder, and describe marked psychopathological phenomena.

Disturbances of Mood.

We now come to the consideration of the affective and emotional changes produced. Like other intoxicating drugs, mescaline can produce an affective change in two directions—those of euphoria and depression, depending upon the stage of the intoxication reached.

The stage of depression is found characteristically at the commencement of the psychosis, usually during the first hour after ingestion of the drug. It takes the form of an acute agitated type of depression, associated with intense anxiety and fear, and a sense of impending dissolution. There may be also ideas of unworthiness, of being irretrievably damned and lost, and of intense hopelessness. Associated with this is a terrifying feeling of unreality of self and of the outside world. Objects may take on an extraordinarily sinister and vaguely menacing appearance. These feelings are identical with those of an agitated melancholia, and can be indescribably terrible and torturing experiences. Alternatively, the depression may occur at the termination of the intoxication as a dull feeling of hopelessness, with ideas of disorder of bodily functions, and a feeling that recovery to the normal state will never occur, even though the subject has experienced the intoxication many times before and has always recovered. In fact, this form is identical with the simple depressive psychosis without agitation.

This stage is quickly succeeded by the stage of euphoria and elation. The euphoria appears to be due to the specific action of the drug on the cerebral cells, and is not secondary to the presence of pleasing and beautiful hallucinations, as it may be present without these, and often some of the most beautiful visions may coincide with the depressive stage. It varies from a delightfully happy and dreamy feeling accompanied by pleasant fantasy, to an intense ecstasy of exaltation, which is often associated with brilliant hallucinations with a religious content. It is usually coincident with the delusions of grandeur and ideas of increased physical power and ability.

The depression and elation are thus of pathological type, and of a closely similar kind to those found in psychotic subjects.

Characteristically associated with these mood-changes are marked emotional decontrol, emotional lability, and fatuousness of the type found in the schizophrenic patient. The mescaline subject also shows incongruity of affect, with complete indifference to events in the outside world, towards which he displays markedly shallow affective response. Thus, he may simply laugh fatuously at a piece of bad news ; or he may wear a mournful and depressed expression whereas he is really inwardly elated and exalted ; or he may laugh fatuously while in the depressive stage.

In the majority of the subjects studied the euphoria showed the typical features of the schizophrenic as described above. In one or two, however, who were of the cyclothymic type, the elation was of the jovial and infectious type found in the hypomanic and manic states.

A remarkable symptom observed by the writer in his own case is that of feeling both depressed and elated at the same moment. At times it is impossible to say what the prevailing affect is. On other occasions waves of elation and depression alternated rapidly and with great regularity; this was seen especially in the early stages of the psychosis.

Under the heading of "affect and emotional changes" should be mentioned the effect of the drug on the sexual functions. Guttmann has pointed out that mescaline is a powerful anaphrodisiac, and produces complete loss of sexual power and frigidity during the period of its action. This has been the writer's experience with most of his cases. In some, however, particularly of the extraverted type, there may be at the commencement of the intoxication a subjective feeling of increased sexual appetite and potency, with consequent erotic and shameless conduct.

Synæsthesia.

We must now consider one of the most remarkable and characteristic phenomena produced by the drug—namely, that of synæsthesia, that is, colour-hearing and sound-seeing, which may truly be described as a "sixth sense".

In a few normal individuals, and often in imaginative children, the close association of certain colours and shapes with certain sounds, and the production of sensory impressions in one modality by stimulation of the sense-receptors of another, is found in the normal state. In mescaline intoxication this sense is greatly heightened, and the hallucinations are found to possess equally qualities of visual and auditory perceptions. Thus, an auditory hallucination may at the same time present itself as a fantastic shape or colour, or both; in the same way a given vision may be accompanied by a corresponding auditory impression. This phenomenon appears to be a specific peculiarity of the mescaline action, and produces the most fantastic and amazingly beautiful mental experiences, which are impossible to describe in ordinary language.

In the same manner, an external stimulus in one sense may evoke a corresponding impression in another; for instance, music may be perceived by the subject as intensely beautiful rhythmically pulsating and changing colours, the musical notes appearing as patterns of exquisitely delicate spirals, scrolls and filigree work, while the visions already present pulsate and change rhythmically to the tune played. Certain notes are found to evoke corresponding shapes and colours. In the same way, looking at an object in the room may evoke a corresponding auditory sensation.

Whether this phenomenon is present in the naturally-occurring psychoses, and if so, what its significance is, is as yet not definitely known. The writer has in no case as yet been able to elicit a history of this symptom by direct questioning of a psychotic patient. It is the writer's view that it is actually the basis of the strange neologisms and expressions used by some schizophrenic patients, and of their almost complete inability to express their mental experiences in ordinary every-day language. In the case of the mescaline subject, as has been pointed out, it gives rise to ideas and concepts for which there are no equivalents known to us in our normal waking life. It is therefore, in the writer's opinion, possible, if not probable, that this process of synæsthesia is the basis of the failure of conceptual thinking found in many psychotic patients, and the almost complete inability of the physician to establish any sort of rapport with the patient, and to understand his mental processes. It is indeed this extraordinary sense of synæsthesia which, in the mescaline subject, more than any of the other phenomena, gives the subject the feeling that he is living in another world.

In connection with these bizarre and indescribable experiences a further noteworthy characteristic of the feelings of the mescaline subject must be mentioned, which is also commonly found in schizophrenic states. This can best be described as the quality of silliness. " I just felt so silly " and " I just feel funny " were typical descriptions given by the subjects. This silliness is exemplified in the hallucinations, in which mingling of the sublime with the ridiculous is one of the outstanding peculiarities, in the actual mental feelings, and in the language and conduct of the subjects. It is this feeling of silliness which often makes the subjects ashamed to talk of their experiences after the termination of their intoxication, and which is probably also one of the factors which make a psychotic patient so evasive and unwilling to talk of his experiences to the physician.

Vegetative Disorders.

Finally, before leaving the subject of the various psychotic phenomena, the striking disorders of the vegetative centres should be pointed out.

Sleep-disorder is characteristic in mescaline psychosis ; the drug appears to have a specific action in abolishing sleep ; thus, the subject always suffers from intractable and absolute insomnia for many hours after the signs of intoxication have ceased. This is generally associated with restlessness and profound anorexia with refusal of food. In these respects the striking resemblance to the naturally-occurring psychoses is again evident. In the catatonic state complete neglect of the bodily functions is found, a state reminiscent once more of the catatonic types of schizophrenia.

Taking the psychosis as a whole, one striking fact should be mentioned, namely, the influence of constitutional make-up on the course and form of the

psychosis. The group of subjects studied by the writer included examples of both the intravert (schizothymic) and extrovert (cyclothymic) types of personality. It was found that the constitutional make-up in every case modified the course of the psychosis considerably.

Thus, in the schizothymic type, the symptoms most strikingly shown were vivid hallucinations, delusions and ideas of reference, and catatonic stupor with withdrawal from reality; similarly, the euphoria was of the introverted type found in schizophrenia—in other words, the clinical picture shown by the subject approximated to a schizophrenic reaction. In the cyclothymes, on the other hand, the reaction tended to resemble much more the hypomanic or manic reaction, with press of activity, flight of ideas, increase of motor activity, manic elation and joviality, and the comparative absence of hallucinations. Indeed, it appears that in this type of personality the psychosis may run its course without the production of hallucinations. In this respect, the mescaline psychosis again appears to be governed by the same conditions as determine the course of a naturally-occurring psychotic illness.

Discussion.

When the nature of the mescaline psychosis is considered generally, we see illustrated in it in a remarkable manner the various mental mechanisms which are of importance in the study of mental illness.

Thus, in the first place, we have the process of turning away from reality and withdrawal inside oneself, with the creation of a fantastic dream-world of one's own to replace the discarded outer world. The subject thus finds satisfaction for all his unconscious wishes in the tremendous burst of wish-fulfilling fantasies which the action of the drug releases. He regresses to a childish mode of thought, an archaic golden age, in which all his desires are fulfilled in fantasy. His thinking processes are dominated by his complexes, which are clearly reflected in the hallucinations described. The mescaline psychosis represents a tremendous "volcanic eruption" of the subconscious, with the repressing forces in complete abeyance, in which respect it appears to bear a close relationship to dream-states.

These characteristics of withdrawal from reality, katathymic thinking and archaic regression have been emphasized as part of the essential mechanism of the schizophrenic by Henderson and Gillespie.

Having now completed a review of the principal phenomena of the mescaline psychosis, the principal points of resemblance between it and the naturally-occurring psychoses will be considered.

As Guttmann has pointed out, the most striking resemblances seen are those to the schizophrenic reaction type. Thus, the extraordinary disorder of personality, the feelings of unreality and of living in another world, the delusions, hallucinations and peculiar disorders of thinking, and the motor signs

such as catatonia make this resemblance extremely striking. Likewise, the self-descriptions of schizophrenic experiences by patients obtained in different cases, and the indications given of the mental life of these patients as shown in their drawings and writings, which are found to be so strikingly reminiscent of the experimental psychosis, would further point to a similar mechanism for the underlying basis of the two conditions.

On the other hand, the type and quality of the visual experiences would appear to relate the mescaline psychosis more closely to the toxic confusional psychoses. So also would the disorders of spatial and temporal perception, and the clouding of consciousness which results from the employment of the very large doses.

The striking changes in the mood and affect produced in the same way bear close resemblances to the manic and depressive reaction types. Again the phenomena of misinterpretation of perceptions and the formation of grandiose, persecutory and somatic delusions under the influence of the drug reproduce almost exactly the clinical picture of the delusional states.

Taking the psychosis as a whole, undoubtedly the most outstanding feature is the complete transformation and alteration in the psychic life of the individual, which is the common factor in all the psychotic states.

Having pointed out these resemblances, we must now, before proceeding to draw any conclusions regarding the mechanism and nature of these changes, indicate and examine the main points of dissimilarity between the two conditions under consideration, namely, the mescaline-produced and the naturally-occurring psychosis. Furthermore, we must also consider the possible fallacies and limitations which must be borne in mind when attempting to interpret the results of the experiments described, and in applying them to the study of diseases occurring in the human subject under natural conditions. As is only to be expected, similar fallacies are found to those which apply to the study of physical disease in the human subject by means of animal experiment.

In the first place, we must bear in mind that mescaline, like any other specific poison, may produce effects which are peculiar to itself, and which are not found in any other type of psychosis, artificial or otherwise. Such effects are the vegetative symptoms, the peculiar qualities of the visual experiences, and perhaps the synæsthetic phenomena. Such effects would therefore be superimposed upon those symptoms common to all psychotic states, and so colour the clinical picture produced in a manner not found in the ordinary forms of mental illness.

Secondly, it is obvious that we cannot, for practical reasons, exactly reproduce the conditions normally found in the psychotic patient. Thus, to give an example, an acute psychosis deliberately induced by the administration of a toxic drug, to a dispassionate observer is obviously not the same thing as a chronic and insidiously developing reaction arising in an ordinary person as a result of a long period of stress and maladaptation.

Thirdly, it will have been perceived from the description of the mescaline intoxication that it is not identical in form with any of the known naturally occurring psychoses. The mescaline psychosis is a medley of all the known psychotic symptoms occurring at random in the course of an acute intoxication, the events of which are crowded together into the space of a few hours.

A fourth point which has been indicated by Guttmann must also be mentioned. This worker has pointed out that in the schizophrenic psychosis the auditory hallucinations are predominant, in the confusional type the visual, so that in this respect the clinical picture produced by mescaline would approximate more nearly to the confusional state than to schizophrenia.

As against this, however, it is known that schizophrenics in the acute phase of their disorder may experience visual hallucinations. In the experience of the writer, almost all schizophrenic patients who have recovered from their acute illness are found, on questioning, to give accounts of such experiences; the same applies to such patients under amytal narcosis. Again, as has been pointed out, the drawings and other art productions of these patients are strongly reminiscent of the visual imagery of the mescaline psychosis. It should also be remembered that a large part of the mental content of the mescaline subject consists of vivid fantasy rather than true hallucination, as in the case of schizophrenic subjects; also that in some subjects it is possible for the mescaline intoxication to run its course without the presence of visual hallucinations. Another point is that with mescaline intoxication, as with many acute psychoses which occur naturally, there is often a gross degree of amnesia for the experiences of the acute stage; also, the auditory hallucinations are much more vividly remembered than the visual; so that the isolated auditory hallucinations of schizophrenics probably constitute only a very small part of the total mental content of the acute psychosis.

An interesting fact which may be mentioned at this point is the close similarity of the art-forms and symbolism of the ancient Mexicans and Central Americans, who used mescaline freely in their religious rites, to the symbolic drawings of schizophrenic patients—a point which has been mentioned by several writers on this subject. This is another fact which suggests strongly a close similarity between the thought-processes of the schizophrenic and those of the subject under mescaline.

Again, there is another fact, well known to those who have daily experience of the psychotic patient, which should be mentioned in this connection. This is that, in spite of the numerous and elaborate classifications of the different forms of mental disorder which have been produced, no hard and fast distinction between the various diseases described can be made. Few patients in actual practice conform closely to the textbook descriptions; thus, to take an example, a case may be admitted in the acute stage with all the classical signs of an acute confusional state; a few months later, when florid symptoms have abated, we may find the patient presenting all the signs of a classical mania; and later,

we may find that the picture has changed to that of a schizophrenic illness. In the same way, the signs of all the various reaction types may alternate in the mescaline subject in the course of one intoxication. This, in the writer's opinion, is a strong piece of evidence for the unity of all the various disease processes described as the psychoses, excluding, of course, the organic reaction types.

It does not seem unreasonable to suppose that, if we assume the fundamental mechanism of the natural and the artificial psychoses to be similar, the causative agent may have a selective action for the various higher centres of the brain. Thus, in confusional patients the visuo-psychic centres, and in schizophrenics the auditory, may be picked out for attack. An analogy could be drawn in the virus diseases of the nervous system, in which the specific virus always selects certain particular parts of the nervous system for its attack.

Finally, in consideration of these arguments, we should not lay too much stress on any one particular symptom or symptom-group in the psychosis under consideration, but rather consider the complete picture—the all-important transformation of the personality, of which the different symptoms are only parts.

The conclusions arrived at by the writer as the result of these experiments are as follows:

Firstly, that in mescaline we have an agent which can reproduce in the normal subject under experimental conditions all those phenomena which are found in the subject of the so-called psychogenic psychoses; the drug is therefore of the greatest importance as a method of approach to the understanding of the nature of mental disorder.

Secondly, that the various diseases commonly known as the psychoses are all variants of the same disease process; and that the causative agent is a toxic body, probably a toxic amine with chemical and pharmacological properties similar to those of mescaline, and having a selective action on the various higher centres of the brain. The particular centres attacked, and the nature and content of the resultant psychosis are determined by the psychophysical make-up of the individual patient and his past mental and environmental experiences.

Finally, that the correct method of approach to the problem of the understanding of the nature and treatment of the psychotic diseases lies in the spheres of biochemistry and pharmacology.

The references used in the compilation of this paper were: *Artificial Psychoses Produced by Mescaline*, by E. Guttmann; *Mescaline and Depersonalization*, by Guttmann and Maclay; and the accounts of the mescaline psychosis given in Lewin's *Phantastica*, and in W. Adams's *Drug Addiction*.

The preparation used in these experiments was a synthetic one of pure mescaline sulphate, kindly supplied specially for the purpose by Messrs. Burroughs Wellcome, of London.

A COMPARISON BETWEEN SOME OF THE EFFECTS OF ISOMYN (BENZEDRINE) AND OF METHYLISOMYN.*

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I. INTRODUCTION.

J. W. TREVAN has shown in some unpublished experiments on mice that the analeptic action of methylisomyn after paraldehyde injections is some 50% greater than that of isomyn (benzedrine), and that the median lethal dose of methylisomyn is 0·16 mgrm. per 20 grm. body weight, compared with 0·29 mgrm. per 20 grm. for isomyn. His findings in regard to the analeptic action have been recently confirmed by Jacobsen, Wollstein and Christensen (1), who found, after injecting mice with barbiturates, that methylisomyn had a somewhat greater analeptic action than isomyn, whereas the other isomyn derivatives they tested were less effective.

d-methylisomyn is closely related to isomyn and ephedrine, as shown in the following structural formulæ:

$C_6H_5.CH_2CHMe.NH_2$	$C_6H_5.CH_2.CHMe.NHMe$	$C_6H_5.CHOH.CHMe.NHMe$
isomyn	methylisomyn	ephedrine

Methylisomyn is the *N*-methyl derivative of isomyn and the desoxy derivative of ephedrine. It exists in two optically active forms, of which the dextro-rotatory modification has been selected for clinical trials. *d*-methylisomyn hydrochloride is a colourless crystalline solid, m.p. 173–174°. It is readily soluble in water, less soluble in alcohol. It is dextro-rotatory in aqueous solution and has a specific rotation of +21° for the mercury green line.

II. GENERAL EFFECTS OF ISOMYN ON HUMAN BEINGS.

Many experimental investigations have been made into the effects of isomyn on human beings. The main findings have been summarized by Guttmann (2) and by Riefenstein and Davidoff (3). The majority of workers emphasize that one of the difficulties in the way of generalizing about its

* A Report to the Therapeutic Trials Committee of the Medical Research Council.

effects is the large individual variability in susceptibility to the drug. Some subjects require as big a dosage as 40 to 50 mgrm. to get as marked an effect as others get from a dosage as low as 2·5 mgrm. Again, the effect of the same dosage on the same subject appears to vary considerably with his mental, physical and physiological state at the time he takes it. Bearing these difficulties in mind, however, we may say that the main psychological effects of isomyn on the majority of subjects are as follows:

(1) An elevation of mood in the sense of a lessening of depression or an increase in cheerfulness, leading sometimes to marked elation, facetiousness, and even uncontrollable laughter. Confidence is also increased and shyness decreased. Interest in and desire for work are increased, and feelings of fatigue are diminished.

(2) An acceleration of the stream of mental activity, and an increase in the content of thought. Alertness and perception are increased. Efficiency is improved and confusion diminished. The desire for sleep and the need for sleep are also diminished.

(3) A decrease in reticence or an increase in talkativeness, even to the point of garrulousness. Frequently subjects are unaware of the change, and will maintain with considerable verbosity that the drug is having no effect upon them. Sometimes, however, subjects are willing to admit that they are more talkative than usual.

(4) An increase in motor activity, in restlessness and irritability. This, with the increase in talkativeness, is often the major symptom noticed by an observer who is acquainted with the subject's normal speed of reaction. Riefenstein and Davidoff hold that mental, speech and motor activity are in general more often affected than elevation of mood.

(5) Other symptoms often noticed are a loss of appetite and a dryness of the mouth. Constipation has been found to result in some subjects, and both an increase and a decrease in the frequency of micturition have been reported. Both an increase and a decrease in sexual potency have been mentioned.

III. General Effects of Methylisomyn on Human Beings.

Similar effects to some of those mentioned above have been found when subjects have taken methylisomyn. Individual variability in susceptibility to the drug is found as frequently as with isomyn. Some subjects, too, regard a dose of, say, 5 mgrm. methylisomyn as stronger in its effects than a dose of 5 mgrm. isomyn; others report that they consider methylisomyn to be "milder" in its effects. So far as one of us is concerned a dose of 5 mgrm. methylisomyn gives similar subjective effects to one of 10 mgrm. isomyn, and a dose of 10 mgrm. methylisomyn is definitely an overdose, leading to a marked hyperkinesis and general restlessness and irritability.

Putting together the subjective reports of a number of reliable subjects,

and bearing in mind the variability in individual reactions to the drug, the following general statement may be made as to the effects of methylisomyn :

About half-an-hour after taking methylisomyn the subject usually gets a slightly euphoric feeling. Restlessness or agitation, with slight palpitation, follow, occasionally for as long as six or seven hours. After this there is sometimes a reaction, and the subject feels physically tired. This is followed, particularly if the subject lies down to rest, by mental clarity and mental activity, combined with physical lassitude. But in spite of the physical lassitude the subject is often prevented from going to sleep.

Subjects sometimes report that the drug is having no effect on them, though their behaviour is obviously different from usual. They have occasionally stayed to tell us much about themselves in a way that is quite different from their usual reserve and control. During such times, however, they have maintained that the drug is having no effect on them at all.

This short statement shows that from the subjective point of view the effects of isomyn and of methylisomyn are very similar.

Confirmatory evidence is provided by Jacobsen, Wollstein and Christensen (1) who made a controlled experiment on students aged between 18 and 33 years. The subjects were given a questionnaire to fill in at the end of every day over a period of time, irrespective of whether they had been given tablets on that day or not. Some of the tablets were made of an inert substance, others contained 15 mgrm. isomyn, 15 mgrm. methylisomyn or other isomyn derivatives. The questionnnaire asked them about their efficiency, their desire for work, their general feeling and mood, and also about various organic symptoms. The percentage of subjects who said they had experienced various symptoms is presented in Table I.

TABLE I.—(*From Jacobsen, Wollstein and Christensen.*)

Group.	Dosage.	Number of experimental days.	Increased efficiency.	Diminished efficiency.	Disturbed sleep.	Poorer appetite.	Palpitations.
Normal	..	566	17	9	6	5	0·4
Control	..	162	19	10	5	8	0
Isomyn	15	192	48	8	15	34	3
Methylisomyn	15	78	40	8	15	28	1

The table shows that there is a close similarity between the effects of isomyn and of methylisomyn. The percentage of subjects who noticed these effects when they were given *other* isomyn derivatives, however, was very much smaller, and in some cases negligible.

One other point of interest emerges from this table. Whereas the analeptic effect of methylisomyn on mice is significantly greater than that of isomyn, there is no such difference between the two substances in human beings—so far as the symptoms mentioned in the table are concerned. If anything the effect of isomyn is slightly stronger than that of methylisomyn, but the

differences between the two substances are small and they should not be regarded as significant.

IV. Excretion in the Urine.

The rate of excretion of isomyn and of methylisomyn has been measured by a method devised by Richter (4). There is considerable similarity between the curves. Two typical curves presented below show that maximal excretion

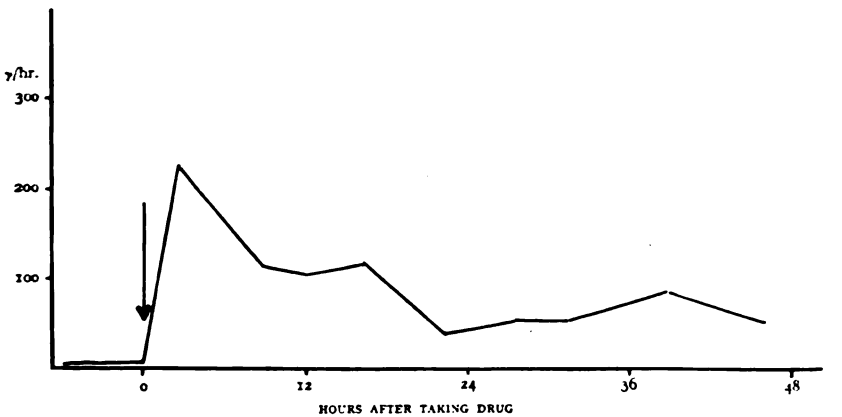

Fig. 1.—Rate of excretion in the urine of 10 mgrm. methylisomyn.

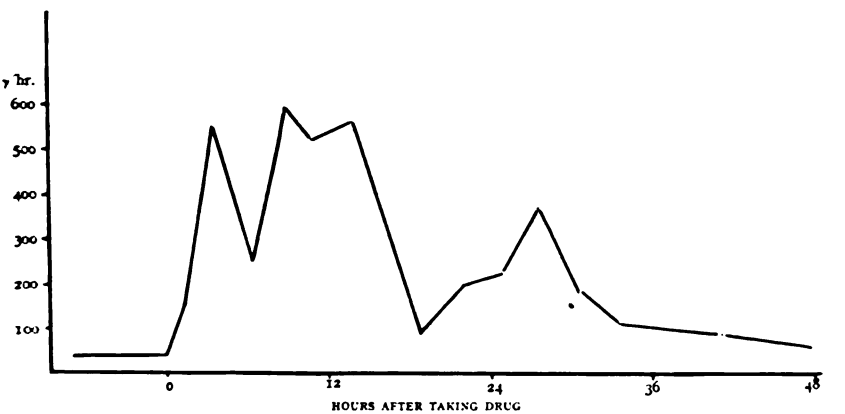

Fig. 2.—Rate of excretion in the urine of 20 mgrm. isomyn.

in the urine occurs between 4 and 13 hours after the administration of isomyn and between 3 and 7 hours after the administration of methylisomyn. The rate of excretion is, however, slow, and it continues for longer than 48 hours after administration in both cases. At the end of 48 hours 70% of the isomyn administered has been recovered, and at the end of the same period 56% of the methylisomyn.

V. Pulse-rate.

Many observers have claimed that the pulse-rate is increased after the administration of isomyn, but Guttmann (2), in his analysis of published work, finds that this is inconstant. In the experiment to be described in Section IX, six of the nine subjects had an increased pulse-rate under isomyn, two had a decrease, and one showed no change. The observations were made one hour after a dose of 20 mgrm. The maximum rise was 12 per minute.

With methylisomyn Jacobsen, Wollstein and Christensen (1) found palpitation in only 1% of their cases after a dosage of 15 mgrm. (see Table I), compared with 3% after 15 mgrm. isomyn. Working with four patients living their ordinary lives in the wards at the Maudsley Hospital, and using doses of 5, 10 and 15 mgrm. methylisomyn, Guttmann found a maximum increase of pulse-rate of 16 per minute.

In the experiments to be described in Section IX we found that one hour after a dose of 10 mgrm. methylisomyn eight of the subjects showed an increase in pulse-rate, three showed a decrease and three showed no change. The maximum increase was 14 per minute.

Another observation was made on one of the present writers when doing a strenuous addition test (see Section VII). His normal pulse-rate is 80, but under the influence of 10 mgrm. methylisomyn (which for him is an overdose), and under the exertion of the test his pulse-rate rose to a maximum of 144 per minute. No such increase has been found in any other subject.

VI. Blood-pressure.

Guttmann maintains that the best indicator for determining the effective dose of isomyn for any individual is the blood-pressure. He adds: "Given sufficient dosage by mouth benzedrine raises the blood-pressure. Marked changes are generally absent after doses of less than 20 mgrm., though susceptible persons may show elevations as high as 140/90 to 210/120 after 10 mgrm. per os. Systolic pressure tends to rise more than the diastolic; in other words the pulse pressure increases" (2).

In his observations on the effect of 5, 10 and 15 mgrm. methylisomyn on four patients living their ordinary lives in the wards of the Maudsley Hospital, Guttmann found a maximum increase of 15 mm. in blood-pressure occurring between 60 and 120 minutes after the administration of the drug.

In the experiment to be described in Section IX, eleven of the subjects showed an increase in blood-pressure one hour after taking 10 mgrm. methylisomyn. In one case the blood-pressure was slightly lower, and in two cases it was practically the same. The maximum rise was 18 mm.

In ten cases the pulse-pressure was increased, in four cases it was diminished.

The one subject doing the addition test described in Section VII has a normal blood-pressure of 115/75. Under the influence of 10 mgrm. methylisomyn this rose to 139/80 during the test.

The findings in regard to pulse-rate and blood-pressure, therefore, are on the whole very similar when the effects of isomyn are compared with those of methylisomyn.

VII. Addition Test.

One subject was practised each day for several weeks in an addition test, until he was adding a page of randomly selected numbers in never less than 1 min. 50 sec. Two hours after taking 10 mgrm. methylisomyn, however, he was given the test again and reduced his time to 1 min. 41 sec.—a decrease of 8%, which may be regarded as significant. Subsequently his score returned to between 1 min. 50 sec. and 1 min. 55 sec., and he never achieved so low a score again as he had obtained when under the influence of methylisomyn.

VIII. Intelligence Test Scores.

Sargant and Blackburn (5) showed in a controlled experiment that the effect of 20 mgrm. isomyn on patients in the Maudsley Hospital was to increase their scores in an intelligence test by about 8%. Bradley (6) has shown that the effect of 10–30 mgrm. isomyn (modal dose 20 mgrm.) on thirty children aged between 5 and 12 years was a marked qualitative improvement in school performance. Molitch and Eccles (7) found in a controlled experiment that when ninety-three boys, aged between 11 and 17 years were given a battery of tests, the effect of doses of between 10 and 30 mgrm. isomyn was to increase their scores on the tests on the average between 15 and 28% more than the corresponding increase after inert tablets instead of isomyn.

Sargant and Blackburn's technique was repeated with methylisomyn, Groups of patients were given an intelligence test (Cattell, Scale 2) one day. and on the next were given an equivalent form of the same test. On the second occasion half the patients were given methylisomyn and the other half were given an inert tablet made to be similar in appearance and in taste to the methylisomyn tablets.

The results indicate that the patients given 10 mgrm. methylisomyn improved their score on retesting, as compared with their control group, but that patients given 5 mgrm. did less well on retesting than their control group. The patient given 15 mgrm. did less well on retesting than he had on his first test. The average scores for the three groups, which are given below, are not nearly so clear as were the results of the same experiment with isomyn. All the patients were tested on the second occasion two hours after having taken the tablets.

TABLE II.—*Effect of Different Doses of Methylisomyn on Intelligence Test Scores.*

	Average score before tablet.	Average score after tablet.
(1) 5 patients given 5 mgrm. methylisomyn.	19·8	21·0
5 ,, ,, inert tablet . . .	20·0	22·4
(2) 3 ,, ,, 10 mgrm. methylisomyn	27·0	30·0
3 ,, ,, inert tablet . . .	24·7	24·0
(3) 1 patient ,, 15 mgrm. methylisomyn	34	27

IX. FURTHER EXPERIMENTS ON THE EFFECTS OF ISOMYN, METHYLISOMYN AND CAFFEINE ON PERFORMANCE IN PSYCHOLOGICAL TESTS.

1. *Description of Procedure.*

The selection of tests designed to evaluate the influence of drugs on mental processes has always suffered from certain technical difficulties. To eliminate the effects of practice it is obviously necessary for the subjects to undergo a long preliminary training till the condition of maximum efficiency has been reached. Such requirements necessarily restrict the number of subjects whose co-operation can be enlisted. Even when this difficulty can be overcome a much greater source of error is attributable to the emotional atmosphere in which such experiments are conducted. Few subjects of any intelligence can fail to be bored by the intrinsic nature of the tests, and this state of boredom or its reciprocal is responsible for the unevenness of results which characterize the majority of mental tests. This again can only be dealt with by averaging a much larger number of subjects than are likely to be available. Another yet more difficult source of error to deal with is occasioned by the expectations on the part of the subject that the drug will help him to overcome any difficulties in his task, and the general sensation of well-being engendered by isomyn and its congeners makes it difficult to rely on the administration of ineffective powders as controls.

It is for this reason that the authors decided to adopt a method which, as far as is known, has not been previously used in psychological experiments. They decided to observe certain movements and performances which are matters of such frequent use that they are unaffected by practice or familiarity of external conditions. The criterion of efficiency in such performances was that of time, and in order to avoid the difficulties which have been mentioned, the observations were done without the knowledge of the subject. The subject, then, comes into the room prepared for an ordinary mental test, but whilst one examiner is occupied with administering and recording this, the other observer is secretly timing a number of actions which are necessarily performed in the same order during the course of the experiment. These are the time taken for the subject to sign his name, the time taken to enter

and leave the room, sitting down and getting up, the selection and throwing of darts, and a number of similar actions. It is true that in themselves these observations will only control the time taken, and not the excellence of the performance. Such timing might, however, be reasonably expected to be related to performance.

It is proposed to extend this technique later so as to allow an appraisal of the accuracy and general efficiency of this performance which the subject does not recognize as part of the test.

In evaluating the results the tests have been divided into two groups—those which the subject knew were being scored (the " overt " tests) and those which were scored without his being aware of it (the " unconscious " tests). The subjects used in the experiment consisted of laboratory assistants, clerks, research workers and doctors. Ambulatory in-patients of the hospital were not used in this experiment.

On the first occasion the subjects were put through the tests so that they should become familiar with the procedure. They returned on three subsequent occasions to repeat the procedure, and on the second of these subsequent occasions they were given 5 or 10 mgrm. methylisomyn or 20 mgrm. isomyn one hour before, or 15 gr. caffein sodium benzoate twenty minutes before the beginning of the experiment.

No subject suspected he was being scored on the " unconscious " tests.

2. *Results.*

(a) *" Unconscious " Tests.*

(i) *Signature.*—There was a significant speeding-up of the time of writing the signature by both methylisomyn and isomyn. Thirteen of fourteen subjects signed their name quicker when under the influence of methylisomyn, and all nine subjects signed their name quicker when under the influence of isomyn. The average increase in speed by both methylisomyn and isomyn was approximately the same. Only five of the eight subjects in the caffein group signed their names faster when under the influence of the drug, and the average time under non-drug and drug conditions was approximately the same.

(ii) *Walking across the room.*—Methylisomyn and isomyn significantly speeded up the rate of walking, but caffein had no significant effect. Eleven of the fourteen subjects in the methylisomyn group walked faster when drugged, eight of the nine subjects in the isomyn group similarly walked faster when drugged, but only three of the eight subjects in the caffeine group walked faster under drug conditions.

(iii) *Rapidity of choosing column to add.*—Methylisomyn and isomyn again appeared to increase the speed of decision in this test, and caffeine may to some extent have increased it also. Ten of the fourteen subjects in the methylisomyn group chose their column faster when drugged, seven of the nine subjects

LESIONS OF THE SPINAL COLUMN RESULTING FROM CONVULSION THERAPY.

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IN the literature the opinion is repeatedly expressed that Von Meduna's convulsion therapy, which is so frequently applied, is a comparatively harmless treatment, and that this method, provided the necessary precautions are taken, occasions more or less serious complications only in rare cases. This notion, however, is contradicted by the observations of others, as well as by our own experience. Lesions of the skeleton and affections of the lungs (putrid pulmonary abscesses and activation of latent tuberculosis) are first among the serious complications which may arise from convulsion therapy.

Descriptions of lesions of the spinal column are comparatively few, although they develop so frequently and may so easily remain unnoticed that separate discussion is justified.

The publications of Stalker (1), Wespi (2), Van der Horst (3), Polatin, Friedman, Harris and Horwitz (4), B. T. Bennett, Fitzpatrick, Gerber and McCusker (5), Hamsa and A. Bennett (6), Palmer (7) and Valsö (8) induced us to make an X-ray examination of the spinal columns of those patients in our hospital to whom convulsion therapy had been applied.

Our examination comprised altogether 51 patients, viz., 13 males and 38 females. The ages of the males varied from 18 to 55; the females were between 21 and 56 years old. The average age of the whole group was 34·5, that of the males being 29·4, and of the females 38·9. The number of fits varied from 1 to 31, the average being 12·2. For the males and the females separately it was 15·7 and 10·9 respectively. It should be remembered that our material is a selection in that we were mainly concerned with patients who could not be discharged, i. e., in whom the result of the treatment was comparatively poor.*

A. *Compression-fractures* were found in 5 cases.

1. No. 5581. Man, aged 38. In January–March, 1938, he had 15 fits. He complained of backache after the first three; later his complaints became sporadic, but they reappeared at the time of the examination. There was then

* Our thanks are due to Prof. Dr. J. van Ebbenhorst Tengbergen and to Dr. J. W. Kamerling, who kindly looked through part of our photographic material.

(iii) *Drawing on paper.*—There was an increase in speed due to isomyn, but no significant increase due to methylisomyn or to caffeine. With isomyn eight of nine subjects were quicker, with methylisomyn six of fourteen, and with caffeine four of seven.

(iv) *Drawing on the blackboard.*—There was an increase in speed due to isomyn and possibly also due to caffeine. There was no increase in speed due to methylisomyn. With isomyn six of eight subjects were quicker, with methylisomyn only seven of fourteen. With caffeine four of six were quicker and the average increase in speed was more than that due to isomyn.

(v) *Writing the alphabet.*—There was a possible increase in speed due to isomyn, but no increase in speed due to methylisomyn or to caffeine. With isomyn six of nine subjects were faster, with methylisomyn six of fourteen, and with caffeine three of eight.

(vi) *Darts score.*—There was no significant improvement due to either methylisomyn or isomyn, and the score was worse after caffeine. With methylisomyn seven out of fourteen improved, with isomyn four out of nine, and with caffeine six out of eight were worse. It should be pointed out that the scores obtained by the subjects in this test were rather more variable than in most of the other tests. In this test the chance factor played an important part in determining the score of those who were not skilled darts players. If the results are confined to those who showed fair ability from the start it is found that the effect of methylisomyn is to improve the score, while the effect of both isomyn and caffeine is to lower it. This is shown in Table IV.

TABLE IV.—*Average Score of Fairly Able Darts Players under Non-drug and Drug Conditions.*

	Non-drug.		Methylisomyn.
(1) Five subjects . .	113	.	118
	Non-drug.		Isomyn.
(2) Three ,, . .	104	.	94
	Non-drug.		Caffeine.
(3) Four ,, . .	108	.	96

TABLE V.—*Effect of Three Drugs on Various "Overt" Tests.*

	Methylisomyn.			Isomyn.			Caffeine.		
	Number faster.	Non-drug (seconds).	Drug (seconds).	Number faster.	Non-drug (seconds).	Drug (seconds).	Number faster.	Non-drug (seconds).	Drug (seconds).
Figures test of memory and attention	11/14	94	89·6	5/8	99·6	94·6	6/8	106·2	100
Addition speed . . .	8/14	17·8	18·1	7/8	23·2	18·9	3/7	24·4	34·1
Drawing on paper speed .	6/14	8·6	8·3	7/9	5·9	5·1	4/7	7·3	6·9
Drawing on blackboard speed .	7/14	7·6	7·5	6/8	5·5	4·4	4/6	6·6	4·9
Writing the alphabet speed .	6/14	14·3	14·6	6/9	15·7	15·1	3/8	16·5	16·6
Darts score	7/14	89·7	91	4/9	83·3	8·9	1/8	87·6	79·1

(c) *Comparison between the Results of Different Subjects in the "Overt" and in the "Unconscious" Tests.*

Both isomyn and methylisomyn affected the performance of subjects in the "overt" and in the "unconscious" tests in a similar direction. That is to say, if one takes all the tests and counts the number in which any subject showed improvement or impairment when drugged, one finds that the subjects who showed more improvement than impairment in the overt tests also tended to show more improvement than impairment in the unconscious tests.

With methylisomyn eight of the subjects showed this agreement and in only two cases were the results of the overt and unconscious tests different from one another. In both these cases the number of improvements was greater than the number of impairments in the unconscious tests but less in the overt (the other four cases showed an equal number of improvements and impairments in either the overt or the unconscious tests). With isomyn five of the subjects showed the agreement and two disagreed. In these two cases the number of improvements was less than the number of impairments in the unconscious tests but greater in the overt. With caffeine only two subjects showed the agreement and two showed disagreement.

These facts may further emphasize the greater influence of methylisomyn and of isomyn than of caffeine on these tests. It is possible, however, that the dose of caffeine was not sufficiently large for any very definite results to emerge from its use.

X. Summary.

1. The general effects of methylisomyn on human beings in causing euphoria, heightened mental activity, heightened motor activity, increased talkativeness, and diminished sleep, are similar to those of isomyn, but there are marked individual differences in susceptibility to the drugs, and some contradictory results are found.

2. Curves for excretion in the urine show similar characteristics for both isomyn and methylisomyn. The excretion rate is slow in both cases, continuing for longer than forty-eight hours.

3. Methylisomyn and isomyn show similar effects on pulse-rate and blood-pressure.

4. Whereas the intelligence test scores of patients have been increased after doses of isomyn, the improvement after methylisomyn in a similar experiment was very small and probably not significant.

5. Experiments were performed to compare the effect of isomyn, methylisomyn and caffeine on the performance of various psychological tests. In some of these tests (the "unconscious" tests) the subjects did not know they were being timed or tested, in others (the "overt" tests) they did. The results showed that in the "unconscious" tests there was a close agreement

between the effects of methylisomyn and of isomyn. Both drugs had the effect of increasing the speed of writing, of walking, of decision and of dart-throwing. Caffeine, however, had no significant effect on the speed of these performances.

In the "overt" tests all three drugs increased the score in a test of attention and memory. Isomyn also increased the speed of adding, drawing and writing, though there was no significant increase in these tests due to either methylisomyn or caffeine. The score in a darts test was not improved by either methylisomyn or isomyn, and it was impaired by caffeine.

6. Methylisomyn and isomyn tended to affect a subject's performance in the "overt" and in the "unconscious" tests in the same direction, those subjects showing improvement in the overt tests also tending to show it in the unconscious tests. With caffeine, however, in the dosage used, there was no such indication.

The methylisomyn used in these experiments was supplied to us by Messrs. Burroughs Wellcome & Co., through the Therapeutic Trials Committee of the Medical Research Council. One of us (J. M. B.) is indebted to the Council for a part-time grant which enabled him to undertake the work.

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A REHABILITATION AND RESOCIALISATION SCHEME FOR PSYCHOPATHIC PATIENTS.

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SINCE the passing of the Mental Treatment Act in 1930 it has been noticed that a number of patients who have been discharged recovered from hospital seek readmission as voluntary patients within a comparatively short time of their discharge.

On investigating the factors which had caused a recurrence of their illness, it was found, in many cases, that inability to obtain any form of employment was often a predominant or deciding factor. An outstanding feature was that patients stated that when applying for employment or on obtaining work the production of their insurance cards (which, of course, were unstamped for the period of their stay in hospital) disclosed a period of unemployment which could only be accounted for by admitting that they had recently been discharged from a mental hospital, and this, in most cases, resulted in termination of their employment or failure to obtain the post.

It was thought that in a number of cases relapses might be avoided by placing the patient in a job before leaving hospital. But it was found that in many cases the patients' employment was unsuitable from a psychiatric point of view, while in others their trades were dying or overcrowded. In 1935, therefore, a scheme was evolved to attempt to deal with these two types of case, and the Mental Hospitals Committee of the L.C.C. gave the hospital a grant of £100 to be spent on the training of suitable patients.

In the early days of the scheme patients were found jobs mainly of the artisan type, but it was soon apparent that many of them were not of a type to be placed in labouring or other similar jobs, and in consequence of this the question of the re-education of patients, either in their own trade or in another more suitable one arose.

In order to cope with this problem a conference between representatives of the hospital, Mental Hospitals Department, and the Education Department

of the L.C.C. was held, and the experiment was keenly supported by the educational officials. Since that date there has been no difficulty in giving suitable candidates training at the numerous polytechnics and training centres in London. Before being sent for training each patient is seen individually by a representative of the Education Department in conference with the medical staff of the hospital, and the potentialities of each such patient explored in the light of his past experience, the type of mental illness and the ætiological factors.

The following two cases show some of the many points which have to be taken into consideration. One man had been a barman for some time prior to admission, and was admitted in an alcoholic confusional state, from which he recovered. It was found that previous to being a barman (a job which he disliked intensely, but which he had been obliged to take for economic reasons) he had worked for a time at engineering. While still a patient in hospital he went through a course of instruction in motor engineering, and he is now doing well in a garage. The other case was that of a window-cleaner who fell from his ladder and was admitted with an anxiety neurosis from which he made a good recovery, except for a residual fear of heights. He was unable to follow his previous employment owing to this fear, so arrangements were made for his instruction in leather work at the Cordwainers' Hall. Just before he was due to start his training there he received exceptionally full compensation; he therefore did not pursue his training, but opened a small shop, and is doing very well.

The problem is complicated by the financial position of the patient, and in this connection patients appear to fall into two categories:

(1) Those who have a home and sufficient resources to tide them over for a brief period;

(2) Those who are homeless and have no friends or relations willing to help.

Regarding the patients in the first category, an attempt was made to find work for them originally either through the Employment Exchange or through special contacts with employers, which were gradually made by the social worker. It must be remembered, however, that many patients who were discharged to their own homes had no difficulty in obtaining work of a kind. In many cases, however, when they came up against the realities of the labour market in competition with more efficient applicants, they were obliged to accept jobs with little or no prospects and for which they were unsuited, physically or temperamentally. Many undertook such jobs as canvassers, ice-cream vendors, etc., types of work which would appear to produce conditions conducive to further breakdowns. For these patients there is now a liaison with the Mental After-Care Association, which will be discussed in detail later in the paper.

For the patients in the second category, there is greater difficulty in carrying

out the process of rehabilitation. Theoretically it would appear desirable that the patient should find a job and make his plans for the future before leaving the security of the hospital. In practice it is difficult to follow this course, partly because of the necessity for personal interview and the geographical position of the hospital, and partly because residence in a mental hospital would appear to be a serious handicap in applying for work.

The following methods have, therefore, been used:

(1) Transfer to a Mental After-Care hostel where the patient can remain for a short period until a job is found, but where permanent accommodation is not available owing to the pressure of patients awaiting admission.

(2) Transfer to Church Army, S.O.S. and similar hostels not specially designed for the use of patients convalescent from a mental breakdown. In some cases this is adequate, but generally the facilities provided are insufficient for the needs of a patient who requires a reasonable period of security following discharge. In almost all cases material resources have been reduced to their lowest ebb and special efforts are required on the part of the patient to re-establish himself on that side alone, apart from any psychological problems arising out of the illness itself.

(3) Boarding-out in specially selected lodgings for some patients has been tried, and is particularly suitable, and on further exploration is likely to prove a constructive form of After-Care. One of the disadvantages, however, is the expense involved.

(4) Finding suitable posts (usually residential) direct from the hospital, with or without the co-operation of relatives or friends. This has only been possible in a few isolated cases.

Those patients whose type of work was unsuitable and who require re-education in a new trade, after a particular line of training has been decided upon at the previously-mentioned conference are sent home and attend the courses from their homes. Patients who are homeless either remain in hospital and travel up to town daily to attend classes, or are boarded out or live in hostels. When the scheme becomes enlarged and more homeless patients are found to need rehabilitation, owing to the pressure on beds in the hospital itself, it may be impossible to allow them to remain in hospital for the requisite time, and residence in a specialized hostel may become necessary.

As the results of the scheme appear to be so hopeful and more patients are being dealt with, the amount of work devolving in this connection on the medical staff and social worker has become excessive. Employment-seeking is a specialized and time-absorbing task, needing special contacts for its successful application, and it has been impossible with the present facilities to engage in it to its fullest extent. It is impossible, however, to ignore the fact

that if a really constructive form of after-care is to be developed, the rehabilitation of patients into suitable forms of employment, combined with the right kind of hostel or home surroundings for at least the period immediately following discharge, will be of the greatest importance.

In order to lessen the strain imposed on the hospital, an experimental liaison for a limited time has been arranged with the Mental After-Care Association who have set up a special department to deal with employment finding, and who have a trained social worker with special contacts with employers.

A number of patients, on recovering from their illnesses, feel capable of finding employment for themselves, and leave hospital in the hope of doing so. Quite a large number, however, find that obtaining work is not such an easy matter, and as contact is maintained with practically all patients discharged from this hospital at a follow-up clinic in London, many of the unsuccessful applicants for work attend there and are referred to the Mental After-Care social worker mentioned above. Although the liaison with the Mental After-Care Association has only been working for about twelve weeks, 10 patients have already been referred, of whom 7 have obtained work.

Below is given a table of diagnoses of the patients' illnesses which does not appear to require any comment, while a few typical case histories are appended.

DIAGNOSIS OF PATIENTS PLACED.

	Males.		Females.
Schizophrenia	6	Psychopath (dep.)	5
Depression	5	Schizophrenia	4
Psychopath (alcoholic)	4	Hysteria	1
Anxiety states	2	Epilepsy	1
Epilepsy	2		
Toxic-confusional	1		
Total	20	Total	11

TYPICAL CASE HISTORIES.

Male, aged 31, labourer, single. Admitted on 7.iv.37 in a state of depression with ideas of reference and delusions that he had venereal disease and gave off an odour. He had had two previous attacks of depression, for which he had been in mental hospitals, and had never had a settled job. He made an excellent recovery, and for twelve months prior to discharge attended one of the London polytechnics for training in electrical engineering. He has since obtained a job in this line and is doing well at it.

Female, aged 15, single, with no occupation. Admitted on 12.i.34 as a case of behaviour disorder. She was the offspring of an incestuous relationship between brother and sister, and had been the victim of several sexual assaults. She had been in various homes for treatment with no benefit, but while here she improved

considerably and eventually was placed in a domestic post and left the hospital on 8.i.37, and is still doing well at her job.

Male, aged 23, single, clerk. Was admitted on 3.xii.35 suffering from schizophrenia. After he had improved considerably and before his discharge he attended a course of training in bespoke shoemaking for several months at the Cordwainers' College, as he was not anxious to return to clerking and the prospects for him in this line of work appeared to be poor. He left the hospital on 24.ix.37 to take up a job and is doing well at the present time.

Female, aged 16, single, domestic. Was admitted on 18.v.37 in a state of depression. She had been in another hospital for almost a year, and previously had been ill-treated and sexually assaulted by her stepfather. She remained depressed for some time, but on 3.iii.38 was discharged and sent to suitable lodgings so that she could attend a polytechnic to learn shorthand, typing and commercial subjects. She attended for about fifteen months and is now in a job and getting on well; this in spite of her having previously been psychologically tested from the vocational point of view and advised against that type of occupation.

Female, aged 20, single, domestic. Admitted on 7.iv.37 in a state of depression. She remained extremely depressed for some time and made several suicidal attempts. She began to improve and was discharged recovered to the Mental After-Care Association on 7.v.38. As she was anxious to take up general nursing, an attempt was made to get her into a general hospital for training. This was done and she has been training for over twelve months, is happy and contented and about to sit for her preliminary nursing examination.

Of these 31 patients placed in jobs, 8 males and 1 female were trained in new trades, as follows:

One girl, who had been a domestic, was trained as a typist, and is now in work. One man, who had been a labourer, was trained in electrical wiring, while another man, who had been an electrician, was retrained in the work, and both obtained posts. One man, who had been a barman, was trained in motor engineering, and placed in work, while another man, who had been a car-cleaner, was trained as a gardener; another, who had been a clerk, was trained at the Cordwainers' College in the bespoke shoemaking trade, while three men, who had been a barman, farm-labourer and cellulose sprayer respectively, were trained as labourers, and all these patients were placed in work. In addition, seven females were placed in domestic jobs, two as typists, one as a seamstress, and one as a nurse in a general hospital.

Five male patients were placed in jobs as labourers, two as clerks, one as a garage hand, one as a motor engineer, one as a tobacconist, one as a research chemist, one as a seaman, and one as milk-roundsman.

All these twelve male and ten female patients were placed in jobs without any special training, and in most cases went back to their original type of work.

Of the thirty-one patients placed in jobs, twenty-five remain well and in work, four have relapsed, one committed suicide and one is in the hands of the police.

Financial Statement.

Below is appended a statement of the total amount expended since the inauguration of the scheme.

		£	s.	d.
1935–36	2 patients	44	18	10
1937	6 ,, ...	27	15	11
1938	4 ,, ...	107	14	7
1939 (6 months)	2 ,, ...	78	19	5
	Total .	£259	8	9

Although at first sight this appears to be a large sum of money, a large proportion of the sum has been expended on the maintenance of the patients during the period of training. In our opinion, however, this sum would have been considerably exceeded, as many of these patients would have been burdens to the State after their discharge for a considerable time, either as unemployed persons, or probably in certain instances as relapsed cases in mental hospitals, while the homeless would have had to be housed in workhouses or hostels.

In conclusion, we should like to emphasize the fact that when most of these patients are admitted to hospital they are not only workless, homeless and penniless, but psychopathic also, and would appear to belong to the social problem group. After a period of treatment, in which special encouragement from the occupational side is given, and they realize that they are not social outcasts and useless members of society, confidence and self-respect begin to appear again, and these potential members of the social problem group are enabled to take their places as self-supporting and useful citizens. The experiment is, therefore, being continued.

We should like to express our thanks to Miss E. Simpson, the social worker at St. Ebba's, for her valuable help and co-operation.

THE MEINICKE CLARIFICATION REACTION: FACTORS INFLUENCING NON-SPECIFIC ZONE PHENOMENA.

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DURING the course of research into an improved method of the Meinicke Klärungs Reaction (Ford Robertson, W. M., and Colquhoun, D. B., 1939) certain undesirable zone reactions occurred. This paper deals with some of the factors responsible for such non-specific precipitations.

Dunlop, E. M., and Sugden, S. (1934) have shown that, in addition to a zone selective for syphilis, a common zone of precipitation for syphilitic and non-syphilitic sera can be obtained with a cholesterinized human heart extract antigen. The non-specific precipitation was dependent on low electrolyte or serum concentration or both together.

Mackie, T. J., and Anderson, C. G. (1937), using a cholesterinized sheep heart extract, failed to confirm the above findings, but nevertheless showed that non-specific precipitation could be induced by a combination of low serum concentration and certain cholesterin-lipoid extracts. Although the antigens employed by us were composed of ox-heart and balsam of Tolu, the factors governing such precipitations were basically similar to those described by the workers mentioned. There is one exception, however, and this concerns the inactivation of the sera. While most of their work was done with inactivated sera (sera heated to 56° C. or higher), we consistently used uninactivated sera. Non-specific precipitation could be induced with most of our antigens merely by inactivating normal sera at 56° C. for 20 minutes. This phenomenon denotes a striking difference between the cholesterol and balsam of Tolu systems, the latter requiring fresh active sera for specificity. Both the original Meinicke extract (Meinicke, E., 1929) and the M.K.R. 2 (Meinicke, E., 1934) entail this procedure.

Under certain conditions of hydrogen-ion concentration, electrolyte molar concentration and serum dilution, in which the type of lipoid used also played a part, zonal reactions were observed.

This paper describes the various factors deemed responsible and the steps

taken to eliminate them. The difference between Meinicke's antigen and some of our experimental antigens was illustrated in the following manner: With strongly reacting syphilitic sera a feature of the Meinicke reaction is complete clarification of the fourth tube (known as the D tube), the other three tubes (A, B and C) failing to clear completely. The appearance of a similar but non-specific D tube zone reaction with our antigen-electrolyte combination on the part of certain normal sera was thus a possible source of error. In comparison the commercial Meinicke antigen exhibited only slight D tube precipitation, and it was therefore necessary to ascertain the causes for such variations.

Before entering into these, a summary of the components of the physico-chemical system of the Meinicke test and the colloidal principles underlying the reaction is given.

The commercial Meinicke antigen is a 2% alcoholic solution of Tolu balsam containing an "ether-rest" alcoholic solution of heart extract. The electrolyte of the disperse medium is composed of four solutions of increasing strength of sodium carbonate incorporated in a 3·5% sodium chloride solution. These "soda-salt" antigen mixtures form separate emulsions termed A, B, C and D. The sodium carbonate serves two purposes; it counteracts the acidity of the natural Tolu balsam, and by means of an increasing alkalinity from tubes A to D, puts a brake on clarification of the emulsion by syphilitic sera. Thus it was possible to grade sera as weak or strong reactors according to the range of carbonate molar concentration overcome. A reversal of this carbonate or alkalinity effect is a property, as already mentioned, of exceptionally strong syphilitic sera. Control of the reactivity of syphilitic sera was also effected by the strength of the heart extract (lipoid) in the antigen. Specificity and sensitivity are largely determined by the amount of lipoid present, this being ascertained by titration against normal and syphilitic sera, the other reagents remaining constant.

For the purposes of testing, 0·2 ml. of unheated serum is pipetted into tubes A, B and C, and 0·1 ml. into tube D, $\frac{1}{2}$ ml. of antigen emulsions A, B, C and D being mixed with the serum. After a period of 16–20 hours at room temperature (approximately 20° C.) the presence or absence of clarification is noted.

The Physico-Chemical Elements of the Meinicke Colloid System.

The following is a short description of some of the interactions taking place between the various components of the soda-salt and salt-antigen mixtures in terms of their colloid chemistry. It makes no pretence to finality, since our knowledge of organic colloids is far from complete.

When in the disperse state, i. e., in antigen-salt or soda-salt mixtures, the two organic colloids, balsam of Tolu and heart extract, appear to have a strong mutual affinity. Balsam of Tolu can be classed as an alcosol which, on contact with water, forms a colloidal emulsion that is hydrophobic in character, i. e., has little or no affinity with the dispersion medium. The gum particles are thus not readily hydrated. Such colloidal emulsions are highly sensitive to electrolytes, being readily discharged and precipitated. Most natural gums and resins have these characteristics. It is worth noting, however, that polymerized resins and also a sample of Damar resin tested by us were found to be completely lacking in affinity with phospho-lipins. Sumatra and Siam benzoins appear, on the other hand, to take an intermediate place in this group of organosols.

Lecithin and allied substances such as kephalin, in spite of their method of preparation, in which they resemble hydrophobic sols, differ from them in various

respects, so that they may be classed among the hydrophilic sols. They, according to the experiments of Koch, W. (1903), Porges and Neubauer (1908) and Long and Gephart (1908), are very insensitive to the salts of alkali metals, e. g., NaCl only coagulates weakly and KCl still less so. Alkalies disperse (peptize) markedly, a characteristic which bears on the carbonate concentrations used by Meinicke in making the alkaline end of his system more resistant to precipitation. The susceptibility to hydration or solvation strongly determines the protective action of the lipoids used apart from the other factors just mentioned.

According to Zsigmondy, R. (1924), protective colloids are those that by themselves are highly stable toward the influence of electrolytes, and capable of imparting this property to hydrophobic sols if added thereto. It seems that particles, e. g., lipoid, with an affinity toward the disperse medium (hydrophilic sols) can be adsorbed on the surface of hydrophobic particles, e. g., gums (those having the opposite affinity with the disperse medium), thus conferring protection by the formation of more or less thick layers. There are many protective colloids such as gelatine, proteins and surface active substances, e. g., soaps and especially saponins. All the evidence points to similar protective qualities of suitable phospholipins, with the exception perhaps of pure kephalin, which by itself would seem to perform a special role, as is later suggested in the text.

Thus we have two organic colloids of widely differing physico-chemical properties, which nevertheless have affinities of such a character that when placed under suitable electrolyte conditions, they are ideally suited as an indicating system for the presence of syphilitic colloid elements in human serum. That phospho-lipins and syphilitic globulins interact by virtue of some strong affinity is established, but precisely in what manner is not quite clear. Eagle, H. (1935), expresses the view that the reagen, a complement-fixing antibody in the proteins of syphilitic sera, acting in a cholesterinized heart extract emulsion, is deposited on the surface of the antigen particle as a unimolecular layer, and submits evidence in favour of this theory. Whatever takes place, a violent discharge of hitherto balanced electro-chemical forces around complex colloidal micellæ occurs, which results in aggregation of the disperse system and finally the phenomenon of clarification.

In our experience of the Meinicke system, the factors just outlined, as well as the composition of the lipoid, play an important role in determining a zone of reactivity selective for syphilitic sera. Comparison of a considerable number of lipoids and lipoid fractions prepared by us indicates how variable their protective and antigenic properties may be. Further reference to this is made in a subsequent section of this paper.

Hydrogen-ion Concentration and Molarity.

The electrolyte sensitivity of Tolu emulsions led to a closer investigation of the effects of hydrogen ion and molar concentration. For experimental purposes an almost neutral alcoholic solution of Tolu was prepared (Ford Robertson, W. M., and Colquhoun, D. B., 1939), with an acid value of 8.* By our method the acid value of natural Tolu varies between 80 and 100. A 2% emulsion was mixed with equal volumes of a range of buffer solutions of a pH from 2 to 10 in unit increments, the molar concentration of 0·1 being equivalent to 0·6% NaCl. The effect of pH on the aggregation and dispersion of the gum particles was clearly evident. At a pH of 2 precipitation was complete; at between 3 and 5 the colloid was respectively just below or above its iso-electric point.†

* Acid value: A figure originally intended to represent the weight in milligrammes of KOH required to neutralize 1 grm. of resin, but now employed as a relative and purely arbitrary index of the free-acid content of resins and balsams.

† Iso-electric point: If the potential difference between the layer of water or layer of dispersion medium which the particle has condensed around it and the outer liquid is zero, then the particle is at the so-called iso-electric point, according to the theory of Michaelis. It does not strictly hold good for colloids, however, because their iso-electric point also depends on the other ions present, not merely H and OH ions.

From pH 6 upwards, and more especially at 8, 9 and 10, solvation of the particles in the disperse medium was apparent from the occurrence of opalescence. Furthermore, throughout the whole range of tubes the aggregating and dispersing influence of H ions and OH ions respectively was recognizable, indicating their role in determining the size of the gum particles. By increasing the molar concentration from 0·1 up to 0·5, complete precipitation occurred over the entire range of buffer solutions. With the addition of lipoid to the balsam of Tolu precipitation could be averted, the proportion of lipoid necessary for protection being dependent on the H ion concentration and molar concentration of the buffer solutions. It can be concluded that while the hydrated lipoid was only slightly affected by H ion and molecular concentrations, as noted by Mackie and Anderson (1937), balsam of Tolu emulsions in particular, and also cholesterol, are the electrolyte labile elements of such colloid systems. The degree of affinity between lipoid and gum or cholesterol is therefore a factor also to be considered as much as the lipoidophile properties of the serum in determining zones of precipitation. A loose combination of the former will give rise to strong H ion and electrolyte effect, off-setting, for example, the role of the serum itself as a protective colloid. The apparent discrepancies between the results of one worker and another would seem to be explained by one or several of such variables. Illustrative of this has been our experience of non-specific zone phenomena occurring with our preparations of the Meinicke antigen. The following experiments indicate how H-ion and molecular concentration participate in zonal reactions. The hydrogen ion concentrations of the commercial Meinicke antigen are determined by the natural acid present in balsam of Tolu. These are cinnamic and benzoic acids in a combined concentration of between 25 and 30%. As the non-specific precipitation of the fourth or D-tube end of the system was more pronounced with the Institute's antigens, some difference in the acid content of the two antigens was suggested. This was verified from comparison of the two sets of hydrogen ion concentration figures. The four commercial antigen emulsions were respectively pH 5·1, 5·3, 6·0 and 7·4, while our series were pH 5·1, 5·2, 7·0 and 8·0. The difference lay chiefly in the D-tube, our antigen emulsion being more alkaline. We were thus led to incorporate a small quantity of an organic acid in our antigen, the effect of which is seen in Table I.

The range of tubes was extended in order to bring the commercial antigen up to the critical H-ion concentration of pH 8 for purposes of comparison, other factors, such as serum dilution and molecular concentration of sodium chloride, being kept constant. The commercial antigen maintained its stability over the extended range of alkalinity at tubes E and F, but our antigens again showed their susceptibility to a certain molar concentration and pH on the alkaline side, seen as a zone of precipitation at tube E. From this was inferred some qualitative difference between the lipoid of the two antigens. This point will be referred to in another section. Under certain conditions the role of

TABLE I.

	A.	B.	C.	D.	"E."	"F."
Meinicke soda-salt system 1·0% Na_2CO_3 in 3·5% NaCl	0·01	0·015	0·020	0·040	0·050	0·060*
Serum volume	0·2	0·2	0·2	0·1	0·1	0·1
Negative serum (Inst. Ant.)	±	—P.Tr.	—P.Tr.	—P.Tr.	+SH	—
,, ,, (M.K.R. Com.)	±	Tr.	..	—P.Tr.	—	—

* Figures represent grm. % sodium chloride.

Key to Table I.

— = Absence of precipitation with no disc.
—P.Tr. = Trace of precipitation without clearing.
+SH = Complete clearing, but with slight residual haze.

OH-ions, or alkalinity, at a specific molar concentration is thus demonstrated in their participation in zonal reactions.

SERUM AS A PROTECTIVE COLLOID: ITS DILUTION AS A FACTOR IN NON-SPECIFIC PRECIPITATION.

The antigen emulsions A and B of the commercial product are self-precipitating, i. e., the control tubes, after 16 to 20 hours, show complete or partial clearing. Free H-ions of the natural Tolu acids, giving a pH of about 5, in conjunction with the sodium chloride, bring this about. The addition of 0·2 ml. of normal human serum to 0·5 ml. of the antigen emulsion is sufficient to inhibit precipitation, the albuminous constituents acting as a protective colloid. Failing this, normal sera could not be differentiated from syphilitic. This protective function of serum is proportional to its concentration in the system, and in the Meinicke commercial test is also operative to some extent in tubes C and D.

In our earlier preparations of Meinicke antigen the method of extracting the lipoid resulted in a certain number of normal sera giving either D-tube precipitation or clarification, although relatively good specificity and sensitivity were obtained. On checking such sera against the commercial antigen, precipitation to a lesser degree was also found. As the volume of serum in this particular tube is half that in the preceding tubes, it seemed probable that even greater serum dilution would enhance this phenomenon. Six diminishing volumes of serum in 0·85% saline were tested against a D tube antigen emulsion. The results are set out in Table II, which is divided into two sections, A and B. These compare the commercial and Institute's antigens.

Since in Section A the D-tube antigen emulsion is stable *per se*, the precipitation leading to partial or complete clarification seen in the range of serum dilutions from 0·025 to 0·0015 ml. is due to some positive action by the serum. In Section B the antigen emulsion is also stable *per se*, but a wider zone of non-specific precipitation is evident. One-tenth of a ml. of serum, the amount

TABLE II.

A. *Meinicke Commercial Antigen.*

	A.	B.	C.	D.					
Serum concentration .	0·2	0·2	0·2	0·1	·05	·025	·003	·0015	·00075 ml.
Normal human serum	−D	−D	−D	−P.Tr.	−P.Tr.	+	+SH	±	−P.Tr.
Syphilitic human serum	+	+	+	+	+	+	±	−P.Tr.	−D

B. *Institute's Antigen.*

Normal human serum	−P.Tr.	−D	−D	+SH	+	+	+SH	±	−D
Syphilitic human serum	+	+	+	+	+	+	±	−D	−D

Key to Table II.

−D = Absence of clarification with formation of disc-like sediment.
−P.Tr. = Trace of precipitation without clarification.
−SH = Almost complete clarification except for slight haze in the supernatant fluid.
+ = Complete precipitation and clarification.

used normally in the D tube, causes clarification; one-fifth of an ml., however, is more than sufficient to prevent this. On the other hand, no difference between the two antigens with the syphilitic serum was noted. The precipitating syphilitic factor was, however, diluted out slightly beyond 0·003 ml., whereas a normal serum still operated beyond 0·0015 ml., thus suggesting a difference in the protein constitution of syphilitic and non-syphilitic sera under the experimental conditions. A certain minimal concentration of serum is thus required in the system to maintain specificity, and a limit to the use of serum dilution as a means of determining the precipitation power of syphilitic serum was thereby shown.

THE INFLUENCE OF EXTRACTIVES IN THE PREPARATION OF ETHER-REST LIPOID SOLUTIONS.

The results of the experiment detailed in Table I suggested some qualitative difference between the two lipoid solutions used in the commercial and Institute antigens. Maclean, H. (1927), in his book on *Lecithin and Allied Substances*, points out that many of the difficulties of comparing the results of one worker with those of another have been due to the quality and nature of the solvents employed. We have also found that the anhydrousness of the extractives is also another factor of greater importance than is generally recognized.*

In our initial lipoid preparations methylated ether (0·730 sp. gr.), which contains about 2% water, was used for preliminary extraction, these producing non-specific zone reactions. We were thus led to examine the effect of purer reagents such as those of "Analar" standards. "Analar" ether was found to eliminate zone phenomena to a great extent, only slight deposit in place of clearing being noticed in a few sera. When "B.P." acetone was used in place

* Colquhoun (*Laboratory Journal*, January, 1939) has shown the importance of using water-free ether for Kahn antigen preparations.

of methylated ether, however, lipoids giving an even more pronounced D-tube reaction were obtained. As this effect was ascribed to the acetone removing some soluble stabilizing or anti-zone lipoid element, it was thought that the loss might be made good by using mixtures of acetone and alcohol as the final solvent.

In the following experiment, set out in Table III, equal weights of methylated ether-rest heart powder were extracted for ten days with varying proportions of " B.P." acetone and absolute alcohol. From these lipoids antigens were made and tested for specificity and sensitivity and control emulsion stability, i. e., lipoid protective power. The weight in grammes % of five extracts was obtained by means of a 1-grm. torsion balance.

TABLE III.

Extract No.	Solvents. Acetone.	Alcohol.	Weight (grm. %).	Sensitivity. Weak + + + − Positive.	Specificity. − − − − Negative.	Antigen controls. A, B, C, D.
1	10 vol.		0·20	+ + + +	± ± ± ±	+ + + +
2	9 ,, +	1 vol.	..	+ + + +	± ± ± ±	+ + + ±
3	8 ,, +	2 ,,	..	+ + + +	± − − −	+ ± ± −
4	7 ,, +	3 ,,	0·32	+ + + +	− − − −	− − − −
5	6 ,, +	4 ,,	..	+ + + ±	− − − −	− − − −
6	5 ,, +	5 ,,	0·50	+ + + −	− − − −	− − − −
7	4 ,, +	6 ,,	..	+ + + −	− − − −	− − − −
8	3 ,, +	7 ,,	0·52	+ + + −	− − − −	− − − −
9	2 ,, +	8 ,,	..	+ + + −	− − − −	− − − −
10	1 ,, +	9 ,,	..	+ + + −	− − − −	− − − −
11		10 ,,	0·46	+ + + ±	− − − ±	± ± − −

It will be seen that the alcoholic extract (No. 11) produced the expected D-tube zone precipitation, while sensitivity was higher than alcoholic extracts containing acetone (Nos. 6 to 10). Protective capacity, as observed from the controls, was only slightly lower than extracts 4 to 10, but much greater than Nos. 1, 2 and 3. In the latter results compensation for the difference in lipoid concentration was duly made. Extracts 1, 2 and 3 indicate some relationship between the protective function of lipoid in the qualitative sense and specificity as seen by the controls. An exception to this is seen with pure lecithin which, though strongly protective to Tolu emulsions, is precipitated by normal sera. Some of the factors entailed are discussed in the next section.

A certain range of proportionality between acetone and alcohol supplied the balance of phosphatides requisite for antigenicity and avoidance of D-tube precipitation. The most suitable range appeared to be from 5 + 5 ratio to 1 + 9 acetone alcohol. The ratio of 3 + 7 was selected mainly on the grounds that the yield of lipoid by weight was optimum. In order to effect as great a degree of uniformity of phosphatide content as possible, "Analar" standard ether and acetone extractives have been used in the making of subsequent preparations of No. 8 extract for antigens. Extensive trials have proved these to be entirely satisfactory.

The Role of a Kephalin-like Phosphatide in the Elimination of Zone Reactions.

A study of the behaviour of lipoid fractions obtained from ether or acetone rest extractions of heart powder on lines similar to the preceding section, indicated that a certain ratio of kephalin (or some closely allied phosphatide) to lecithin was probably necessary for specificity.

Kephalin is insoluble in anhydrous ether, but is soluble if a small percentage of water be present (Maclean, 1927). Methylated ether is an example of a hydrated extractive. If this or "B.P." acetone is used to extract heart powder, some disturbance of the kephalin-lecithin balance can be expected, owing to the removal of water-soluble kephalin. On the other hand, a minimal disturbance of this ratio could be anticipated by using "Analar" ether.

If a certain proportion of kephalin, or some closely-allied substance, is necessary to maintain the antigenicity of the lipoid fraction, it follows that pure lecithin should be lacking in such properties. Substantiation of this view was afforded by the behaviour of B.D.H. egg yolk lecithin purified with cadmium chloride. Precipitation by normal sera occurred more readily at all soda-salt levels over a wider range of lecithin concentrations than with syphilitic sera. A similar but less pronounced lack of specificity was also noted in the cadmium chloride purified lecithin obtained from ox heart. Lecithin prepared by us according to Maclean's method did not behave as the cadmium preparation, and failed even to give a D-tube zone precipitation. There was reason to suspect, however, that the method of purification had not entirely disposed of kephalin. Supporting this was the following evidence: On evaporating the alcohol from the ox heart lecithin, dissolving the residue in methylated ether and then evaporating this off immediately, alcohol-soluble and alcohol-insoluble fractions were obtained. The latter fraction was found to be insoluble in acetone, but soluble in water and in chloroform. In so far as solubility tests are concerned, these are in every respect similar for kephalin.

Identical fractionation of the cadmium-purified egg yolk and ox-heart lecithin failed to show the presence of this kephalin-like substance.

So far, evidence as to the role of kephalin was purely circumstantial, and more direct experimental proof was indicated.

Kephalin was prepared according to the method given by Maclean (1927), and for the purpose of the experiment was dissolved in distilled water. Varying dilutions of this solution were made by adding 0·1 ml. to 0·9 ml. of an antigen giving pronounced zone reactions. Further dilutions were made by adding an equal volume of the kephalin-antigen mixture to an equal volume of antigen, this procedure being repeated until the requisite range of dilutions had been obtained. Normal and syphilitic sera were tested at the usual D-tube concentrations, i.e., 0·1 ml., and in four other dilutions as in Table I, in order

to accentuate the non-specific precipitations. The antigen emulsion represented the fourth tube of the Meinicke series containing 0·04% sodium carbonate. The possible effect of hydration on the antigens due to the water contained in the added kephalin was controlled and found to be absent. The stabilizing action of kephalin on a zone-producing antigen is clearly shown in Table IV.

TABLE IV.

Serum concentration.	Normal D-tube 1–2.	D-tube dilutions. 1–4.	1–8.	1–16.	1–32.	Antigen controls.	Kephalin concentration.
Positive serum	+	±	−P.Tr.	−D	−D	−D	*Nil.*
Negative ,,	±	+SH	+	+	+	−D	
Positive ,,	−D	−D	−D	−D	−D	−D	1/10–1/40 dilution.
Negative ,,	−D	−D	−D	−D	−D	−D	
Positive ,,	±	−D	−D	−D	−D	−D	1/80 dilution.
Negative ,,	−D	−D	−P.Tr.	±	+SH	−D	

On the one hand it eliminated the non-specific precipitation occurring with normal sera, and on the other it also inhibited precipitation by syphilitic sera if present in too great a concentration. For our kephalin preparation a concentration between 1/40 to 1/80 appeared to be required. A similar effect was shown on a cadmium chloride egg yolk lecithin which resulted in the absence of zonal precipitation characteristic of pure lecithin. Kephalin-like material obtained by fractioning ox-heart lecithin with methylated ether was likewise found to have stabilizing properties.

The antigenic role of two kephalin substances has been examined, a pure kephalin and a kephalin-like material from an alcoholic solution of heart muscle. Both react alike as zone eliminators, though they may not necessarily be strictly similar in chemical composition. In its colloidal properties kephalin is more readily hydrated than lecithin or mixtures of lecithin and kephalin. Pure lecithin is relatively insoluble in water, and requires to be in alcoholic solution before it is dispersed into a colloidal state. Our observations on the physical properties of kephalin in water indicate its affinity to soaps or saponins from the readiness with which frothing takes place on shaking. These and other more complex physical-chemical properties will partly explain the role of kephalin as an element of the phosphatide complex. It is suggested also that its stabilizing action seen in the experiment in Table IV is due to its marked hydrosol properties and surface tension activity. This should enable the likewise hydrated serum proteins and their associated electrolytes to come into more intimate contact with the outer layers of the protective colloidal micellæ of the antigen emulsion. In this way the protective function of normal serum protein is likely to be more effective, thus avoiding non-specific precipitation due to some degree of affinity between normal serum globulins and lecithin.

Excessive kephalin has been seen to reduce the precipitation by syphilitic

sera, an observation which may be accounted for by the adsorption of the syphilitic globulins on to the kephalin, thereby reducing its linkage with lecithin, which is a highly protective agent for the gum particles. If this assessment be correct, kephalin and its analogues are likely to behave as antigenic factors, while the function of lecithin will be mainly restricted to a protective role. A suitable balance of these two phosphatides appears to be necessary at least for the Meinicke colloid system.

Differentiation between normal and syphilitic sera is therefore dependent on a balance of numerous factors, namely, hydrogen-ion concentration, provided by the balsam of Tolu, which can be graded by sodium carbonate, electrolyte molarity obtained by sodium chloride, serum dilution and the phosphatide composition of tissue extract.

Conclusions and Summary.

1. Zonal precipitation of the Meinicke soda-salt electrolyte system by non-syphilitic sera has been demonstrated by the use of certain lipoid fractions.

2. Dilution of zonal reacting non-syphilitic sera resulted in enhanced precipitation.

3. It has been shown that highly-purified specimens of lecithin are unsuitable owing to their interaction with non-syphilitic sera.

4. Kephalin or kephalin-like substances, when added to pure lecithin antigens, inhibit this non-specific interaction.

5. A brief description of the physico-chemical nature of the colloids and their inter-relationships has been attempted.

6. The importance has been shown of using extractive reagents of known water content and chemical purity in the preparation of ether-rest heart muscle extracts for the Meinicke reaction.

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LESIONS OF THE SPINAL COLUMN RESULTING FROM CONVULSION THERAPY.

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IN the literature the opinion is repeatedly expressed that Von Meduna's convulsion therapy, which is so frequently applied, is a comparatively harmless treatment, and that this method, provided the necessary precautions are taken, occasions more or less serious complications only in rare cases. This notion, however, is contradicted by the observations of others, as well as by our own experience. Lesions of the skeleton and affections of the lungs (putrid pulmonary abscesses and activation of latent tuberculosis) are first among the serious complications which may arise from convulsion therapy.

Descriptions of lesions of the spinal column are comparatively few, although they develop so frequently and may so easily remain unnoticed that separate discussion is justified.

The publications of Stalker (1), Wespi (2), Van der Horst (3), Polatin, Friedman, Harris and Horwitz (4), B. T. Bennett, Fitzpatrick, Gerber and McCusker (5), Hamsa and A. Bennett (6), Palmer (7) and Valsö (8) induced us to make an X-ray examination of the spinal columns of those patients in our hospital to whom convulsion therapy had been applied.

Our examination comprised altogether 51 patients, viz., 13 males and 38 females. The ages of the males varied from 18 to 55; the females were between 21 and 56 years old. The average age of the whole group was 34·5, that of the males being 29·4, and of the females 38·9. The number of fits varied from 1 to 31, the average being 12·2. For the males and the females separately it was 15·7 and 10·9 respectively. It should be remembered that our material is a selection in that we were mainly concerned with patients who could not be discharged, i. e., in whom the result of the treatment was comparatively poor.*

A. *Compression-fractures* were found in 5 cases.

1. No. 5581. Man, aged 38. In January–March, 1938, he had 15 fits. He complained of backache after the first three; later his complaints became sporadic, but they reappeared at the time of the examination. There was then

* Our thanks are due to Prof. Dr. J. van Ebbenhorst Tengbergen and to Dr. J. W. Kamerling, who kindly looked through part of our photographic material.

slight pain on pressure, which soon disappeared. The photograph (30.vi.39, see Fig. 1) shows compression-fractures of Th. IV, V, VI and VII most marked in Th. V. The nucleus pulposus is pressed into the body of Th. VII. There is evident kyphosis.

2. No. 5675. Man, aged 55. In March, 1939, he had one fit (azoman), after which he complained of pains in the loins, which soon disappeared. The photograph (10.viii.39, see Fig. 2) shows a compression-fracture of L. I. On the antero-posterior photograph there is an angle of spondylosis deformans seen on Th. XI.

3. No. 5522. Man, aged 31. On June 16, 1939, he had one fit (azoman), and for a short time complained of backache. The photograph shows slight compression-fractures of Th. VI and VII, which are wedge-shaped and have an irregular upper edge (20.vi.39).

4. No. 5613. Woman, aged 31. In July, 1937, she had 16 fits and did not complain of pain. The photograph (12.vii.39) shows evident compression-fractures of Th. VI and VII, while in the antero-posterior view Th. IV is seen to be lower on the right than on the left.

5. Man, aged 31. In June and July, 1938, he had 9 fits, and especially after the first attacks he complained of a violent backache, which, however, soon disappeared. In the photograph taken by our colleague, Dr. C. P. H. Teenstra (Fig. 3), and here published with his kind permission, Dr. Teenstra took the abnormalities of the vertebræ to be traumatic. The photograph (January, 1939) shows compression-fractures of Th. VI and VII, which are wedge-shaped. The superficial layers of these vertebræ do not show evident defects, but those of Th. VIII, in which a " Knörpelknötchen " without sclerosis, hence probably of recent date, has developed, do.

B. *Lesions of the vertebral bodies (infraction) without evident compression* were found in 3 cases.

6. No. 5540. Man, aged 22. In October–November, 1937, he had 4 fits and did not complain of pain. In the photograph Th. VII is slightly wedge-shaped. The upper as well as the lower edges are somewhat concave, whereas the front is a little convex. Th. VI and VIII are not altogether normal.

7. No. 5535. Man, aged 33. In June–August, 1937, he had 25 fits, complaining of a pain in the back after the first 4. In the photograph (21.vi.39) Th. VI, VII and VIII are slightly wedge-shaped, while Th. VI is plainly convex anteriorly. In Th. VIII the nucleus pulposus seems to be slightly pressed into the vertebral body.

8. No. 5587. Woman, aged 34. In May–June, 1939, she had 10 fits, and for a short time complained of a slight pain in the back. The photograph (3.vii.39) shows slight lesions of Th. VI. The upper and lower edges are irregularly shaped, the front is convex. There may be some callus formation on the anterior part of the lower edge. Presumably Th. VII is also defective.

C. We observed *doubtful lesions of the vertebral body* in 5 cases.

In a 36-year-old woman (15 fits) the upper and lower edges of Th. V and VI are somewhat irregular, the spinal column there showing a slight bend ; in a woman, aged 45 (15 fits), with spondylosis deformans, there is doubtful callus formation and an indication of wedge-shape in Th. VII; in a woman, aged 32 (5 fits), a line in Th. VI seems to point to infraction; in a woman, aged 32 (14 fits), there is doubtful infraction in the upper anterior part of Th. VI, VII and VIII ; in a woman, aged 42 (8 fits), Th. VI and VII are wedge-shaped, with irregular upper and lower edges. There is kyphosis, but it is not clear whether the abnormalities were caused by violence, or if it is a case of adolescence kyphosis.

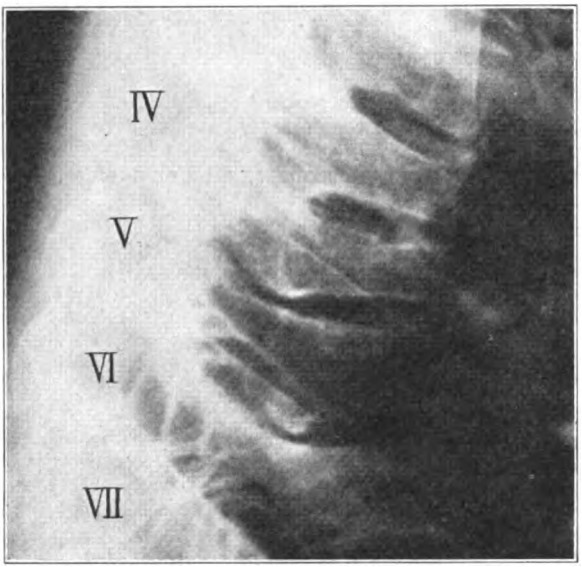

FIG. 1.—Compression-fractures of Th. IV, V, VI and VII after cardiazol treatment.

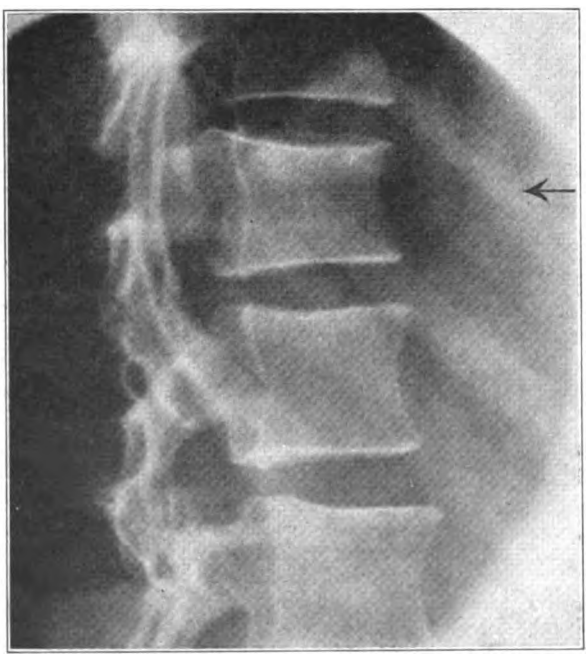

FIG. 2.—Compression-fracture of the first lumbar vertebra after one azoman fit.

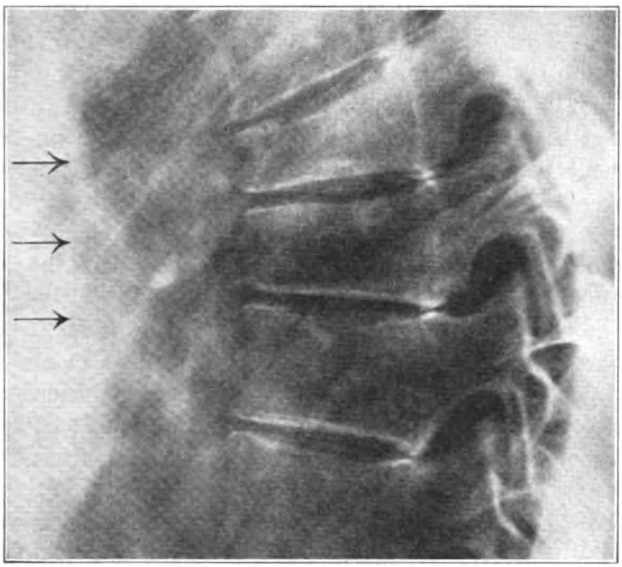

FIG. 3.—Compression-fractures of Th. VI and VII. Th. VIII shows a " Knorpelknötchen ". After cardiazol treatment.

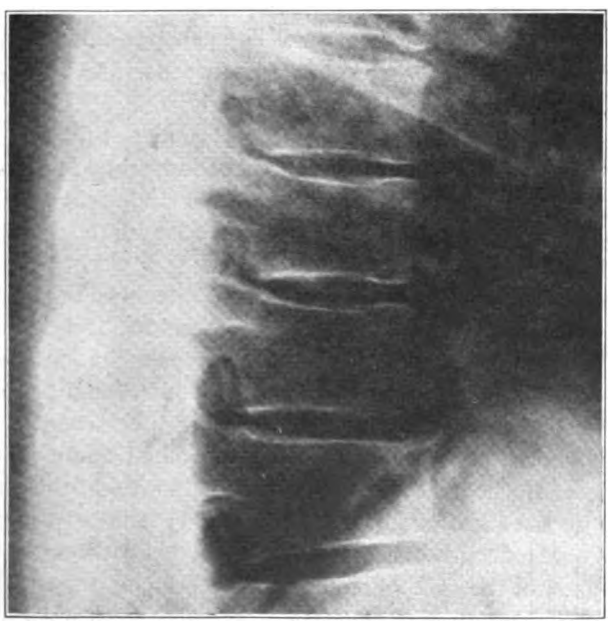

FIG. 4.—Compression-fracture of Th. XI in a case of epilepsy.

D. The so-called "*Schmorl'sche Knötchen*", usually multiple, were found in 17 patients. This is a comparatively high figure in comparison with the result of Wissing's investigation (9), where in 421 cases "Knorpelknötchen" were found in 13·5%. Our low absolute figures do not justify any positive conclusion, but we are inclined to assume some causal connection between the lesions and the fits, especially in several of our cases there was no evident thickening round the herniæ, which makes recent development seem probable, and also because the majority of the "Knötchen" were found in the central thoracic vertebræ, whereas they usually occur on the lower thoracic and on the lumbar vertebræ.

E. In 4 patients we saw one or more *very flat intervertebral discs.*

In 2 of them we also found the doubtful infractions mentioned under C, which two signs together may point to a traumatic cause. In another case there were already "Knötchen" with a considerable calcium accumulation near the narrow disc a short time after the last fit, so that there a connection between trauma and fit is not likely.

F. *Non-traumatic abnormalities* were found in 4 patients, viz., twice spondylosis deformans, and twice a wedge-shaped vertebra with a fine outline and structure, without any other peculiarities.

G. A perfectly *normal spinal column* was found in 25 of our patients.

The 5 men and 24 women of Groups F and G had an average age of 24·4 and 37·5 respectively. The men had an average of 21, the women of 11·5 fits. It is worth while to compare these figures with those of the 6 men and 2 women of Groups A and B, whose average ages were 35 and 32·5 respectively, the men having had an average of 10·5 and the women 13 fits. As in Cases A2 and A3, where the abnormalities already developed after one fit, these figures point to the comparatively small significance of the number of fits met with.

Altogether, therefore, we found lesions of the vertebræ in 8 patients, which can be attributed with certainty to the violence caused by the cardiazol (or azoman) attacks, because in none of these patients was there any considerable trauma in the anamnesis.

The injuries found agree with those often described in the literature on tetanus as a consequence of the action of the muscles. The explanation which Reddingius (10) has given for the development of lesions in that disease we also consider applicable to cardiazol attacks. Reddingius supposes that, owing to the contraction of the abdominal muscles attached to sternum and ribs, which he assumes to work like a lever, the spinal column is bent forward while, exactly in the central and upper part of the chest, this bending is not counteracted by the sacrospinalis muscle. This hypothesis is supported by the observations made during artificial attacks, in which considerable bending of the upper part of the spinal column is often seen to occur. Moreover, the fact that the same vertebræ are preferably affected in tetanus would point to analogy in the ætiology.

It is not clear, however, why such lesions do not attend ordinary epileptic fits, which, as a matter of fact, show more similarity to a cardiazol fit than the latter does to a tetanus attack. As far as the psychiatric literature is concerned, we have found no mention of this problem. It is true that the muscle contractions seem much stronger in an artificial attack than in epileptic fits, and it must be owing to this circumstance that affections of the skeleton of the limbs are occasionally found after cardiazol, but hardly ever—except luxations—after epileptic fits. Yet, if the difference is only a quantitative one, affections of the spinal column should also be found, although less frequently, in epileptic subjects, considering the great frequency of spinal lesions after cardiazol.

These considerations have induced us to make a Röntgen examination of a number of epileptic subjects. We selected 21 patients, 6 males and 15 females, who had often had, or were still often suffering from fits. The ages of the males varied from 25 to 62, the average being 42·3, the females were between 26 and 58 years old, the average age being 42·4. Here follow the results of this investigation :

A. A *compression-fracture* was found in one case.

1. No. 5638. A woman, aged 51. She has no complaints which point to an affection of the spinal column. The photograph (13.vii.39) gives the following picture (see Fig. 4) : Th. XI is flat and wedge-shaped. The upper edge has a double line anteriorly and is rostriform.

C. In one case we saw a *doubtful lesion of a vertebral body.*

2. No. 5651. A man, aged 62. He has no complaints, but on account of his deep dementia it is impossible to make out whether the spinal column is perfectly flexible in all directions. There are certainly no severe functional disturbances. The photograph shows Th. VI to be wedge-shaped. Th. VII is very flat with indented upper and lower edges. Th. VIII has the same abnormality to a less extent. In this vertebra the concave anterior edge is striking. There is some slight but evident osteoporosis. It cannot be ascertained which is of greater significance, the effect of the repeated traumata or the osteoporosis.

D. "*Schmorl'sche Knötchen*" were found in 4 cases.

E. In one case there were some *very flat intervertebral discs.*

F. *Non-traumatic abnormalities* were seen in 3 cases, namely once some slight osteoporosis, once a slight spondylosis deformans, and once an *abnormality* which was reminiscent of Bechterew's disease. The case mentioned under C is not included here.

G. A *perfectly normal spine* was found in 11 cases.

Our material is not extensive enough to draw any positive conclusions from the above findings in epileptic patients. Chance may have played a more important role than the epileptic fits. Although there is no evidence of exterior injury in the anamnesis of either patient, the possibility of injury due to a fall during the attacks should be reckoned with. So there is no proof that

there is a connection between the abnormalities found and the muscle contractions in the attacks. In view of our investigation, however, the assumption that there is such a connection is certainly justified. Therefore it seems desirable to us that others, who have more extensive material at their disposal, should make a similar examination of epileptic subjects.

The lesions of the spinal column found by us after cardiazol treatment do not yield a standard which allows us to determine a percentage which would be of universal application. The ratio found by us is considerably lower than that given by Polatin *et al.*, but it is high enough for us to agree with the authors mentioned when they conclude that the complications described are of frequent occurrence, and of a serious nature. It is true that only one of our patients has any serious complaints; but we should allow for the possibility that disturbances develop later on, such as, for instance, Kümmell's disease, or herniæ of the nucleus pulposus in the spinal canal, although probably this chance is not great. The complications are of a serious nature, because during convulsion therapy *we have no control whatever of the seriousness of the injuries which may ensue.*

We are not optimistic about the possibility of somehow preventing injuries. Polatin *et al.* have thought of making the patient suffer the attack lying on his side in a strongly flexed position. Hamsa and A. E. Bennett give lumbar anæsthesia in order to eliminate the muscles of the lower part of the body; in other cases they give the fits during insulin hypoglycæmia. Palmer makes vague mention of three possibilities, viz., curare, lumbar anæsthesia, and finding the best possible position. Valsö applies a preliminary medication with calcium gluconate, and tries to mitigate the convulsions with calcium and barbituric-acid preparations.

In our opinion, however, these attempts do not alter the fact that the lesions found should be a strong counter-indication to the application of convulsion therapy. For all that, it does not seem desirable to abandon this treatment altogether; the beneficial results in certain cases are too great, and greater than the chance of injury. The indications, however, should be stronger than is now customary, and it should be borne in mind that the interference is of a serious nature. In cases of hesitation between convulsion therapy and insulin cure, this consideration ought to turn the balance in favour of the latter.

For obvious reasons the following precautions should finally be taken:

1. If possible a Röntgen examination should be made beforehand.
2. This examination should be made in any case if the patient complains of a backache.
3. If possible a Röntgen examination should be made after the treatment, even if the patient does not complain and, eventually, after every third or fourth attack.
4. Any abnormalities found should be regularly controlled röntgenologically.

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Summary.

In 51 patients who had been treated according to Von Meduna's convulsion therapy, the authors found 8 cases of more or less serious lesions of the spinal column; in 21 epileptic subjects 1 certain and 1 doubtful traumatic injury were found. The indications for convulsion therapy should be studied with great care, and a Röntgen examination is necessary as soon as the patients complain of pains in the back.

Resumé.—Les auteurs trouvaient chez 8 entre 51 malades traités d'après Von Meduna des affections plus ou moins graves de la colonne vertebrale; chez 2 entre 21 épileptiques ils trouvaient 1 lésion certaine et 1 lésion dubieuse. Il faut limiter l'indication de la thérapie convulsante et il est nécessaire de faire un examen radiologique aussitôt que les malades accusent des douleurs au dos.

Zusammenfassung.—Bei 8 von 51 Patienten die nach Von Meduna behandelt wurden fanden die Autoren mehr oder weniger schwere Affektionen der Wirbelsäule; bei 2 von 21 Epileptikern wurden 1 sichere and 1 zweifelhafte Läsion gefunden. Die Indikation zur Krampfbehandlung muss sehr streng gestellt werden, und Röntgenuntersuchung ist notwendig sobald die Kranken über Rückenschmerzen klagen.

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OBSERVATIONS ON THE SYMPTOMS OF HYPERINSULINISM IN RELATION TO BLOOD SUGAR AND KETO-BODIES OF THE BLOOD.

By RUDOLF FREUDENBERG, M.D.Freiburg, L.R.C.P.&S.E.,
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THE investigation described below has as its object the determination of the influence of massive doses of insulin, such as are used in treatment of schizophrenia, on the concentration of the sugar and the ketone bodies of the blood with a view to analysing some of the causative factors of the symptoms of hyperinsulinism.

The changes in the blood sugar during insulin-shock treatment of schizophrenia have been investigated by several workers (1, 2, 3). They concluded that there was a disparity between the blood-sugar level and the severity of hypoglycæmic symptoms. This fact led to much discussion as to whether the symptoms of hypoglycæmia were due to some toxic action of the insulin itself rather than to the lowered blood sugar. Others (4 and 5) regarded some products of metabolism as possibly responsible for the convulsions occurring during hypoglycæmia, especially mentioning pyruvic acid and methylglyoxal. Finally the diminished use of oxygen of the tissues during hypoglycæmia was considered of great importance by some workers (6). Not all the possible factors leading to the symptoms of hypoglycæmia can be discussed here, only some of the most important ones being considered. Himwich (11) recently reviewed the work concerning the effects of hypoglycæmia on the brain.

The procedure adopted has been to inject large doses of insulin into the fasting patient sufficient in all cases to produce hypoglycæmic coma and sometimes convulsions, the coma dose having been previously determined by gradually increasing the insulin dose by 5–10 units per day. After several hours, interruption of coma was carried out by a solution of 200 grm. of glucose administered by stomach tube, the patient finally awaking about half-an-hour afterwards.

Samples of blood were obtained at approximately half-hourly intervals in 4 curves and at about hourly intervals with the remaining 15.

METHODS.

The blood sugar was determined according to the method of Hagedorn and Jensen modified by using a Folin and Wu blood filtrate. In 4 curves true blood-sugar values were obtained by fermenting the glucose with yeast (7).

Two different methods were used for the estimation of the ketobodies. Firstly, the bisulphite binding capacity of the blood introduced by Clift and Cook (1932)

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(8) was determined; estimates the bisulphite binding substances (B.B.S.), such as pyruvic acid, methylglyoxal and other ketone and aldehyde compounds. Secondly, acetone and aceto-acetic acid were estimated by the ordinary distillation method (9). For both methods Folin and Wu blood filtrates were used.

RESULTS.

True Blood Sugar (*Ref.* 3).

	Dose units.	Time after injection.	True blood sugar.	Clinical notes.
No. of curve, 1*a*. Patient V.	155	..	96	Fasting.
		1 00	13	..
		1 30	15	Slight perspiration.
		2 05	14	Drowsy.
		2 40	20	,,
		2 45	..	Unconscious corneal; reflex positive.
		3 00	15	Ditto.
		3 45	12	,,
		4 15	14	,,
		4 45	13	,, negative.
		4 55	11	200 grm. glucose by stomach tube.
		5 08	51	Awake.
No. of curve 2*a*, Patient W.	80	..	79	Fasting.
		0 15	38	..
		0 45	14	Slight perspiration.
		1 15	12	Drowsy.
		1 45	9	,,
		1 55	..	Unconscious corneal; reflex positive.
		2 30	6	Ditto.
		2 45	2	,,
		3 35	14	,, 200 grm. glucose by stomach tube.
		3 45	52	Awake.
No. of curve 3*a*, Patient X.	120	..	82	Fasting.
		0 25	96	..
		1 00	55	..
		1 30	30	..
		2 15	19	..
		3 15	26	Drowsy; perspiring
		3 30	28	,,
		3 00	27	Unconscious; corneal reflex positive.
		4 30	39	Awakes spontaneously; 200 grm. glucose.
No. of curve 4*a*, Patient Y.	55	..	79	Fasting.
		0 20	60	..
		0 35	50	..
		1 05	47	Perspiring.
		1 35	28	Drowsy.
		2 05	24	,,
		3 20	28	Unconscious; corneal reflex positive.
		4 05	26	Ditto, negative.
		4 20	22	,, ,, 200 grm. glucose by tube.
		4 35	75	Awake.

Ordinary Blood Sugar and Keto-bodies.

	Dose units (insulin).	No. of specimen.	Time after injection. hr.	min.	Glucose mgrm. %	B.B.S. mgrm. %	Acetone aceto-acetic acid mgrm. %	Clinical notes.
		1	..	..	..	2·3	..	Fasting.
No. of curve 1, Patient A	85	2	1	00	..	1·5	..	Drowsy.
		3	2	00	..	1·1	..	Unconscious; corneal reflex positive, plantar flexor response.
		4	3	00	..	1·1	..	Unconscious; corneal reflex positive, Babinski positive both sides.
		5	4	00	..	1·2	..	Ditto.
		..	4	30	..	..	..	200 grm. glucose by stomach tube.
		6	5	00	..	3·3	..	Awake.
		1	..	..	113	4·7	..	Fasting.
No. of curve 2, Patient A	80	2	1	00	45	2·6	..	Unconscious; twitchings, corneal reflex positive, plantar flexor response.
		3	2	00	38	4·4	..	Twitchings ceased, awake.
		..	2	15	..	..	..	Unconscious; corneal reflex positive, plantar flexor response, twitchings returned.
		4	3	00	41	3·8	..	Unconscious; restless.
		5	3	30	36	3·7	..	Unconscious; Babinski positive both sides.
		..	4	00	..	..	..	Stridor. 200 grm. glucose by stomach tube.
		6	4	45	68	4·1	..	Awake.
		1	..	..	84	5·6	..	Fasting.
No. of curve 3, Patient B	240	2	1	00	35	4·8	..	Drowsy.
		3	2	00	31	5·3	..	"
		..	2	40	..	..	..	Unconscious; corneal reflex positive, plantar flexor response.
		4	3	00	31	4·1	..	Unconscious; Babinski both sides.
		5	4	00	28	4·8	..	Unconscious; corneal reflex negative.
		6	4	55	28	3·2	..	Ditto. Glucose 200 grm. by stomach tube.
		7	5	20	64	6·7	..	Unconscious; corneal reflex again positive, Babinski both sides; restless, hypertonic, opisthotonus, rolling movements, flushed face. 9·9 grm. glucose intravenous.
		8	6	10	40	6·2	..	Still unconscious; waking delayed.
		..	..	..	..	..	..	Awake (complete amnesia).

	Dextrose units (insulin)	No. of specimen	Time after injection hr. min.	Glucose mgm. %	B.B.S. mgm. %	Acetone and diacetic acid mgm. %		Clinical notes
curve 1, ient A	85	1	..	..	2·3	..		Fasting.
		2	1 00	..	1·5	..		Drowsy.
		3	2 00	..	1·1	..		Unconscious; corneal reflex positive, plantar flexor response.
		4	3 00	..	1·1	..		Unconscious; corneal reflex positive, Babinski positive both sides.
		5	4 00	..	1·2	..		Ditto.
		..	4 30	..	..	..		200 grm. glucose by stomach tube.
		6	5 00	..	3·3	..		Awake.
No. of curve 2, Patient A	80	1	..	113	4·7	..		Fasting.
		2	1 00	45	2·6	..		Unconscious; twitchings, corneal reflex positive, plantar flexor response.
		3	2 00	38	4·4	..		Twitchings ceased, awake.
		..	2 15	..	..	..		Unconscious; corneal reflex positive, plantar flexor response, twitchings returned.
		4	3 00	41	3·8	..		Unconscious; restless.
		5	3 30	36	3·7	..		Unconscious; Babinski positive both sides.
		..	4 00	..	..	..		Stridor. 200 grm. glucose by stomach tube.
		6	4 45	68	4·1	..		Awake.
No. of curve 3, Patient B	240	1	..	84	5·6	..		Fasting.
		2	1 00	35	4·8	..		Drowsy.
		3	2 00	31	5·3	..		,,
		..	2 40	..	..	..		Unconscious; corneal reflex positive, plantar flexor response.
		4	3 00	31	4·1	..		Unconscious; Babinski both sides.
		5	4 00	28	4·8	..		Unconscious; corneal reflex negative.
		6	4 55	28	3·2	..		Ditto. Glucose 200 grm. by stomach tube.
		7	5 20	64	6·7	..		Unconscious; corneal reflex again positive, Babinski both sides; restless, hypertonic, opisthotonus, rolling movements, flushed face. 0·9 grm. glucose intravenous.
		8	6 10	40	6·2	..		Still unconscious; waking delayed.
			7 30	..	..	..		Awake (complete amnesia).

No. of curve 4, Patient C	130	1	..	99	6	..		Fasting.
		2	1 00	34	5·6	..		..
		3	1 45	31	4·5	..		Unconscious; corneal reflex positive, plantar flexor response.
		4	2 10	34	2·9	..		Unconscious; Babinski positive both sides, cornear reflex positive.
		5	4 00	34	3·5	..		Ditto. Glucose 200 grm. by stomach tube.
		..	4 20	..	..	..		Awake.
		6	5 00	122	4·4	..		,,
No. of curve 5, Patient C	80	1	..	104	6·6	..		Fasting.
		2	1 00	36	3·5	..		Drowsy.
		3	2 00	34	4·0	..		,,
		4	3 15	36	4·3	..		Unconscious; corneal reflex positive; twitchings started.
		..	3 55	..	..	..		Unconscious; corneal reflex negative, hypertonic, Babinski both sides.
		5	4 00	38	5·3	..		Corneal reflex again positive; Babinski both sides, hypertonic.
		6	4 30	38	5·4	..		Ditto.
		..	4 45	..	..	..		Corneal reflex negative. Glucose 200 grm. by stomach tube.
		7	5 00	114	2·2	..		Awake.
No. of curve 6, Patient C	100	1	..	76	4·5	..		Fasting.
	2	2	1 00	17	1·4	..		..
		3	2 00	14	1·1	..		Drowsy.
		4	2 45	26	1·7	..		Unconscious; corneal reflex positive.
		..	3 45	..	..	..		Unconscious; corneal reflex negative, Babinski positive both sides, hypertonic.
		5	4 45	22	2·2	..		Ditto. Glucose 200 grm. by stomach tube.
		..	5 00	..	..	..		Awake.
		6	5 20	114	2·2	..		,,
No. of curve 7, Patient C	160	1	..	90	5·4	1·4		Fasting.
		2	1 00	43	1·1	·9		Slight twitchings beginning.
		3	3 00	33	1·3	1·5		Unconscious; corneal reflex positive.
		4	4 00	36	2·1	1·7		Unconscious; corneal reflex positive, Babinski positive both sides, stridor. Glucose 200 grm. by stomach tube.
		5	4 30	124	2·7	0·7		Awake.

Ordinary Blood Sugar and Keto-bodies—continued.

	Dose units (insulin).	No. of specimen.	Time after injection. hr.	min.	Glucose mgrm. %.	B.B.S. mgrm. %.	Acetone aceto-acetic acid mgrm. %.	Clinical notes.
No. of curve 8, Patient D	130	1	..		69	5·7	..	Fasting.
		2	1	00	31	2·9	..	Unconscious; corneal reflex positive, plantar flexor response.
		3	2	00	24	1·5	..	Unconscious; restless.
		..	2	40	..	..	..	Unconscious; corneal reflex negative.
		4	3	00	23	0·7	..	Ditto. Opisthotonus, hyperextension, pronation arms, hyperextension legs, no plantar response.
		..	3	20	..	..	..	Ditto. Glucose 200 grm. by stomach tube.
		5	3	45	34	5·0	..	Awake.
No. of curve 9, Patient E	220	1	..		110	5·1	..	Fasting.
		2	1	00	34	5·9	..	..
		3	2	10	29	3·4	..	Drowsy.
		4	2	30	33	3·4	..	Unconscious; corneal reflex positive, Babinski positive both sides.
		5	3	40	29	6·2	..	Unconscious; corneal reflex negative, hypertonic, Babinski both sides positive.
		..	4	00	..	..	..	Ditto. Glucose 200 grm. by stomach tube
		..	4	20	..	..	..	Awake.
		6	4	50	99	5·2	..	,,
No. of curve 10, Patient E	170	1	..		83	2·9	..	Fasting.
		2	2	20	24	2·9	..	Unconscious; hypertonic, corneal reflex positive.
		..	4	10	..	..	..	Ditto. Glucose 200 grm. by stomach tube.
		3	4	45	76	2·9	..	Awake.
No. of curve 11, Patient E	180	1	..		74	5·6	1·5	Fasting.
		2	1	00	20	3·5	2·1	Drowsy.
		3	2	30	20	2·0	0·4	Unconscious; pronounced twitchings.
		4	3	00	37	3·2	2·0	Slight twitchings.
		5	4	00	44	2·0	0·4	Babinski positive both sides.
		..	4	05	..	..	..	Glucose 200 grm. by stomach tube.
		6	4	30	73	3·8	1·1	Still unconscious; corneal reflex positive, Babinski positive on both sides. Glucose 18 grm. intravenous (20% solution).

	Dose units (insulin).	No. of specimen.	Time after injection. hr. min.	Glucose mgrm. %	B.H.S. mgrm. %	Acetone + diacetic acid mgrm. %		Clinical notes.
f curve 8,	130	1	..	69	5·7	..		Fasting.
tient D		2	1 00	31	2·9	..		Unconscious; corneal reflex positive, plantar flexor response.
		3	2 00	24	1·5	..		Unconscious; restless.
		..	2 40	..	..	..		Unconscious; corneal reflex negative.
		4	3 00	23	0·7	..		Ditto. Opisthotonus, hyperextension, pronation arms, hyperextension legs, no plantar response.
		..	3 20	..	..	..		Ditto. Glucose 200 grm. by stomach tube.
		5	3 45	34	5·0	..		Awake.
No. of curve 9,	220	1	..	110	5·1	..		Fasting.
Patient E		2	1 00	34	5·9	..		..
		3	2 10	29	3·4	..		Drowsy.
		4	2 30	33	3·4	..		Unconscious; corneal reflex positive, Babinski positive both sides.
		5	3 40	29	6·2	..		Unconscious; corneal reflex negative, hypertonic, Babinski both sides positive.
		..	4 00	..	..	..		Ditto. Glucose 200 grm. by stomach tube
		..	4 20	..	..	..		Awake.
		6	4 50	99	5·2	..		,,
No. of curve 10,	170	1	..	83	2·9	..		Fasting.
Patient E		2	2 20	24	2·9	..		Unconscious; hypertonic, corneal reflex positive.
		..	4 10	..	..	..		Ditto. Glucose 200 grm. by stomach tube.
		3	4 45	76	2·9	..		Awake.
No. of curve 11,	180	1	..	74	5·6	1·5		Fasting.
Patient E		2	1 00	20	3·5	2·1		Drowsy.
		3	2 30	20	2·0	0·4		Unconscious; pronounced twitchings.
		4	3 00	37	3·2	2·0		Slight twitchings.
		5	4 00	44	2·0	0·4		Babinski positive both sides.
		..	4 05	..	..	..		Glucose 200 grm. by stomach tube.
		6	4 30	73	3·8	1·1		Still unconscious; corneal reflex positive, Babinski positive on both sides. Glucose 08 grm. intravenous (20% solution)
		7	4 55	103	4·0	0·0		Awake after injection.
								Awake.

No. of curve 12,	100	1	..	85	3·5	3·3		Fasting.
Patient F		2	1 00	31	2·5	2·1		..
		3	2 00	31	2·9	0·8		Drowsy.
		4	2 35	17	2·4	0·8		Unconscious; twitchings beginning.
		5	2 50	..	..	..		Pronounced twitchings.
		5	3 00	33	4·4	5·7		Twitchings ceased; awake.
		..	3 20	..	..	..		Unconscious again.
		..	4 00	..	..	..		Unconscious; corneal reflex negative, Babinski positive on both sides.
		6	4 20	15	2·4	1·1		Ditto. Hyperextension, pronation arms, hyperextension legs, opisthotonus. Glucose 200 grm. by stomach tube.
		..	4 45	..	..	..		Awake.
		7	4 55	71	3·4	3·3		,,
No. of curve 13,	120	1	..	59	3·8	1·9		Fasting.
Patient F		2	1 00	7	2·3	1·1		Unconscious; marked twitchings.
		3	2 30	7	1·5	0·6		Awake; twitchings ceased.
		..	3 40	..	..	..		Unconscious again.
		..	4 00	..	..	..		Glucose 200 grm by stomach tube.
No. of curve 14,	130	1	..	55	3·2	1·9		Fasting.
Patient G		..	3 05	..	..	..		Unconscious; corneal reflex positive.
		..	3 50	..	..	..		Unconscious; corneal reflex negative, Babinski positive on both sides.
		2	4 05	7	2·0	0·3		Ditto. Hyperextension, pronation arms, hyperextension legs. Glucose 200 grm. by stomach tube.
		3	4 45	50	3·0	1·8		Awake.
No. of curve 15,	180	1	..	82	3·5	4·5		Fasting.
Patient H		2	1 00	33	1·4	2·1		..
		3	2 00	26	1·0	3·2		..
		..	2 50	..	..	..		Epileptiform attack.
		4	2 52	37	4·1	4·0		Sample taken just after attack. Glucose 200 grm. by stomach tube
		..	3 00	37	..	..		Awake.
		5	3 50	78	2·9	4·4		,,

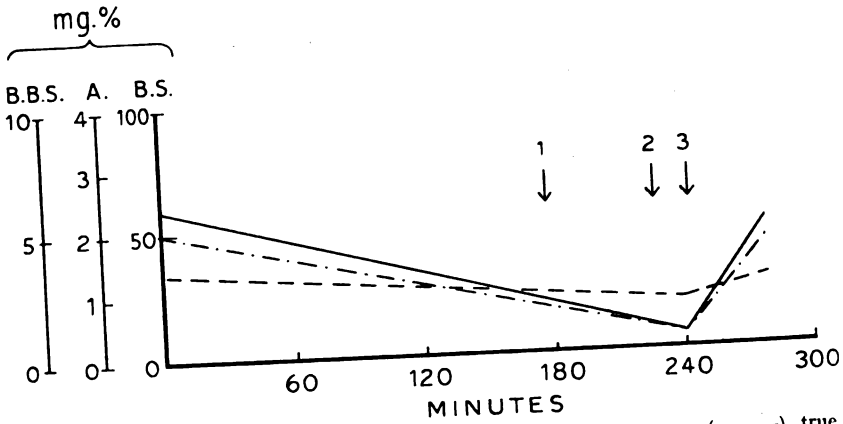


FIG. 1.—This shows simultaneity of the fall of total reducing substances (———), true blood sugar (—.—) and non-sugar-reducing substances (– – – –). Details, see curve 1*a*. Arrow 1, onset of coma; arrow 2, corneal reflex lost; arrow 3, interrupted with 200 grm. of glucose.

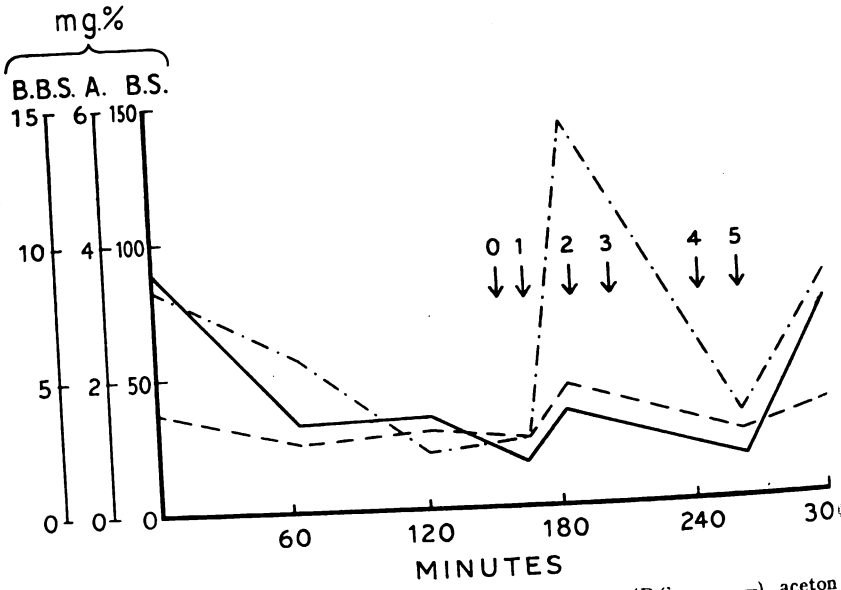
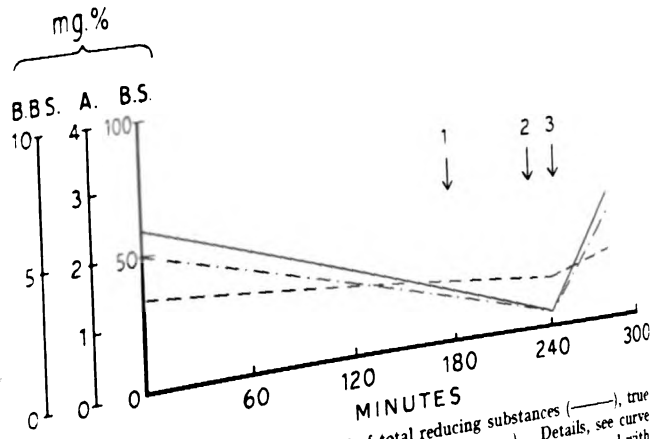


FIG. 2.—This shows simultaneity of the fall and rise in glucose (B.S., ———), aceton (A., —.—) and B.B.S. (– – – –) values. Details, see curve 14. Arrow 1, onset coma; arrow 2, corneal reflex lost; arrow 3, interrupted with 200 grm. of glucose.



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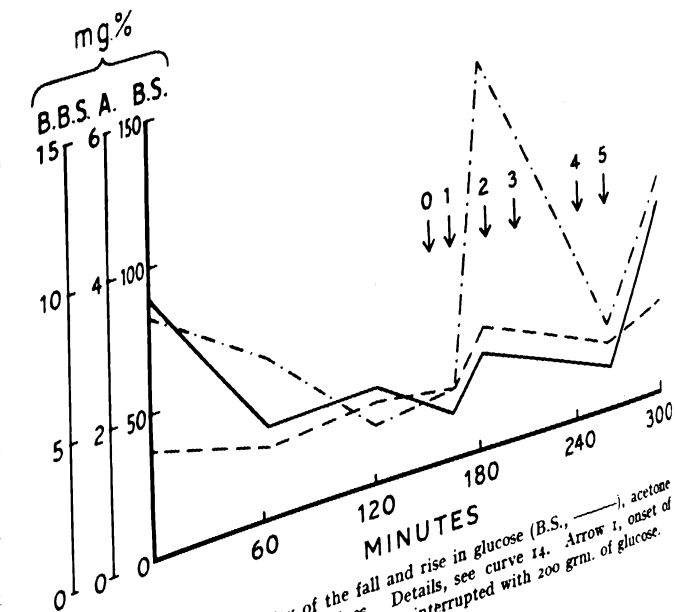

This shows simultaneity of the fall and rise in glucose (B.S., ——), acetone (—.—) and B.B.S. (– – –) values. Details, see curve 14. Arrow 1, onset of corneal reflex lost; arrow 3, interrupted with 200 grm. of glucose.

Discussion of Results.

The blood-sugar curves confirm the work previously done (1, 2, 3), and show that low blood-sugar levels have to exist for a certain time before coma occurs (Fig. 1). After interruption with glucose the patient usually awakes within half an hour, in some cases (1*a*, 2*a*, 3*a*, 8, 11, 14) the blood sugar remains much below normal after interruption with glucose, in spite of the fact that the patient is quite awake. Keer's (10) experiments suggest that

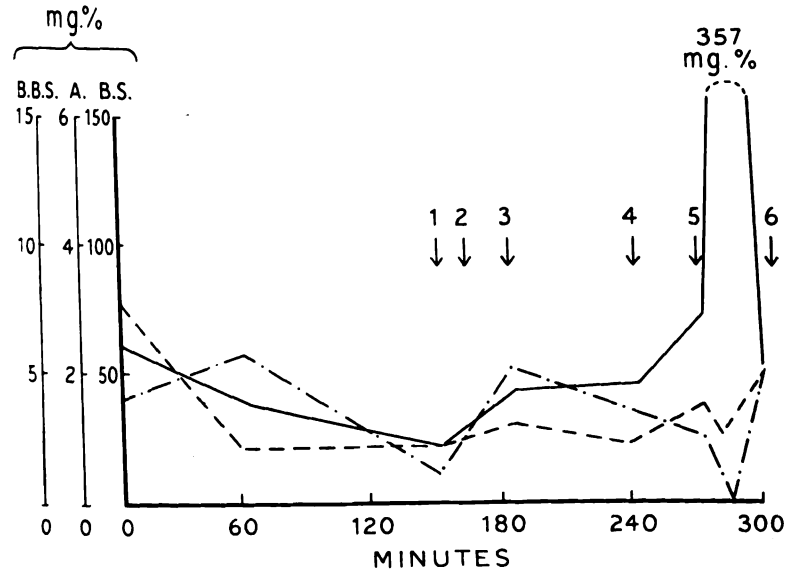

Fig. 3.—This figure illustrates the initial fall in all values and the parallel course taken by glucose (B.S., ——), acetone (A., —.—), and B.B.S. (– – –); it also shows the slight rise in these substances following twitchings. Arrow 0, onset of coma; arrow 1, onset of twitchings; arrow 2, twitchings ceased, awake; arrow 3, again in coma; arrow 4, corneal reflex lost; arrow 5, interrupted with 200 grm. of glucose. (For further details see curve 12.)

twitchings and convulsions only occur after the blood sugar has been low for a certain time, leading to a decrease in the carbohydrate content of the brain. After interruption apparently the opposite process takes place, the sugar being first taken up by the brain and other organs. The patient may, therefore, be found awake with blood-sugar levels much below normal. The decrease in the carbohydrate content of the brain induces a parallel decrease in the oxygen consumption of the brain cells, since they mainly live on glucose (11). It was also thought that a change in oxidative ferments might be connected with the decreased oxygen utilization of the brain. We have therefore examined the oxidase of the leucocytes by means of the oxidase reaction and

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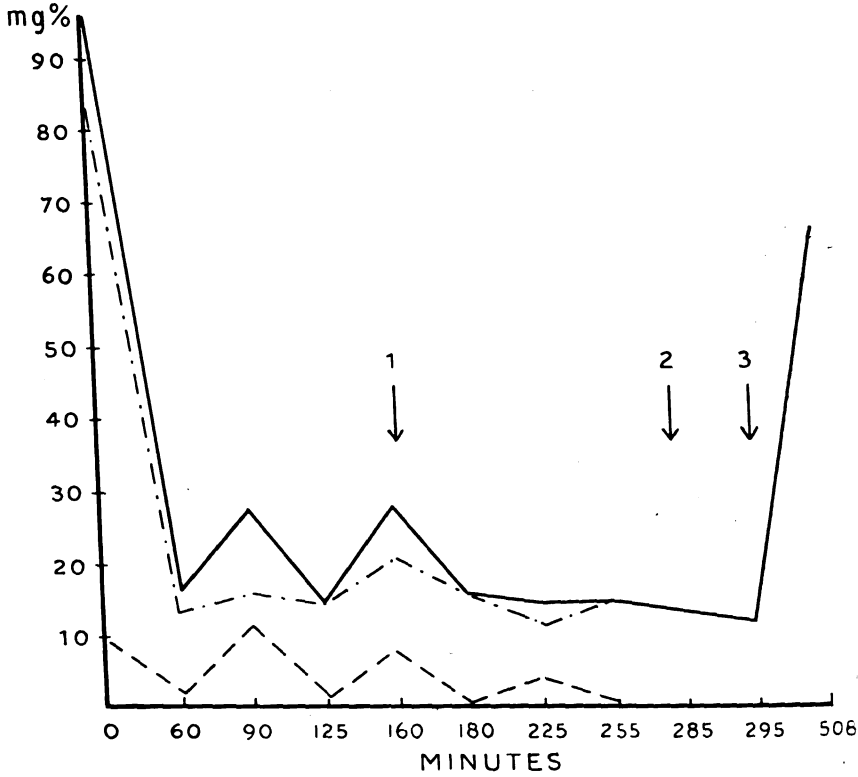

FIG. 4.—This figure illustrates the increased speed with which sugar is utilized in hyperinsulinism after an intravenous injection of glucose (B.S., ———) and that this is accompanied by a further decrease in the B.B.S. (– – – –) and acetone (A., —.—.) values. Arrow 1, indicates onset of coma; arrow 2, onset of twitchings; arrow 3, twitchings just ceased; arrow 4, interrupted with 200 grm. of glucose by stomach tube; arrow 5, awaking delayed, intravenous injection of 18 grm. of glucose in 20% solution; arrow 6, awake. (For further details, see curve 11.) It is of interest to note that the patient remained in coma with a blood-sugar value of 73 mgrm.% (arrow 5) and awoke with a value of 51 mgrm.% (arrow 6); this is one example of the fact that no direct relationship exists between the degree of hypoglycæmia and the symptoms of hypoglycæmia.

Taylor, Weiss and Wilkins (13) regard 4·7 mgrm.% ± 1 as the normal range for the B.B.S., values above 6 mgrm.% being considered as ra Out of 84 B.B.S. estimations 3 values were above 6 mgrm.%. In one the fasting value was 6·6 mgrm.% (curve 5); in another patient the B increased to 6·7 mgrm.% 25 minutes after interruption and was 6·2 mgr

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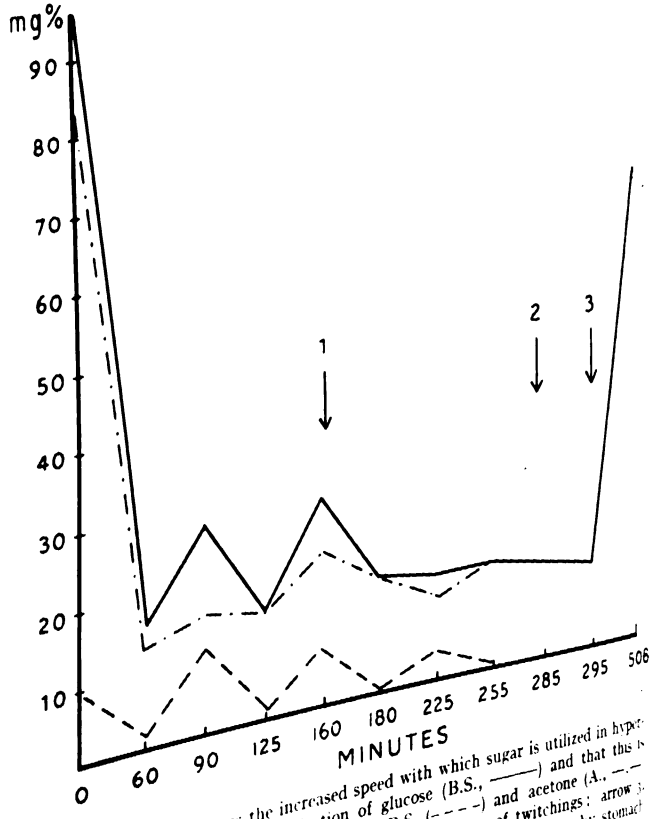

FIG. 4.—This figure illustrates the increased speed with which sugar is utilized in hyper-
insulinism after an intravenous injection of glucose (B.S., ——) and acetone (A., —·—
accompanied by a further decrease in the B.B.S. (– – –) and acetone values. Arrow 1, indicates onset of coma; arrow 2, onset of twitchings; arrow 3,
twitchings just ceased; arrow 4, interrupted with 200 grm. of glucose by stomach
tube; arrow 5, awaking delayed, intravenous injection of 18 grm. of glucose in 20%
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another 50 minutes later, the patient still remaining unconscious, his waking was delayed. He regained consciousness 2 hours and 25 minutes after interruption with glucose. Just before interruption the B.B.S. was 3·2 mgrm.% (curve 3).

The normal values for acetone and aceto-acetic acid in the blood are 1-3 mgrm.% (12). Out of 31 determinations 27 were under 3·3 mgrm.%. The highest value being 4·5 mgrm.% in a patient (curve 15) who was very liable to epileptiform attacks during hypoglycæmia; it decreased to 2·1 mgrm.% after the insulin injection, was 4·0 mgrm.% after an epileptiform attack and 4·4 mgrm.% after interruption with glucose.

Where both acetone plus aceto-acetic and B.B.S. curves were obtained a parallelism was evident, which was striking in most cases (Fig. 2). The insulin injections showed a definite influence on the B.B.S. and on the acetone plus aceto-acetic acid. In most cases there was a tendency to fall and especially an initial decrease (Fig. 3) (curves 1, 2, 3, 5, 6, 7, 8, 11, 13, 15). All keto-bodies were usually higher following restlessness, hypertonus, twitchings or epileptiform convulsions than before the onset of those symptoms (Figs. 3 and 4) (curves 2, 3, 5, 9, 11, 12, 15). It seems unlikely therefore that the symptoms of hyperinsulinism, especially convulsions, or, on the other hand, any delay in waking after interruption (curve 3), are due to an increase in pyruvic acid or methyglyoxal, as recently suggested by Silberschmidt (4), because these substances were never found to be increased before the onset of these symptoms.

Many workers (14) found a decrease in liver glycogen after high doses of insulin. Others (15) believe that there is an antagonism between glycogen content of the liver and the amount of keto-bodies in the blood. In this investigation the keto-bodies were usually found to decrease following insulin injections. It seems doubtful therefore whether this antagonism occurs in hyperinsulinism. The amount of keto-bodies in the blood seems to be regulated by the periphery, mainly the muscles, because the keto-bodies were usually found to increase after muscular movements or twitchings.

SUMMARY.

(1) Blood specimens were taken from schizophrenic patients undergoing insulin treatment. Estimations were made of—

(*a*) blood sugar,

(*b*) bisulphite-binding substances,

(*c*) acetone and aceto-acetic acid.

(2) There is a disparity between blood-sugar level and the symptoms of hypoglycæmia. The blood sugar has to be kept below about 30 mgrm.% for a certain time before coma occurs.

(3) The B.B.S. and acetone and aceto-acetic acid values showed a definite tendency to depression.

Ordinary Blood Sugar and Keto-bodies—continued.

	Dose units (insulin).	No. of specimen.	Time after injection. hr.	min.	Glucose mgrm. %.	B.B.S. mgrm. %.	Acetone aceto-acetic acid mgrm. %.	Clinical notes.
No. of curve 8, Patient D	130	1	..		69	5·7	..	Fasting.
		2	1	00	31	2·9	..	Unconscious; corneal reflex positive, plantar flexor response.
		3	2	00	24	1·5	..	Unconscious; restless.
		..	2	40	..	..	..	Unconscious; corneal reflex negative.
		4	3	00	23	0·7	..	Ditto. Opisthotonus, hyperextension, pronation arms, hyperextension legs, no plantar response.
		..	3	20	..	..	..	Ditto. Glucose 200 grm. by stomach tube.
		5	3	45	34	5·0	..	Awake.
No. of curve 9, Patient E	220	1	..		110	5·1	..	Fasting.
		2	1	00	34	5·9	..	..
		3	2	10	29	3·4	..	Drowsy.
		4	2	30	33	3·4	..	Unconscious; corneal reflex positive, Babinski positive both sides.
		5	3	40	29	6·2	..	Unconscious; corneal reflex negative, hypertonic, Babinski both sides positive.
		..	4	00	..	..	..	Ditto. Glucose 200 grm. by stomach tube
		..	4	20	..	..	..	Awake.
		6	4	50	99	5·2	..	,,
No. of curve 10, Patient E	170	1	..		83	2·9	..	Fasting.
		2	2	20	24	2·9	..	Unconscious; hypertonic, corneal reflex positive.
		..	4	10	..	..	..	Ditto. Glucose 200 grm. by stomach tube.
		3	4	45	76	2·9	..	Awake.
No. of curve 11, Patient E	180	1	..		74	5·6	1·5	Fasting.
		2	1	00	20	3·5	2·1	Drowsy.
		3	2	30	20	2·0	0·4	Unconscious; pronounced twitchings.
		4	3	00	37	3·2	2·0	Slight twitchings.
		5	4	00	44	2·0	0·4	Babinski positive both sides.
		..	4	05	..	..	..	Glucose 200 grm. by stomach tube.
		6	4	30	73	3·8	1·1	Still unconscious; corneal reflex positive, Babinski positive on both sides. Glucose 18 grm. intravenous (20% solution).
		7	4	35	357	2·6	0·0	Awake after injection.
		8	5	00	51	5·1	2·3	Awake.

No. of curve 12, Patient F	100	1	..	85	3·5	3·3	Fasting.
		2	1 00	31	2·5	2·1	..
		3	2 00	31	2·9	0·8	Drowsy.
		4	2 35	17	2·4	0·8	Unconscious; twitchings beginning.
		5	2 50	..	..	..	Pronounced twitchings.
		5	3 00	33	4·4	5·7	Twitchings ceased; awake.
		..	3 20	..	..	..	Unconscious again.
		..	4 00	..	..	..	Unconscious; corneal reflex negative, Babinski positive on both sides.
		6	4 20	15	2·4	1·1	Ditto. Hyperextension, pronation arms, hyperextension legs, opisthotonus. Glucose 200 grm. by stomach tube.
		..	4 45	..	..	..	Awake.
		7	4 55	71	3·4	3·3	,,
No. of curve 13, Patient F	120	1	..	59	3·8	1·9	Fasting.
		2	1 00	7	2·3	1·1	Unconscious; marked twitchings.
		3	2 30	7	1·5	0·6	Awake; twitchings ceased.
		..	3 40	..	..	..	Unconscious again.
		..	4 00	..	..	..	Glucose 200 grm by stomach tube.
No. of curve 14, Patient G	130	1	..	55	3·2	1·9	Fasting.
		..	3 05	..	..	..	Unconscious; corneal reflex positive.
		..	3 50	..	..	..	Unconscious; corneal reflex negative, Babinski positive on both sides.
		2	4 05	7	2·0	0·3	Ditto. Hyperextension, pronation arms, hyperextension legs. Glucose 200 grm. by stomach tube.
		3	4 45	50	3·0	1·8	Awake.
No. of curve 15, Patient H	180	1	..	82	3·5	4·5	Fasting.
		2	1 00	33	1·4	2·1	..
		3	2 00	26	1·0	3·2	..
		..	2 50	..	..	..	Epileptiform attack.
		4	2 52	37	4·1	4·0	Sample taken just after attack. Glucose 200 grm. by stomach tube
		..	3 00	37	..	..	Awake.
		5	3 50	78	2·9	4·4	,,

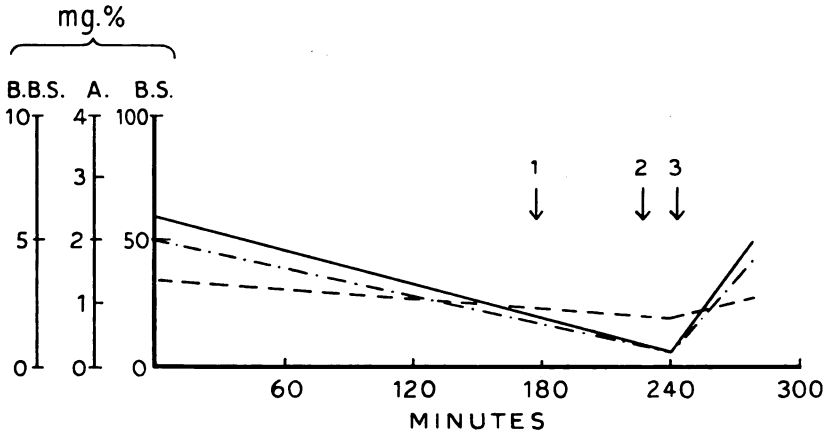


FIG. 1.—This shows simultaneity of the fall of total reducing substances (———), true blood sugar (—.—) and non-sugar-reducing substances (– – – –). Details, see curve 1*a*. Arrow 1, onset of coma; arrow 2, corneal reflex lost; arrow 3, interrupted with 200 grm. of glucose.

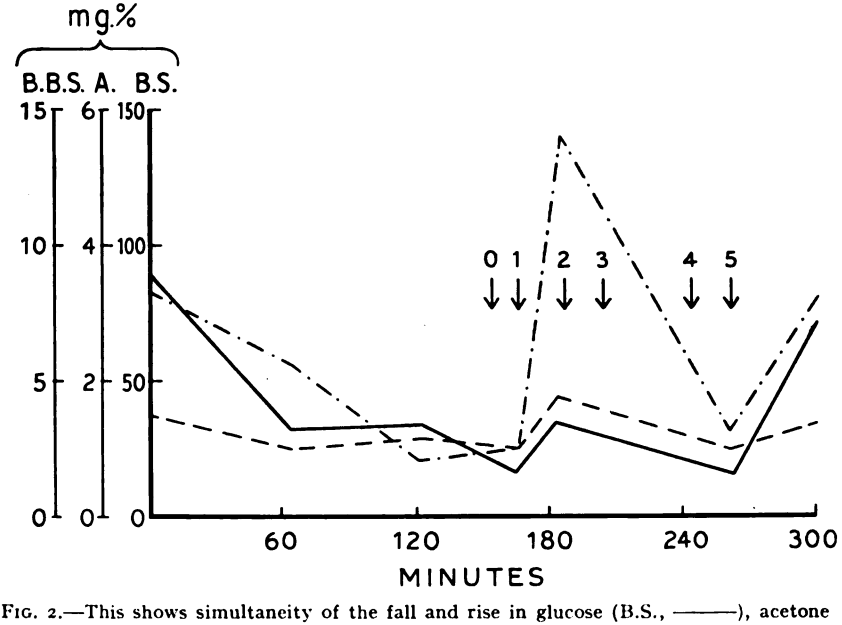
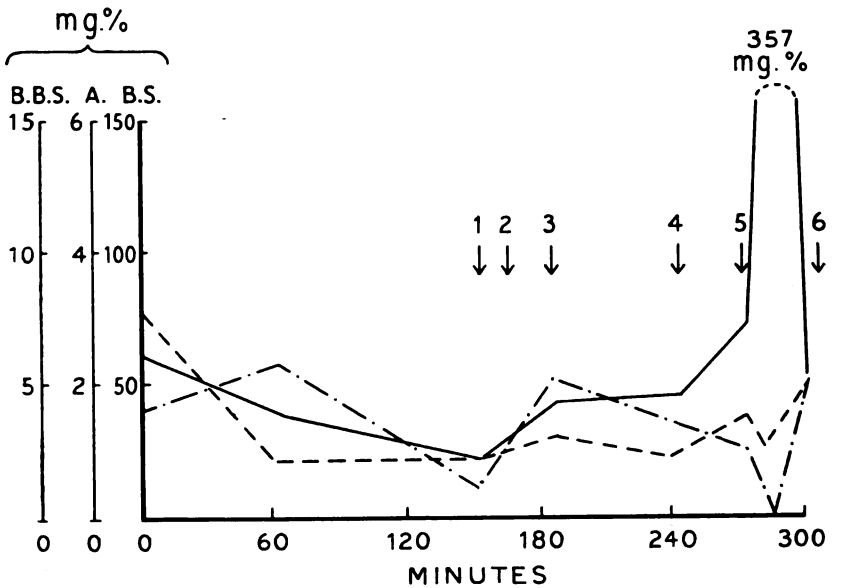


FIG. 2.—This shows simultaneity of the fall and rise in glucose (B.S., ———), acetone (A., —.—) and B.B.S. (– – – –) values. Details, see curve 14. Arrow 1, onset of coma; arrow 2, corneal reflex lost; arrow 3, interrupted with 200 grm. of glucose.

Discussion of Results.

The blood-sugar curves confirm the work previously done (1, 2, 3), and show that low blood-sugar levels have to exist for a certain time before coma occurs (Fig. 1). After interruption with glucose the patient usually awakes within half an hour, in some cases (1*a*, 2*a*, 3*a*, 8, 11, 14) the blood sugar remains much below normal after interruption with glucose, in spite of the fact that the patient is quite awake. Keer's (10) experiments suggest that



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did not find any change during insulin coma. The decrease in oxygen consumption is therefore regarded as secondary to the decrease in glucose. Any toxic action of the insulin itself is unlikely, because an injection of glucose immediately counteracts the symptoms of hyperinsulinism.

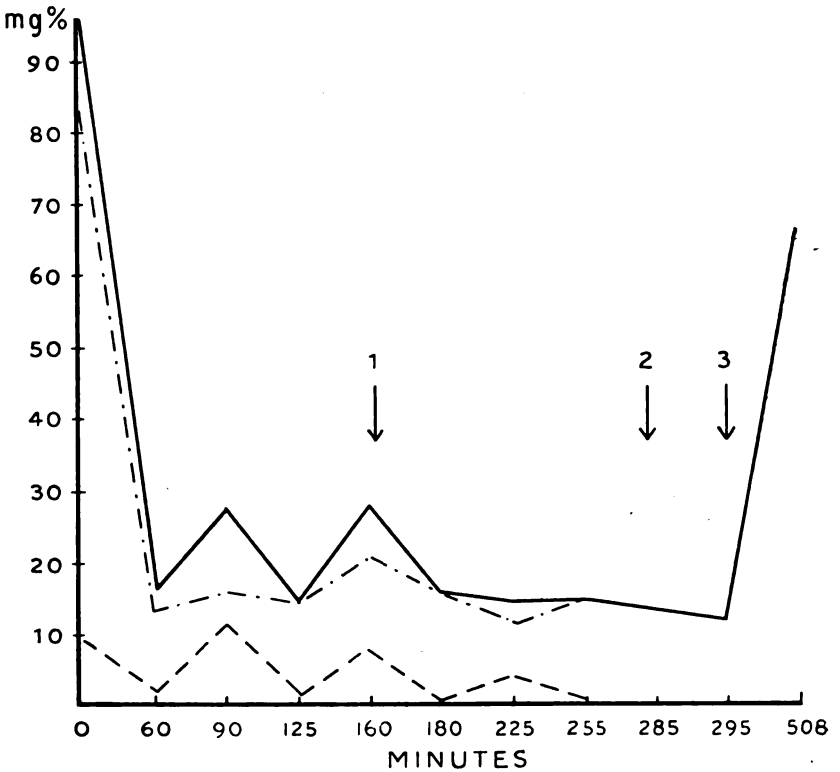

FIG. 4.—This figure illustrates the increased speed with which sugar is utilized in hyperinsulinism after an intravenous injection of glucose (B.S., ———) and that this is accompanied by a further decrease in the B.B.S. (– – – –) and acetone (A., —.—) values. Arrow 1, indicates onset of coma; arrow 2, onset of twitchings; arrow 3, twitchings just ceased; arrow 4, interrupted with 200 grm. of glucose by stomach tube; arrow 5, awaking delayed, intravenous injection of 18 grm. of glucose in 20% solution; arrow 6, awake. (For further details, see curve 11.) It is of interest to note that the patient remained in coma with a blood-sugar value of 73 mgrm.% (arrow 5) and awoke with a value of 51 mgrm.% (arrow 6); this is one example of the fact that no direct relationship exists between the degree of hypoglycæmia and the symptoms of hypoglycæmia.

Taylor, Weiss and Wilkins (13) regard 4·7 mgrm.% ± 1 as the normal range for the B.B.S., values above 6 mgrm.% being considered as raised. Out of 84 B.B.S. estimations 3 values were above 6 mgrm.%. In one case the fasting value was 6·6 mgrm.% (curve 5); in another patient the B.B.S. increased to 6·7 mgrm.% 25 minutes after interruption and was 6·2 mgrm.%

another 50 minutes later, the patient still remaining unconscious, his waking was delayed. He regained consciousness 2 hours and 25 minutes after interruption with glucose. Just before interruption the B.B.S. was 3·2 mgrm.% (curve 3).

The normal values for acetone and aceto-acetic acid in the blood are 1–3 mgrm.% (12). Out of 31 determinations 27 were under 3·3 mgrm.%. The highest value being 4·5 mgrm.% in a patient (curve 15) who was very liable to epileptiform attacks during hypoglycæmia ; it decreased to 2·1 mgrm.% after the insulin injection, was 4·0 mgrm.% after an epileptiform attack and 4·4 mgrm.% after interruption with glucose.

Where both acetone plus aceto-acetic and B.B.S. curves were obtained a parallelism was evident, which was striking in most cases (Fig. 2). The insulin injections showed a definite influence on the B.B.S. and on the acetone plus aceto-acetic acid. In most cases there was a tendency to fall and especially an initial decrease (Fig. 3) (curves 1, 2, 3, 5, 6, 7, 8, 11, 13, 15). All keto-bodies were usually higher following restlessness, hypertonus, twitchings or epileptiform convulsions than before the onset of those symptoms (Figs. 3 and 4) (curves 2, 3, 5, 9, 11, 12, 15). It seems unlikely therefore that the symptoms of hyperinsulinism, especially convulsions, or, on the other hand, any delay in waking after interruption (curve 3), are due to an increase in pyruvic acid or methyglyoxal, as recently suggested by Silberschmidt (4), because these substances were never found to be increased before the onset of these symptoms.

Many workers (14) found a decrease in liver glycogen after high doses of insulin. Others (15) believe that there is an antagonism between glycogen content of the liver and the amount of keto-bodies in the blood. In this investigation the keto-bodies were usually found to decrease following insulin injections. It seems doubtful therefore whether this antagonism occurs in hyperinsulinism. The amount of keto-bodies in the blood seems to be regulated by the periphery, mainly the muscles, because the keto-bodies were usually found to increase after muscular movements or twitchings.

Summary.

(1) Blood specimens were taken from schizophrenic patients undergoing insulin treatment. Estimations were made of—

(*a*) blood sugar,

(*b*) bisulphite-binding substances,

(*c*) acetone and aceto-acetic acid.

(2) There is a disparity between blood-sugar level and the symptoms of hypoglycæmia. The blood sugar has to be kept below about 30 mgrm.% for a certain time before coma occurs.

(3) The B.B.S. and acetone and aceto-acetic acid values showed a definite tendency to depression.

(4) The significance of these findings is discussed and it is concluded that the symptoms of hyperinsulinism are neither due to any toxic keto-substances nor to some toxic action of the insulin itself, but probably to a decrease in the carbohydrate content of the brain cells. There is apparently no antagonism between glycogen content of the liver and the amount of keto-bodies in the blood in hyperinsulinism.

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SOME FURTHER OBSERVATIONS ON VITAMIN C ESTIMATIONS IN PSYCHOTIC AND PSYCHOPATHIC PATIENTS.

By Louis Minski, M.D., M.R.C.P.,
Deputy Medical Superintendent, St. Ebba's Hospital, and

N. D. Constantine,
Technical Assistant.

In a previous paper published in the Journal for July, 1938, the vitamin C content of the urine of 50 psychotic patients was estimated. Although it was found that the urine content was on the low side, no definite conclusion could be reached as to whether there was any correlation between the form of mental disorder and the deficiency of vitamin C. Since that time the urines of another 256 patients have been examined, which, together with the original 50, make a total of 306.

The diagnosis of the mental states was as follows, while the average output of vitamin C in the urine in mgrm. % was :

Schizophrenia . . .	88	·908
Epilepsy	81	·723
Depression	53	·843
Involutional depression .	32	·989
Psychopathy . . .	31	·905
Cerebral arteriosclerosis .	8	·850
Korsakov psychosis . .	5	1·300
Toxic-confusional state .	5	·920
Cerebral tumour . . .	1	1·000
Disseminated encephalomyelitis	1	1·000
Post-encephalitic Parkinsonism	1	·960
Total . .	306	

Although the average level was definitely low, individual patients showed higher levels, e.g. the highest reading among the psychopaths was 20 mgrm., and among the epileptics 14·3 mgrm., while the lowest reading was 4 mgrm.

The modified technique of Harris and Abbasy (1) was used in the estimations and in all cases duplicate tests were carried out with very little variation in the results. Where it was impossible to titrate the specimens immediately, they were stored in the dark after adding 10% by volume of glacial acetic acid. In no case did the time between testing and titrating exceed three hours, and usually the specimens were titrated within fifteen minutes of the urine being voided.

No correlation between the mental state and the vitamin C level was possible, nor did the administration of ascorbic acid produce any material change in the mental state. For instance, a number of patients with different mental diagnosis, as shown in the above list, were given 300 mgrm. of ascorbic acid per day for six days. The previous average low level of 5 mgrm. rose to 15 mgrm. in the urine by the fourth day, and remained at this level until the administration of ascorbic acid was discontinued, when it again fell to its previous low level.

At the same time no change was observed in the mental state during or after the administration of the ascorbic acid.

Rietschel (2) found that after giving 100–500 mgrm. of vitamin C for several days, both infants and adults showed an increased thrombocyte count, restlessness and insomnia, but these changes were not evident in any of the cases in this series.

Estimations were made on recent admissions to hospital; the average reading was 10 mgrm., while the average of the convalescent patients was the same. During the patients' stay in hospital there was little or no variation in the output, unless of course the patient received ascorbic acid by mouth, when it temporarily increased.

Full blood-counts, together with estimations of hæmoglobin, colour index and size of red cells were carried out on 56 patients in an attempt to correlate these with vitamin C estimations. Here again no correlation could be drawn, as patients with low levels of vitamin C showed high red cell-counts, normal colour index and size of cells. Thus, one patient with a reading of 5 mgrm. vitamin C showed a red cell-count of 5,430,000 per c.cm., and a hæmoglobin reading of 86%.

Other patients with vitamin levels of 4 mgrm. showed red counts of 4½ millions and hæmoglobin readings of 82%. Intensive iron therapy had no effect on the vitamin C content, but the hæmoglobin rose by 7%. Ascorbic acid had no effect on the blood-counts which were on the low side.

In four cases of pernicious anæmia and one of carcinoma of the stomach, all with achlorhydria, the vitamin C estimations were normal, while ascorbic acid given by mouth caused no alteration in the results of gastric analysis.

Issler and Demole (3) found that after the ingestion of vitamin C the vitamin content of the gastric juice is increased, but there was no characteristic variation in the volume or acidity of the gastric juice.

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Other patients with vitamin levels of 4 mgrm. showed red counts of 4½ millions and hæmoglobin readings of 82%. Intensive iron therapy had no effect on the vitamin C content, but the hæmoglobin rose by 7%. Ascorbic acid had no effect on the blood-counts which were on the low side.

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Liver extract caused an improvement in the blood-picture, but no alteration in the vitamin C excretion. Platelet counts were carried out by Lamport's (4) modification of the Kristenson method, but no marked deviation from the normal was found in cases with a low vitamin C content.

There appears to be no correlation between body weight and vitamin C content.

It will be seen, therefore, on the physical side that there is no correlation between the excretion of vitamin C and these laboratory findings.

Conclusions.

(1) There appears to be no relation between mental disease and vitamin C content, and the mental state is not altered by its administration.

(2) There does not appear to be any relation between vitamin C content and the blood-picture or gastric acidity.

(3) There is no relation between vitamin C content and body weight.

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"STATIONARY" GENERAL PARALYSIS OF THE INSANE. A REPORT ON A CASE OF THIRTY-ONE YEARS' DURATION.

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(Received September 25, 1939.)

CLINICAL HISTORY.

Mr. W. T. O—, aged 48. Admitted to Hanwell (now St. Bernard's) Hospital on 15.iv.1904.

The patient was admitted from Wormwood Scrubs prison, and there is no available information regarding his condition before his admission to hospital. At this time it was stated that he was confused and unable to give any accurate information about himself. He was garrulous and his conversation was largely incoherent. There are no details of his physical condition on admission. In 1908 he is described as being elated and garrulous. He expressed many delusions of grandeur, stating, for instance, that he was owed large sums of money and possessed his own private carriages, etc. He was rather childish and his memory was impaired. His physical condition was stated to be " much improved " and he was able to be up and about. Even so he showed definite and obvious physical signs of general paralysis (unequal pupils, reacting only sluggishly to light, tremor of lips, etc.).

Between 1908 and 1922 the patient's condition does not seem to have altered to any appreciable extent. Thus, in 1915 he was elated, childish and facile, entertaining a very high opinion of himself. He showed no insight into his position, and believed that his previous employers would be only too glad to have his services again. He also expressed delusions of wealth. He was very loquacious and at times almost incoherent, owing to his inability to confine himself to one subject for any length of time. He occupied himself doing some simple work in the ward, but was constantly changing from one job to another, so that he rarely completed any set task. Often his conversation consisted entirely of a rapid enumeration of the enormous amount of work that he supposed he had accomplished. His general physical health was fair, but obvious neurological signs of general paralysis continued to be manifest: irregular and unequal pupils (right " pinpoint " and the left slightly larger) which did not react to light. The knee-jerks were accentuated and unequal. Marked muscular tremors were present. Speech was slurred. In 1919 the Wassermann reaction of the cerebro-spinal fluid was +++ (strongly positive).

During the period 1922–28 the patient's mental condition began to show further signs of deterioration, and he was described as being very simple and childish, showing pronounced impairment of memory. Although still mildly elated, he no longer expressed any delusions.

In 1931, when the patient had attained the age of 75, quite advanced dementia was present, and he was very amnesic and quite unable to give any account of himself. He was still mildly euphoric and seemed contented with his position.

By 1933 general physical deterioration had set in. He was partially confined to bed, very unsteady on his feet, and generally feeble. By March, 1935, he had become bedridden; on 4.iv.35 he commenced to have slight convulsive attacks and he died on 6.iv.35.

Post-mortem Findings.

Brain.—The leptomeninges covering the cerebral hemispheres were thick and opaque. There was much cortical wasting. The subarachnoid fluid was much increased in amount. (P.M. Wassermann reaction + 30.)

Microscopic examination of brain.—Sections taken from the cerebral hemispheres showed that the pia-arachnoid was enormously thickened (Fig. 1) and in addition it showed much infiltration with plasma cells and lymphocytes, especially in the deeper layers. The pial vessels were very congested. These changes, typical of chronic syphilitic meningitis, were most marked in the temporal regions. In

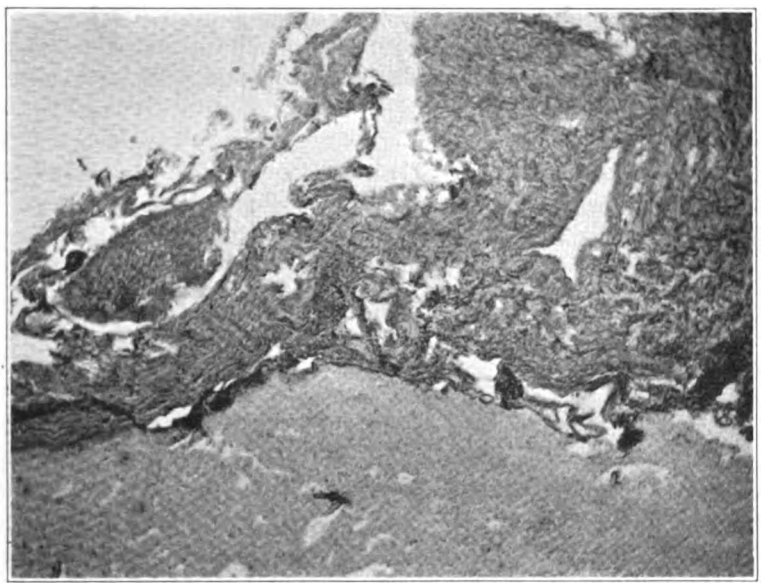

Fig. 1.—Temporal region—lepto-meninges greatly thickened as the result of chronic syphilitic meningitis. (Van Gieson.)

the underlying cortex there was generalized and gross disturbance of the cyto-architectonic structure. There was much diffuse loss of ganglion cells and the surviving elements were irregular in their disposition. There was great proliferation of glia and a number of Hortega " rod " cells (hypertrophied microglia) could be distinguished. The signs of active inflammation in the cortex were limited to a slight but definite " cuffing " of the vessels with plasma cells.

Other organs.—Apart from some broncho-pneumonia consolidation in both lungs there were no noteworthy features.

Discussion.

Spontaneous remissions are known to occur in general paralysis of the insane, and when an untreated patient survives for a number of years without obvious deterioration, the condition has frequently been designated

"stationary". Jahnel (1) has reviewed the cases of "stationary" general paralysis published in the literature and, before discussing the present case, reference will be made to the more important of these publications.

Gaupp (2) reported on a series of nineteen cases of general paralysis, all of at least eight years' duration. Of these nineteen cases, five were analysed in detail, including two cases in which a histological examination was made by Alzheimer. The first of the two cases examined by Alzheimer was of thirty-two years' duration, and the histological findings were those of moderate perivascular infiltrations and cytoarchitectonic disturbances, with pronounced glial proliferation in the cortex. All these changes were considered to be mild in comparison with the typical paretic process. The second case was of nine years' duration, and here there was much cortical atrophy, but again only slight inflammatory changes. Schultze (3) published a case of what he termed "healed" general paralysis where, during a prolonged remission, the patient had died of pyloric carcinoma. Alzheimer was again responsible for the histological examination, and reported that there were no gross changes in the cytoarchitectonic structure of the brain, and that signs of inflammation were slight.

In Tuczek's (4) case, of twenty-two years' standing, the symptoms of general paralysis had subsided during the first two years, but later evidence of tabes dorsalis was noted and still later further psychic disturbances arose. This case also showed comparatively mild histological changes.

Next Jakob (5) reported on five cases of "stationary" general paralysis, one of which requires special mention. In this case, which was of twenty years' duration, the cerebro-spinal fluid became spontaneously negative, and four years before the patient died a biopsy had been performed and examination of the material thus obtained showed only very slight degeneration of ganglion cells and capillary infiltrations. At post-mortem examination it was found that progressive parenchymatous degeneration had taken place since the biopsy and fairly marked infiltrations were present.

Plaut and Spielmeyer (6) published a report on a patient whose symptoms had subsided and the cerebro-spinal fluid become negative, but who developed further psychotic manifestations (hallucinatory) before he died, some nine years after the onset of the original general paralysis. Histologically, there was no evidence of recurrence of the paretic process, the changes being merely the "residue" of the previous attack, and these authors considered that the terminal psychosis was an independent illness.

Schmidt-Kraepelin (7) investigated a series of thirteen cases of slowly progressive general paralysis, and the histological examinations were made by Spatz. Only a proportion of these cases showed findings typical of the "stationary" type, while in others there was evidence of marked and recent inflammatory changes.

In comparing the present case with those published in the literature, and which

Jahnel has outlined, it will be seen that in actual time of survival it fell little short of the record case reported on by Gaupp and Alzheimer, the patient living for thirty-one years after his admission to hospital, as compared with thirty-two years in Gaupp's case. Secondly, from the clinical viewpoint, the patient's condition was not merely stationary, but in some respects tended to improve during the first twenty years of his illness. The subsequent gradual deterioration which he showed may have in part been accounted for by developing senility.* The mild nature of the inflammatory changes in the cerebral cortex corresponds to those usually found in the "stationary" type. Nevertheless, it cannot be said that this man had a complete remission, as his cerebrospinal fluid yielded a strongly positive Wassermann reaction fifteen years after the onset of his illness, and so also did the fluid removed at post-mortem. Further, the severity of the cytoarchitectonic disturbances evident on histological examination was hardly in keeping with the patient's reasonably well preserved intellect during the quiescent phase of his illness, but corresponded to the severe dementia which was present in the terminal stages. It is probably more accurate to describe this case as slowly progressive rather than as stationary, although for many years there was little or no evidence of progressive deterioration. Finally, it must be stated that as yet no acceptable explanation of the exact factor responsible for the chronic nature of such cases has been offered. It is, however, interesting to note that Klarfeld has remarked on the frequently protracted and atypical course of the disease in cases showing a concomitant syphilitic meningitis such as was present in this instance.

I am indebted to Dr. J. B. S. Lewis, Medical Superintendent of St. Bernard's Hospital, for permission to publish this case, and to Dr. S. A. Mann, Central Pathological Laboratory, who first drew my attention to the case and provided access to the patholigical material.

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* Owing to the available material being alcohol fixed, it was not possible to apply staining methods selective for senile changes.

Part II.—Reviews.

The Report of the Feversham Committee. (Published by Messrs. W. H. Barrell, Ltd., Portsmouth.)

This comprises 268 pages and is a full report of the voluntary mental health services in this country. It is divided into six parts.

Part I explains the composition of the Committee, which consisted of two representatives each from the National Council of Mental Hygiene, the Central Association of Mental Welfare, the Child Guidance Council and the Home and School Council of Great Britain, as a result of their preliminary meeting on April 8, 1936, at which Lord Feversham presided. The Mental After-Care Association were also invited to attend this meeting, but were not represented.

The terms of reference decided upon were "*to consider the scope and activities of the law affecting the existing voluntary organizations rendering mental health services*, and to report on their usefulness in relation to—

"(1) Their co-operation with government departments, local authorities and other bodies interested in mental health work.

"(2) The co-ordination of their activities.

"(3) The extension of the services rendered by them."

Part II contains a general survey of the mental health services. With regard to mental hospitals it is pointed out that the complexities of the Lunacy Act of 1890 still exist and involve *detention* in many cases if treatment is to be effective, whereas the Royal Commission of 1926 gave it as their opinion that "*the treatment of mental disorders should approximate as nearly as possible to those of physical ailments*" and the Mental Treatment Act of 1930 is quoted as an effort to bring this about.

The Acts relating to mental deficiency are also reviewed and the anomalies between the Mental Deficiency Act of 1913 and the Educational Act of 1921 referred to, whereby only children in attendance at special schools can be notified to the Mental Deficiency Committee. It is also explained that many mental defectives still find their way wrongly into mental hospitals.

Part III deals with general observations on the evidence given to this Committee. Drawing attention to the importance and size of the problem presented, it is estimated that on a conservative estimate not less than 30% of illnesses lasting twelve months or over are functional disorders, and that a mean average of 8 per thousand of the population (in rural and urban areas together) represents the incidence of cases of mental deficiency.

Mental disorders.—It is evident, from the immediate success of out-patient clinics, 100 of which had been established in 1936, that there is urgent need for their further extension in areas where they do not at present exist, and that on the other hand their duplication in other areas is undesirable. The evidence presented showed that the general consensus of opinion was that "in-patient

beds " in association with the out-patient clinic was desirable, and that the close association of the same with a general hospital was the best arrangement; that at least 3 beds for each sex should be provided for such cases, and that the full hospital services should be readily available. It is also thought that the time has come for a much closer co-operation between the statutory authority and the voluntary hospital. It appears that 60% of local authorities make no provision at all for social work, and that in the remainder no uniformity exists. Some social workers are full-time officers of mental hospitals, some are employed by the local authority and some are the officers of a voluntary association.

Mental deficiency.—It is observed that there are still large numbers for whom the statutory authority has no responsibility and that there are many gaps in the law which need to be filled. In one county area no less than four separate committees deal with mental defectives and yet there are serious gaps still left, e.g., no arrangement for voluntary treatment and no supervision for cases between 14 and 16 years of age. The need for a central co-ordinating committee is obvious when one sees the overlap of work by different existing committees with no contact between them.

Delinquency.—The evidence showed that there are wide differences of opinion on the relative merits of different methods of treatment, but it was generally accepted that psychological examination by experts should be made available in every juvenile court. In the majority of areas there is no system of reference of delinquents to out-patient clinics. There also seems an urgent need for the appointment of more full-time probation officers with high standards of training. Comment is also made on the fact that there is lack of accommodation for the " difficult " or " maladjusted " children who are not mentally defective, whereas many of the cases coming under the care of moral welfare associations or " rescue workers " are mental defectives for whom no treatment has been provided.

The evidence further showed that there was almost complete lack of preventative work on the side of mental health, and that such did not fall within the duty of any government department. That where this is being attempted the work suffers from lack of funds and co-ordination.

Part IV consists of a general review of the situation, and draws attention to the need for a revision of the laws relating to mental disorders and the making of these as simple and as free from formality as possible.

Part V contains a summary of the recommendations which are to be found throughout the report generally, and include the establishment of a Mental Health Committee in each area which should consist of representatives of mental hospital, mental deficiency, educational and public assistance committees, with power to contribute to the cost of convalescent or specialist treatment and deal with and co-ordinate all matters relating to mental health in their area. There should be a uniform standard of training of social workers and special observation centres established for juvenile delinquents and the overlapping of probation and other social services should be eliminated. There should also be a clearer definition of the powers of the local authority to contribute to the funds of voluntary associations interested in the promotion of mental health, and these should cover all the ground not covered by the statutory authority.

Part VI emphasizes the need of co-ordination of the voluntary associations dealing with these problems in their respective spheres (i.e., the National Council for Mental Hygiene, the Child Guidance Council, the Mental After-Care

Association, the Central Association for Mental Welfare and the Home and School Council). A draft of the suggested constitution of a National Council for Mental Health is given in Appendix I, and the Questionnaire used by the Committee in Appendix II. The report is full of matters of interest to anyone who is dealing with mental health problems, and if only half its recommendations are adopted, a great advance will have been made. RICHARD EAGER.

The Body Image (L'Image de notre corps). By JEAN LHERMITTE. Paris: Editions de la Nouvelle Revue Critique, 1939. Pp. 254. Price 36 frs.

In this monograph evidence is amassed in favour of the theory that each of us has, at the fringe of consciousness, a plastic and tridimensional bodily schema. This body image is composed of various perceptive elements, including superficial and deep sensibility, the sense of vision, and above all, the vestibular sense. Normally hardly appreciated, in certain neuro- and psycho-pathological conditions this image, in part or wholly, may be strongly presented to consciousness. It is from a study of the various abnormal manifestations of the body image that the author arrives at his conclusions.

There is an interesting, if speculative, chapter on the development of the body image in the child. Here is shown how the child gradually distinguishes self from non-self, and at a later stage learns to appreciate the self as a unit. Play is believed to be a most important factor in helping to form the body image. It is considered unlikely that this image is fully developed before the age of eight.

A large section is concerned with the phenomenon of the phantom limb. This is a subject upon which the author has previously made a number of important studies, which are incorporated here. There is also a careful review of the theories of other workers, including those of Head and Schilder. Besides the well-recognized phantom limb of the amputated, a number of case-histories are presented in which the same phenomenon is met with in those suffering from various lesions of the central nervous system. The author favours the central rather than the peripheral theory of origin, maintaining that the body image is intimately associated with the cerebral cortex, more particularly the inferior parietal, marginal and angular gyri.

A second phenomenon from which the author elaborates his theory is the illusion of doubles. He believes that, besides the mutilations and distortions which portions of the body image undergo in cases of phantom limbs, under certain conditions the whole image may be projected into space as an illusion of a double. He brings forward some evidence to show that even normal people have produced this phenomenon by a process of introspection. He is, however, prepared to admit that during the experiment the subject's mental state may have been abnormal. Much more evidence is, of course, obtained by a study of psychopathological personalities. Here, besides studies of clear psychotic cases, the experiences of Goethe, de Maupassant, de Musset, E. A. Poe and others are reviewed. It seems rather curious that on this subject there is no reference to the most recent and exhaustive contribution, that of Otto Rank.

This book should be of interest to both neurologists and psychiatrists. Such a controversial subject is perhaps at times treated in a rather didactic manner, but the work, nevertheless, will well repay careful study. There is a fairly exhaustive bibliography. S. M. COLEMAN.

Conscious Orientation. By Dr. J. H. VAN DER HOOP. London: Kegan Paul, Trench, Trubner & Co., 1939. Pp. vi + 352. Price 15*s*.

This book by Prof. van der Hoop is divided into three parts—psychology and the types of conscious orientation, psychiatry and the types of conscious orientation, and a philosophical commentary. The author, who was analysed by Jung, nevertheless considers that Freud is more thorough and employs Freudian analysis in the treatment of the neuroses. The book is written from the standpoint of a practising physician, and is an interesting blending of the two schools of thought. G. W. T. H. FLEMING.

Introduction to Experimental Psychology. By C. W. VALENTINE. Third edition. London: University Tutorial Press, 1939. Pp. x + 283. Price 4*s*. 6*d*.

This small book is written primarily for students of educational psychology. This, the third edition, is a considerable enlargement of the first and second editions. As in the second edition, the new material is placed at the end of the book. The book is divided into two parts, the first detailing the experiments and the second the discussion of the results of the experiments. It is an extremely lucid and coherent account and will be most useful to those for whom it is written. G. W. T. H. FLEMING.

A Survey of Child Psychiatry. Edited by R. G. GORDON. London: Oxford University Press, Humphrey Milford, 1939. Pp. xii + 278. Price 10*s*. 6*d*.

This book, which is published by the Child Guidance Council, contains contributions by twenty-one authors. The book is divided into four divisions, dealing with problems related to physical illness, problems related to mental illness, sociological aspects, and special syndromes. The attempt to crush mental disorders associated with biochemical and metabolic disturbances into one small chapter of eight pages seems a great pity, as it is a most important subject. It is probably true that most cases of children suffering from mental disorders do not have their biochemistry adequately investigated.

G. W. T. H. FLEMING.

The Study of Society: Methods and Problems. Edited by F. C. BARTLETT *et al*. London: Kegan Paul, Trench, Trubner & Co., 1939. Pp. xii + 498. Price 10*s*. 6*d*.

This is an extraordinarily good book on the various problems presented by society looked at from a variety of angles. The book is divided into sections dealing with "some problems of social psychology", "social applications of psychological tests and other methods," "some methods of social anthropology", and "some methods of sociology". The nineteen chapters are written by seventeen different authors, and it would be invidious to select any chapter as being better done than another. The book is the result of the work of a social psychological discussion group and is very well worth reading.

G. W. T. H. FLEMING.

The Surgery of Pain. By RENÉ LERICHE. London: Baillière, Tindall & Cox, 1939. Pp. 512 + xix. Price 21*s*.

Prof. Young is to be congratulated on a good translation of Prof. Leriche's book on the *Surgery of Pain*. Young was a disciple of Hilton's *Rest and Pain*,

which is familiar to many English medical men as a very fine classic. Leriche's, book is in many ways a similar classic.

Leriche has steadily vanquished one opponent after another during the years, but he may truthfully be said to have intentionally avoided dealing with tabetic and thalamic pain. As is to be expected, a considerable portion of the book is devoted to dealing with the surgical treatment of the neuralgias, of nerve injuries, and causalgia. The surgery of vessels and their sympathetic supply is fully dealt with, including the pain of vaso-motor attacks, vaso-constriction attacks, Raynaud's disease, angina pectoris, arteritis.

G. W. T. H. FLEMING.

Technique of Analytical Psychotherapy. By WILHELM STEKEL. London: John Lane, The Bodley Head, 1939. Pp. xvii + 402. Price 21s.

The psychotherapist of whatever school should find in this book valuable and practical hints for the conduct of his practice. Dr. Stekel, with thirty years' experience, is out to put psychotherapy on a business-like footing. To this end he leads off with the matter of fees. His observations on this subject are not without humour and show his keen appreciation of human weakness where money is concerned. He advises that fees should be broached at the first session, before anything else is discussed, and fixed once and for all. Associated subjects are time of payment, bonuses for a cure, stipulations by the analysand regarding payment, gratuitous treatment and reduced fees.

At the preliminary interview, Dr. Stekel proposes a trial week. By the end of that time he is in a position to decide whether the subject is likely to be suitable for analysis. As is well known, analysis by Stekel seldom lasts more than three months, this abbreviation being brought about by the active intervention of the analyst. For success with this method intuition and empathy—by means of which the analyst sees into the complexes of the analysand—are considered essential attributes. The author's objective viewpoint is best shown by his terminology. The analysand suffers from a psychological scotoma; he cannot, or more usually will not, see the secret core of his own complexes. It is the analyst's job to remove this blind spot. Stekel finds that many analysts suffer from a similar scotoma; they are blind to such complexes as they themselves have when they present themselves in the patient, and also tend to transplant their own complexes into the analysand.

All psychoneurotics are grouped together as parapaths, of which there are two types, objective and subjective. The former falls ill because of an unwholesome relationship to some particular person. He can be cured when this relationship is bettered. The latter falls sick on his own account from his own defects in character. He needs a much more penetrating and long-lasting analysis. For Stekel, hysteria is a subjective and the obsessional state an objective parapathy. It is doubtful if many psychotherapists would endorse the statement that obsessionals are more responsive to treatment than hysterics.

Stekel is struck by the fact that in recent years, while hysteria has rapidly decreased, obsessional states have been on the increase. He has an interesting explanation for this. Hysteria is a subjective disease due especially to suppression of the sexual instinct; it has practically vanished because since the last war there has been so much more sexual freedom. Obsessional parapathy, on the other hand, is directed against a loved and guilty object, usually a parent. Its increase is due to the fact that young people now are brought up to a double standard of morality. Parents, teachers and the church continue to advocate

traditional morality, though individual exponents frequently in practice ignore their own creed. In case after case it is shown that the patient had discovered the loved object guilty of some sexual misdemeanour.

Large sections of the book are devoted to the subject of resistance and transference. Resistance may present itself in many disguises. For instance, as argumentation, somatic symptoms or by a hyperethical state, which blinds the subject to his own fundamental complexes. Characteristically Stekel thinks that Freud's discovery of the transference is indubitably one of the greatest of his scientific achievements. Formerly teachers, doctors and lovers took the devotion of pupils, patients and mistresses as the inevitable result of contact with their own super-excellence. It was for Freud to show that these individual experiences are no more than an expression of a universally valid law. Stekel also makes some interesting points on the counter-transference of analyst for analysand, and on a form of resistance which he terms a subsiduary transference. During analysis the analysand may attempt to weaken the transference by making a *confidente*, with whom the analysis is discussed, by indulging in a love affair, or even by undergoing a simultaneous analysis by another doctor.

S. M. COLEMAN.

Part III.—Bibliography and Epitome.

An attempt is being made to provide as far as possible a complete bibliography compiled from the specialist journals dealing only with Psychiatry and Neurology (which are really inseparable) and their ancillary subjects, psychology, anatomy of the nervous system, criminology, etc.

A number of titles may appear to have a very remote relation to psychiatry, but they are included for the sake of completeness.

If any reader can add the names of journals to the following list, which it is hoped to publish each year in the January number, the addition will be gratefully received and acknowledged.

Those journals which are available in the Library of the Royal Medico-Psychological Association are marked " 1 ", those available in the Library of the Royal Society of Medicine are marked " 2 ", those in the Library of the British Psychological Society are marked " 3 ", and those in the Library of the British Medical Association are marked " 4 ".

The titles of these journals are mostly in the form given by the Board of Editors of Publications of the American Psychological Association, January, 1939. Contributors are requested to use the exact form given below.

PSYCHIATRIC JOURNALS.

2, 4 *Acta Psychiatrica et Neurologica.*
3 *Acta Psychol., Hague.*
Acta Psychol., Keijo.
Aliéniste Français.
2 *Allgemeine Zeitschr. f. Psychiat. u. i. Grenz.*
Altersprobleme.
2, 3 *Amer. J. Ortho-psychiat.*
1, 2, 3, 4 *Amer. J. Psychiat.*
2, 3 *Am. J. Psychol.*
An. Inst. Psicol. Univ. B. Aires.
Analele Psihol (Rumania).
Anales de psicologia, Buenos A.
2, 3 *Année Psychol.*
2 *Ann. Méd. Psychol.*
2 *Ann. Osp-psichiatri. Perugia.*
Arb. Psychiat. Inst. Sendai.
Arch. Anthrop. crim.
2 *Arch. Argentinos de Neurologia.*
Arch. Argent. Psicol. norm. pat.
Arch. Brasileiros de Hygiene Mental.
2 *Arch. Brasileiros de Neuriatrica e psiquiatria.*
Arch. Chilenos de Crim.
Arch. Ital. di Studi Neuropsich.
1, 2 *Arch. Neurobiol.*
4 *Arch. Neurol. Paris.*
Arch. de Neurol. de Bucarest.
1 *Arch. de Neurologia.*
2 *Arch. di Antropol. Criminale.*
Arch. di Criminol. neuropsiquiatria y disciplina conexas.
2, 4 *Arch. Psychiat. Nervenkr.*
2, 3 *Arch. di Neur., Psichiat. Psich. e Psichoter.*

2, 3 *Arch. ges. Psychol.*
Arch. Internationale de Neurologia.
Arch. Ital. Psicol.
Arch. Krim. Anthrop.
1, 2, 3, 4 *Arch. Neurol. Psychiat.*
2, 3 *Arch. Psychol. Genéve.*
3 *Arch. Psychol., N.Y.*
Arch. Relig. psychol.
Arch. Speech.
Arquivos da Assist. a Psicopatas de Pernambuco.
3 *Austr. J. Psychol. Phil.*

Beih. Z. angew. Psychol.
Beih. Zbl. Psychother.
Bol. Inst. Psiquiatria.
2, 4 *Brain.*
3 *Brit. J. Educ. Psychol.*
2, 4 *Brit. J. Inebriety.*
2, 3, 4 *Brit. J. Med. Psychol.*
2, 3, 4 *Brit. J. Psychol.*
3, 4 *Brit. J. Psychol. Monogr. Suppl.*
2, 4 *Bull. de la Soc. de Psychiatrie de Bucarest.*
2 *Bull. de la Soc. Roumaine Neur. Psychiat., Psychol., Endocrin.*
Bull. du Groupement Français d'études de neuro-psychopathologie infantile.
2 *Bull. Los Angeles Neur. Soc.*
Bull. Menninger Clin.
Bull. Soc. Psihol. med. Sibiu.

4 *Canad. Journ. Occup. Ther.*
3 *Cath. Univ. of Amer. Studies in Psychol. and Psychiat.*
2 *Cervello.*
2, 3, 4 *Character and Per.*
2 *Child Develpm.*
Child Develpm. Abstr.
Child Develpm. Monogr.
Child Study.
Chin. J. Psychol.
3 *Comp. Psychol. Monogr.*
2 *Confinia Neurologia.*
Contr. del Lab. di Psichologia.
Contr. psychol. Theor.

2 *Deutschr. Zeitschrift f. Nervenheilk.*

1, 2, 3, 4 *L'Encéphale.*
2 *Epilepsia.*
Evolut. Psychiat.

Fiziol. Th. S.S.S.R.
2 *Folia Neuropath. Esthon.*
2 *Folia Psychiat. et Neurol. Japonica.*
2 *Fortsch. Neur. Psychiat.*

3 *Genet. Psychol. Monogr.*
Giornale di Psich. e di Neuropat.

4 *Hum. Factor.*
2, 3, 4 *Hygiène Mentale.*

2, 3 *Imago.*
3 *Indian J. Psychol.*
Industr. Psychol.
Industr. Psychotech.
2 *Int. J. Indiv. Psychol.*
1, 2, 3, 4 *Int. J. Psychoanal.*
3 *Int. Z. Indiv. Psychol.*
2, 3 *Int. Z. Psychoanal.*

Jap. J. appl. Psychol.
Jap. J. Exp. Psychol.
Jap. J. Psychol.
1, 2, 3 *J. Abnorm. Soc. Psychol.*
3 *J. App. Psychol.*
2, 4 *J. Belge Neur. Psychiat.*
2 *J. Comp. Neur.*
1, 3 *J. Comp. Psychol.*
J. Consult. Psychol.
J. Crim. Law and Criminol.
J. Crim. Psychopathol.
J. de Psychiatrie Infantile.
3 *J. Educ. Psychol.*
J. Except. Child.
3, 4 *J. Exp. Psychol.*
2 *J. f. Psychiat. u. Neurol.*
3 *J. Gen. Psychol.*
J. Genet. Psychol.
J. Juvenile Res.
1, 2, 3, 4 *J. Ment. Sci.*
1, 2, 3 *J. Nerv. Ment. Dis.*
1, 2, 3, 4 *J. Neurol. Psychiat.*
J. Neuropath. and Psychiat. Leningrad.
2, 4 *J. Neurophysiol.*
J. Neuropsychiatrique du Pacifique.
J. Parapsychol.
J. of Psichical Research.
J. Psihoteh.
2 *J. Psycho-Asthenics.*
3 *J. Psychol.*
J. Psychol. Moscou.
J. Psychol. Neurol. Leipzig.
2 *J. Psychol. Norm. Path.*
J. Soc. for Psychical Research.
3 *J. Soc. Psychol.*
J. Speech Disorders.

Kriminalistik.
3 *Kwart. Psychol.*

Mag. psychol. Szle.
2, 4 *Mental Hyg., Lond.*
Ment. Hyg., N.Y.
3 *Mind.*
Mschr. Krim. Biol.
2 *Mschr. Psychiat. Neurol.*

Ned. Tijdschr. Psychol.
2 *Neopsichiatrica.*
2 *Nervenarzt.*
3 *Neue psychol. Stud.*
Nevropath. i. Psikhiat.
Note e Riv. di Psichiatrica.
Nowiny Psychjaryczne.
Nuova Riv. di Clin. ed Assistenza Psichiatrica.

Obshch. Klin. Nevropat.
3 *Occup. Psychol.*
2 *Occup. Ther. and Rehabil.*
2 *Onderzoekingen Psychiat-Neur. Klin. Utrecht.*
2 *Ospedale Psichiatrico.*

Person. J.
Pisani.
Polsk. Arch. Psychol.
Prace Psychol.
Proc. Amer. Assoc. Stud. Ment. Def.
Psicoterapia (*Cordoba*).
Psyche.
2 *Psychiat. en Neurol. Bladen, Utrecht.*
2 *Psychiat. et Neurol. Japonica.*
2 *Psychiat. Neurol. Wochens.*
Psychiatry.
1, 2, 4 *Psychiat. Quart.*
2, 3 *Psychoanal. Quart.*
1, 2, 3 *Psychoanal. Rev.*
2, 3 *Psychol. Abstr.*
3 *Psychol. Bull.*
Psychol. Clin.
Psychol. Exch.
3 *Psychol. Forsch.*
Psychol. Index.
Psychol. Monogr.
Psychol. Rec.
3, 4 *Psychol. Rev.*
3 *Psychol. Rev. Monographs.*
Psychol. wychow.
3 *Psychometrika.*
Psychometr. Monogr.
Psychosomatic Medicine.

Quart. Journ. Speech.

Rass. Neurologia Vegetativa.
Rass. Studi Psichiat.
Rev. di Neur. e Psychiatry, S. Paolo.
Rev. di Psiquiatria, Chili.
Rev. di Psiquiatria y Crim.
3 *Rev. Franç. Psychanal.*
Rev. Ibero-Amer. de Anal. Biblio. de Neurol. y Psiquiat.
Rev. Mex. Neurol. Psiquiat.
1, 2, 4 *Rev. Neurol.*
Rev. Neurol. Psychiat. Praha.

Rev. Neuropsiquatr.
Rev. Psicol. Pädag.
Rev. Psihol.
Rev. Psiquiat.
Rev. Tchèque de Neurol. et de Psychiat.
La Ricerca Psichica.
2, 3, 4 *Riv. di Neurol*
Riv. di Neuro-psiquiatria, Peru.
3 *Riv. di Psichologia.*
Riv. Ital. di Endocrin. e Neurochir.
Riv. Neurol. di Buenos-Aires.
2 *Riv. Patol. nerv. ment.*
Riv. Psichol. Norm. Pat.
2, 4 *Riv. Sper. Freniat.*
1 *Rocznik Psychjatryczny.*
Rorschach Res. Exch.

1 *Schizofrenie.*
2 *Schweiz. Arch. Neurol. Psychiat.*
Skand. Arch. Psychol.
Sov. nevropatol., psichiatri, psichoguoguia.
Sovetsk. Psikhotekh.

Tohoku Psychol. Folia.
Trans. Beritov. Inst. Tiflis.
Trans. Kostchenko Ment. Hosp. Moscow.
Trud. fiziol. Lab. Pavlova.
Trud. tsentral. psikhonevrol. Inst.

Univ. Calif. Publ. Psychol.
Univ. Ia. Stud. Psychol.
Untersuch. Psychol. Phil.

3 *Z. angew. Psychol.*
Z. Arb. Psychologie u. praktische im Allgemeinen.
Z. Berufsbildung des Pflegepersonals.
Z. Individ. Psychologie.
2, 4 *Z. ges. Neurol. Psychiat.*
3 *Z. Pädag. Psychol.*
Z. Parapsychol.
Z. Psychoanalyse (Tokyo).
3 *Z. psychoanal. pädag.*
2, 3 *Z. Psychol.*
Z. Psychother. med. Psychol.
Z. Tierspsychol.
2 *Z. Neurochir.*
1, 2 *Zbl. ges. Neurol. Psychiat.*
Zbl. Psychotherap.

ACTA PSYCHIATRICA ET NEUROLOGICA.

VOL. XIV. 1–2, 1939.

EIGHTH CONGRESS OF SCANDINAVIAN NEUROLOGISTS.

3–4.

THE THIRD INTERNATIONAL NEUROLOGICAL CONGRESS.

Suppt. XXI.

Ether-soluble Plasma Phosphatides in Schizophrenia. Jokirartio, E.

The normal mean value of the ether-soluble plasma phosphatides is 10·22 mg.%, with extremes of 8·72 and 12·87. The values for women are generally higher than those for men. In schizophrenics, the 40 acute cases showed a mean value of 5·79 mg.%. 37 out of the 40 cases showed values below the lower limit of normal cases. The 18 chronic cases showed a mean value of 5·76 mg.%. In defective-state schizophrenics the mean value was 8·30 or slightly below the lower limit of normal cases.

Cardiazol or insulin treatment causes no important changes in the phosphatide values. G. W. T. H. FLEMING.

ACTA PSYCHOL., HAGUE.

VOL. IV. 1939.

ACTA PSYCHOL., KEIJO.

VOL. III. 1939.

ALLGEMEINE ZEITSCHR. F. PSYCHIAT. U. I. GRENZ.

VOL. CXI. JUNE, 1939.

AMER. J. PSYCHIAT.

VOL. XCVI. JULY, 1939.

Age of Onset of Epilepsy: Differences between Deteriorated and Non-deteriorated Patients.

In this study the age of onset of 368 adult non-deteriorated patients with epilepsy was determined and compared with similar data for institutional deteriorated patients.

The trends observed were as follows:

1. Fewer non-deteriorated patients have the onset before 5 years of age.
2. Fewer non-deteriorated patients have the onset before 10 years of age.
3. More non-deteriorated patients have the onset after 20 years of age.
4. More non-deteriorated patients have the onset after 40 years of age.

It is concluded that deteriorated patients with epilepsy differ from the non-deteriorated ones in that there is a tendency to later onset in the non-deteriorated patients. (Authors' abstr.)

Cell Minerals in Amaurotic Idiocy, Tuberous Sclerosis and Related Conditions, Studied by Microincineration and Spectroscopy. Examples of Degenerative and of Neoplastic Cell Disease.

(1) The ganglion-cell disease of amaurotic idiocy is characterized by demineralization, that of tuberous sclerosis by hypermineralization of the cytoplasm. In this respect the ganglion-cell disease of amaurotic idiocy aligns itself with other degenerative conditions; that of tuberous sclerosis with other conditions of a blastomatous or neoplastic nature. The actively proliferating reactive glia-cells in amaurotic idiocy are hypermineralized, like all actively growing tissues.

(2) The demineralization of the diseased ganglion-cells in amaurotic idiocy is of especial interest in view of the associated increase in lipoid material. In our studies thus far, it appears that wherever lipoid is accumulated, normally or pathologically, heat-resistant mineral ashes are absent. This is well exemplified by the lipoid body of the normal myelin sheath, which is completely lacking in heat-resistant mineral ash.

(3) The "periventricular spongioblastomatous hæmatoma", presumably an attenuated form of tuberous sclerosis, which has been described and three new cases of which are reported here, shows gross hypermineralization which corresponds to that generally found in tumours and other actively growing tissues.

(4) The mineral ash picture of the brain in "mongolian idiocy" (Langdon-Down's disease) does not show significant alterations from the normal.

(Authors' abstr.)

Pathologic Considerations on Insulin Treatment of Schizophrenia.

The study of the present material while confirming the indirect evidence of functional changes based on the type and distribution of the nerve-cell changes, offers direct evidence of the vascular origin of the lesions based upon actual morphologic alteration of the blood-vessels. The striking pathologic changes of the brain blood-vessels described seem to indicate a direct damaging action of insulin, or some other substance formed in hyperinsulinism, upon the cells of the vessel-walls. The reaction of the adventitial and endothelial elements appears to be mainly hyperplastic and, to a lesser extent, degenerative in character. Neo-formation of capillaries may be explained partly as a secondary vascularization of an altered tissue that is undergoing new organization; partly, however, as a direct effect of proliferative stimuli, since cellular proliferation of vessel-walls was also observed in the absence of major parenchyma destruction. The pathologic features of the vascular changes bear striking similarities to the "productive type" of vascular reaction found in lead "encephalitis" (Bonfiglio, Hassin). This type of vascular changes has not been described as yet in insulin-treated patients, although in experimental hyperinsulinism Dunner *et al.* and Accornero have mentioned the finding in the central nervous system of proliferation of vascular endothelium and neo-formation of capillaries.

It seems reasonable to assume that the cellular waste of the brain tissue in severe hypoglycæmia is brought about by a mechanism of anoxia in which not only biochemical factors but also vascular alterations appear to play a role. In the majority of cases of hypoglycæmic shocks the vascular reaction is likely to be functional in character at the beginning. However, high doses of insulin may produce proliferative changes in the wall of the vessel, leading to narrowing and obliteration of the lumen. In both functional and anatomical vascular alterations, the quantity of oxygen conveyed to the tissue by the blood-vessels is forcibly reduced and cellular anoxia, eventually leading to destructive changes of the nerve-cell, is the ultimate result.

Functional disturbances and productive changes of the blood-vessels might be regarded as two successive stages of the same process; evidence has been offered, in fact, in favour of the hypothesis that angiospastic states of long duration and frequently repeated may determine endarteritic proliferation.

(Authors' abstr.)

Cerebral Damage in Hypoglycæmia: A Review.

Four personal cases are reported, three of which are still alive, but handicapped by varying neurological and psychiatric disabilities.

From a review of the literature and a study of these cases it seems very apparent that continued repeated hypoglycæmia may definitely produce a depression of the cerebral function and even an irreversible degeneration of the brain-tissue and cells, resulting in long-continued or permanent functional damage or even death.

The factors behind the different individual responses to hypoglycæmic insults are at present unknown, hence making it impossible to predict or adequately control the more severe reactions or the resulting brain damage.

(Author's abstr.)

Metrazol Shock Treatment: Pharmacological and Biochemical Studies.

It was found that the level of serum calcium and potassium remained almost unchanged before and after convulsive seizures. The characteristic increase in blood sugar may be due to an increased output of adrenaline. Serum sodium chloride was also slightly increased. The blood sedimentation rate was retarded after convulsions, and is interpreted as reflecting an increase of serum albumin.

Central nervous system stimulants such as carbon dioxide and ephedrine decreased the minimal convulsive dose of metrazol. Adrenalin and pituitrin were less effective in this regard. Strychnine, caffeine and theophylline had no such effect. Hypnotic and narcotic drugs—phenobarbital, sodium barbital and rutonal—exhibited a marked antagonistic action to metrazol, while this effect was less with paraldehyde and chloral hydrate. Sodium bromide also has no antagonistic action. All of these observations tend to corroborate the Pick-Molitor theory of the action of hypnotics. The dose of metrazol required to produce a convulsion during insulin hypoglycæmic shock is much smaller, which tends to show that unconsciousness in insulin shock is pharmacologically and neurologically different from the coma induced by hypnotics and narcotics.

In the human subject the results obtained were similar to those found in animal experiments. Previous administration of thyroxin to rats caused a decrease in the minimal convulsive dose of metrazol.

Metrazol convulsions in man are produced by an intense stimulation of the vegetative and motor centres of the brain-stem. (Author's abstr.)

ARCH. GEN. DI NEUR., PSICH. E PSICHANAL.

VOL. XX. 1938.

Supplement, Bibliography.

ARCH. DE NEUROL. DE BUCAREST.

VOL. III. 1939.

ARCH. NEUROL. PSYCHIAT.

VOL. XLII. OCTOBER, 1939.

Pathologic Laughing and Crying.

From an analysis of the clinico-pathologic material presented, the cases reported in the literature and animal experiments, it is possible to reconstruct the centres and pathways regulating these affective responses.

The cases of cortical lesions indicate that certain cortical areas, namely the frontal, premotor, motor, parietal, temporal and hippocampal, may act as centres for integration of these affective responses. These impulses are mediated by pathways which are in intimate connection with the hypothalamus. This is illustrated best by series of cases in which there were lesions at the cortico-diencephalic level. The hypothalamus or some of the other diencephalic nuclei which are under cortical inhibitory influence are the main centres or stations for the release of affective responses. A lesion of the corticohypothalamic tract removes cortical control, thereby inducing excessive affective responses. The secondary involvement of the nuclei, striatum and pallidum in many of the clinico-pathologic cases, and the œdema of these structures in the experimental animal, suggest that these areas

may also act as centres for the production of these affective responses and that, by means of pathways, they are in intimate association with the hypothalamus.

The group of cases of selective lesions of the mesencephalon and metencephalon and the animal experiments indicate that there are pathways, and possibly independent centres, in these regions for the production of laughing and crying. Some of these pathways are in intimate connection with the hypothalamus and the facio-respiratory nuclei.

The various psychologic theories for the emotions are discussed. It is emphasized that the pathways and centres aforementioned, particularly those of the facio-respiratory mechanism, are important for the expression of the emotions, and that the stimuli setting them off may be cortical or subcortical, or both. No single structure is all-important, and all must be integrated for control of feeling and expression.

A psychodynamic study of pathologic laughing and crying indicates that a number of variations may occur. These emotions apparently may be adequate or exaggerated in their form or feeling tone, as described by the patient. The responses may also be actually or seemingly disjointed and inappropriate. The spontaneous laughing and crying in the psychoses and neuroses are not included in this study. Although these will have to be explained on purely psychological grounds, the seat of their origin and their transmission most likely depend on the centres and pathways described. (Authors' abstr.)

Treatment of Schizophrenia with Glandular Extracts.

1. In every case of schizophrenia there is a disturbance in the gaseous metabolism, which begins with decrease in the specific dynamic action of protein.

2. The specific dynamic action of protein depends, at least in part, on secretions from the anterior lobe of the pituitary gland.

3. The treatment of schizophrenic patients with an extract containing anterior pituitary-like substances from the urine of pregnant women produces good therapeutic results, and has the added advantages of not being a dangerous form of therapy. (Author's abstr.)

Capillary Structure in Patients with Schizophrenia.

1. Schizophrenia is associated with a defect in the capillaries.

2. The observations indicate that the severity of the disease is related to the degree of derangement of the capillary structure.

3. The studies suggest that schizophrenia falls in the category of vegetative and metabolic disorders. (Author's abstr.)

Cerebral Changes in Fatal Cases following Treatment with Barbital, Soluble Barbital U.S.P., Insulin and Metrazol.

Barbiturates, insulin and metrazol produce morphologic changes in the ganglion-cells of the brain, often associated with neuronophagia, but without marked macroglial or microglial reactive phenomena.

The changes are diffuse and appear to be somewhat more marked in the medulla, especially the olivary bodies.

Distension of the subarachnoid space and the cerebral tissue spaces—œdema—is a dangerous occurrence, and is much more significant than the changes in the ganglion-cells.

The changes in the ganglion-cells are not specific, for they are the same regardless of the type of poison; they also resemble changes produced experimentally by injections of a variety of organic or inorganic poisons. (Author's abstr.)

Histopathologic Changes in the Brain following Experimental Injections of Metrazol.

Metrazol in a 10% solution was injected intravenously twice a week into rabbits, in imitation of the treatment of dementia præcox in man. The average dose

injected was 22 mgrm. per kilogram of body-weight, and was sufficient to produce a convulsive seizure. Resistance to metrazol developed gradually, and the initial dose had to be increased after about five to seven injections.

Definite histopathologic changes were observed after injections of a total of more than 700 mgrm. of metrazol. The intensity of these changes was roughly parallel to the dose injected, the number of injections and the time of survival after the last injection. They were characterized by more or less severe shrinkage of both cytoplasm and nuclei of neurons and hyperplasia and hypertrophy of the different types of glia-cells. The pathologic effect was more pronounced in the striatum and hippocampus than in the cerebral cortex. (Authors' abstr.)

Mode of Action of Brilliant Vital Red in Epilepsy.

1. The endothelium concerned with the formation of cerebro-spinal fluid forms an effective protective barrier to the central nervous system.

2. In animals with experimental epilepsy brilliant vital red renders this " barrier " relatively impermeable to the passage of cocaine hydrochloride. The same effect presumably holds for the other convulsive agents (picrotoxin, strychnine, camphor and triphenylphosphite) tested in connection with brilliant vital red.

3. Brilliant vital red affords protection in cases of human epilepsy. This fact, in addition to various other considerations which are discussed, affords strong evidence in support of the hypothesis that " convulsive toxins " and the endothelium of the hæmato-encephalic barrier are factors of ætiologic importance in human epilepsy, and that the relation between them is analogous to that demonstrated in experimental epilepsy. (Author's abstr.)

Skin and Body Temperatures of Schizophrenic and Normal Subjects under Varying Environmental Conditions.

Schizophrenic and normal subjects were exposed to varying mental conditions in the nude and under fasting conditions. Skin and rectal temperatures were measured by means of thermocouples. It was found that immediately after exposure the schizophrenic patients tended to have warmer extremities than the normal subjects. Exposure to cold conditions (15°, 20° and 24° C. [59°, 68° and 75·2° F.]) resulted consistently in greater cooling of the skin in the patients than in the normal controls. Exposure to hot conditions (44° C. [110·2° F.]) resulted in no difference in the response of normal and of schizophrenic subjects. Exposure to high humidity at low and high temperatures showed no difference between the patients and the normal subjects. The rectal temperatures of schizophrenic and normal subjects reacted similarly under all conditions. (Author's abstr.)

NOVEMBER.

Effect of Epinephrine on Convulsions.

1. The intravenous injection of epinephrine hydrochloride in minute quantities (0·004 to 0·015 mgrm. per kilogram of body-weight) diminishes or inhibits temporarily insulin and metrazol convulsions in rabbits, although the blood sugar remains unchanged in the insulin experiments.

2. The injection of epinephrine may induce sleep in rabbits which have been awakened by metrazol from narcosis induced with soluble barbital.

3. Hyper-reflexia as seen in cats under chloralosane anæsthesia is abolished by epinephrine.

4. Experiments on narcotized cats show that the anticonvulsant action of epinephrine is linked with carotid sinus and depressor reflexes. The action is abolished by bilateral vagotomy and denervation of both carotid sinuses, but is still present after carotid sinus denervation if one vagus nerve is intact. These facts, and the observation that convulsions are frequently increased when the blood-pressure is lowered by amyl nitrite, make it probable that pressor reflexes from the carotid sinus and arch of the aorta regulate the excitability of the somatic nervous system in a manner similar to that shown by Darrow and Gellhorn for the autonomic system.

5. The increase of metrazol convulsions with epinephrine occurs only with higher concentrations and is therefore of pharmacologic rather than of physiologic significance. (Authors' abstr.)

Follow-up Study of Five Hundred Patients with Schizophrenia Admitted to the Hospital from 1913 to 1923.

A survey of 500 schizophrenic patients has been made, 222 of whom have been followed for an average of twenty years.

At the time of discharge from the Phipps Clinic, 42·7% of the patients were well or improved ; slightly more than half (57·34%) left the hospital unimproved.

The course of the illness seems more favourable for women than for men.

At the end of twenty years the picture is less favourable than at the end of nine years, or at the time of discharge. After twenty years 27% of patients show recovery ; an additional 13% give evidence of some productivity.

There is great variability in the course of the disorder as regards rehospitalization : 33·5% of the total series of patients were never able to leave a hospital ; 32·6% were never readmitted to any hospital.

While rehospitalization is frequent, this does not necessarily affect the final outcome.

A relatively brief period of hospitalization is the rule for patients who recover. The largest number of deaths occurs in the age decade of 21 to 30. The chief cause of death is tuberculosis. (Authors' abstr.)

ARCH. PSYCHIAT. NERVENKR.

VOL. CIX. APRIL, 1939.

VOL. CX. JUNE, 1939.

ARCH. PSYCHOL. N. Y.

Some Psychological Correlates of the Electro-encephalogram.

Depression of alpha rhythm depended on at least two factors designated as stimulation and attention to stimulation. Attention without stimulation produced no depression. Facilitation of the alpha rhythm accompanied a third factor characterized as a change in the general psychological state of the subject. It appeared following the induction in the subject of states of awareness, attentiveness, readiness, relaxation, etc., and as bursts of high amplitude, regular alpha waves, clearly distinguishable from the level of alpha activity in other portions of the record. Stimulation and attention tended to increase the amounts of the beta and delta potentials. Tasks involving a motor response were also accompanied by an increase in the amount of beta and delta. It is suggested that depression of alpha results from interfering impulses coming from sensory stimulation or from other areas of the cortex, whereas facilitation is produced by increasing the activity of pacemakers, possibly located in subcortical areas.

G. W. T. H. FLEMING.

BRAIN.

VOL. LXII. SEPTEMBER, 1939.

Acute and Subacute Necrotic Myelitis.

One case of acute and two of subacute myelitis (Foix and Alajouanine) are described, and their clinical and pathological relationships to previously published cases is discussed.

The clinical picture of progressive amyotrophic paraplegia, with dissociated sensory changes and loss of tendon reflexes and of sphincter control, is sufficiently characteristic, if taken in conjunction with the condition of the cerebro-spinal fluid, to allow of clinical diagnosis.

The condition consists essentially of primary obliterative sclerosis of the small intramedullary and meningeal vessels in the lower segments of the spinal cord, and is associated with great thickening of the walls of the larger meningeal veins, and sometimes also of the larger arteries.

The degeneration of the parenchyma of the spinal cord appears to be altogether secondary to the vascular lesion. (Authors' abstr.)

Some Observations on Central Pain.

An attempt has been made to correlate certain features of pain resulting from central lesions and observations on the consequences of experimental disturbances of the peripheral nerves. Attention is drawn to the occurrence in both of over-reaction to certain stimuli, irradiation, and delay in the perception of pain.

It is suggested that the double conducting pathway in the peripheral nervous system described by Gasser *et al.* exists also in the central nervous system, and that the pathways differ in the rate at which impulses are conducted by them. It is further suggested that, in normal circumstances, the rapidly conducted impulses produce a relatively refractory state centrally, which has a modifying effect on the impulses conducted slowly. (Author's abstr.)

The Abnormal Cortical Potentials associated with High Intracranial Pressure.

The changes in cortical electric potentials in patients with abnormally high intracranial pressure have been studied in relation to the clinical state and the height and duration of the abnormal pressure. There was little correlation between the pressure and its effects on the state of consciousness of the subject and on the changes seen in the electro-encephalogram.

Experimental modification of cerebro-spinal fluid pressure showed that the abnormal waves of electrical potential were due to secondary osmotic changes in the cerebral tissues. Evidence has been produced that this change is probably an œdema of the nerve-fibres in the white matter of the hemispheres.

The underlying mechanisms causing the changes in cortical electrical activity and in consciousness have been discussed. (Author's abstr.)

BRIT. J. MED. PSYCHOL.

VOL. XVIII. JULY, 1939.

Psychological Observations on Hæmatemesis.

From a study of 50 patients suffering from hæmatemesis the writer arrives at the following conclusions: Hæmatemesis is associated with a certain personality type, characterized by high sensitivity to problems of security, dependence and responsibility. Precipitating conditions are threats to security and independence, or sudden increase in responsibility. In most cases the illness meant a self-punishment, in a few it was used to evade responsibility. Answering the question, Why does the illness take this form?, some evidence is brought forward to suggest that the abnormal gastric response to threats to security may arise as a late result of abnormal conditions during the breast period of development.

S. M. COLEMAN.

The Symbolic Significance of Glass.

From his experience as an ophthalmic surgeon, the writer has come to regard loss of or damage to glasses as psychologically determined. He finds that glasses are in the unconscious equated with virginity, while broken or lost glasses are associated with the patient's reactions to the act of defloration. Since glasses so closely resemble the cornea, and indeed are frequently worn because of some defect in that structure, the idea is carried further and made the starting-point in the investigation of the psycho-genesis of diseases and injuries of the front of the eye.

S. M. COLEMAN.

The Case of a Middle-aged Embezzler.

An instructive case-history of a man, aged 40, who on two occasions had served sentences for embezzlement. Hypnosis revealed an amnesia of twenty years' duration for certain exceptional and unorthodox war experiences. His antisocial conduct was shown to be directly determined by these experiences, by the attitude of the authorities to his war service, and by his failure to obtain a pension.

S. M. COLEMAN.

Symposium on Aggression.

In the opening paper Dr. Fairbairn discusses how far and in what sense aggression may be regarded as a primary instinctive tendency. The inquiry provides an examination of the McDougall, Drever, Freud and Jung theory of instincts. It is concluded that aggression is a primary instinctive tendency, and therefore an irreducible factor in the economy of human nature. As to how far aggression is a quantitatively irreducible factor, the writer finds that it can be modified in two ways: (i) in an economic sense, by regulation of the channels along which it is distributed, and (ii) in a dynamic sense, by mitigation of the frustrations which provoke it.

Dr. Wolters suggests that the term "aggression" should be reserved to denote a perversion of pugnacious behaviour. He believes that there are two patterns of behaviour—retreat and attack—associated with corresponding indefinite modes of reaction—fear and rage. Destructiveness and aggression should be restricted to

designate behaviour which is directed immoderately to the mastery of the environment without reasonable regard to profit or safety, and without economy of the material mastered. Applying these concepts to the group, he finds that group members will fight to maintain their integrity; this is a fundamental biological reaction; it should not be termed "aggression". The group may also fight to advance its own interests and do so deliberately. This, in common usage, is aggression. Lastly there is fear-induced aggression, the most dangerous of all, because inaccessible to reason. Dr. Wolters, supporting Dr. Fairbairn, is pessimistic of any absolute reduction of aggression.

Dr. Stephen takes up the subject of aggression in early childhood. She apologizes for never having undertaken the analysis of a young child, but feels that her views should carry weight because she is "constantly in touch with the repressed unconscious side of human nature". S. M. COLEMAN.

Some Interpretations of a Painting called "Abstraction".

A surrealistic oil painting called "Abstraction" is described. It was painted impulsively by a male student in his early twenties, who was not trained as an artist, and who was in a normal state of health at the time. The painting was done in a fit of anger during a period of overwork. Psycho-analytical interpretation shows how the painting expresses the artist's conflicts, particularly aggression directed towards the father and father-surrogates. S. M. COLEMAN.

BRIT. J. PSYCHOL.

VOL. XXX. OCTOBER, 1939.

CONFINIA NEUROLOGIA.

VOL. II. NO. 5.

L'ENCÉPHALE.

VOL. XXXIV. MARCH, 1939.

Cataplexy.

A report of two cases of cataplexy is followed by a study of the pathology of the condition. It is pointed out that persons subject to cataplectic attacks also often suffer from narcolepsy. The writer supports Lhermitte's dual conception of sleep as the physio-pathological basis of cataplexy. Cataplexy presents in a state of isolation the somatic element of sleep, without involvement of the psychical factor, inhibition of consciousness. Regarding the pathology, this is considered to be due to disequilibrium of the subcortical neuro-vegetative tonus. Here it is noted that cataplectics have a well-marked vagotonic constitution. Repercussions from the disordered subcortical centres on the cerebral cortex, in whole or in part (motor areas), will result in narcolepsy or cataplexy.

S. M. COLEMAN.

Pharmacological Estimation of Histamine in the Blood of Schizophrenics and Controls.

The histamine content in the blood of 11 schizophrenics and 15 controls was estimated by the Barsoum and Gaddum method. On the whole the content was higher for women than men. Schizophrenics and controls showed no essential difference, and in some normals the histamine value was far above that of the schizophrenics. It is concluded that the metabolic disorders believed to be associated with schizophrenia are not due to histamine intoxication.

S. M. COLEMAN.

FORTSCH. NEUR. PSYCHIAT.

VOL. XI. MARCH, 1939.

APRIL.

MAY.

JUNE.

JULY.

AUGUST.

GENET. PSYCHOL. MONOGR.

VOL. XXI. AUGUST, 1939.

The Capacity of the Rhesus and Cebus Monkey and the Gibbon to Acquire Differential Response to Complex Visual Stimuli.

Several primate types (three rhesus and two cebus monkeys, and one gibbon) were tested on a progressively complex discrimination task involving ambivalent and antagonistic cue-combinations. The monkeys were all in the very early stages of adolescence and the gibbon was somewhat pre-adolescent. The task included four series of stimulus-combinations representing as many stages of difficulty. The reaching-method was used throughout except that a shift was made to the pulling-in technique when failure occurred at any stage. The norm of mastery for each series was 40 correct trials in succession in random presentation. The criterion of failure on a step was 1,000 trials by the reaching-method, in which no significant progress was made, usually followed by 500 trials by the pulling-in technique. The results of the experiment based upon random order presentation appear to warrant the following conclusions:

1. The rhesus monkeys failed to master Series I, consisting of two pairs of stimuli involving antagonistic cue-combinations.

2. The gibbon was successful on Series I, but failed to master Series II, consisting of two antagonistic stimulus-combinations that represented ambivalence with respect to the pairs in Series I.

3. The cebus monkeys were successful on Series I, II and III, but failed on Series IV, comprising four pairs of antagonistic and ambivalent stimuli, although they showed some progress in the earlier stages of this series.

4. The rank-order of primate types on this task (cebus monkey, gibbon, rhesus monkey) corresponds to the order in which the animals ranked in the frequency in which comparison-behaviour was observed. This type of behaviour favoured correct response.

5. In the final series the task was complicated enough to set up marked "neurotic" behaviour in one of the cebus monkeys, a mild phase of which still remained seven months later.

6. An attempt has been made to explain the main findings regarding limits of ability in the several primate types in terms of structural and behavioural differences. A tentative interpretation of the results in terms of abstraction and related processes has been offered. (Author's abstr.)

INT. Z. PSYCHOANAL. AND IMAGO.

VOL. XXIV. 1939.

JAP. J. PSYCHOL.

VOL. XIV. 1939.

J. BELGE NEUR. PSYCHIAT.

VOL. XXXIX. JUNE, 1939.

JULY.

AUGUST.

SEPTEMBER.

J. COMP. NEUR.

VOL. LXXI. OCTOBER, 1939.

J. COMP. PSYCHOL.

VOL. XXVIII. OCTOBER, 1939.

J. CRIM. PSYCHOPATHOL.

VOL. I. JULY, 1939.

J. EXP. PSYCHOL.

VOL. XXIV. 1939.

J. GEN. PSYCHOL.

VOL. XXI. OCTOBER, 1939.

The Goodenough Test in Insulin and Metrazol Treatment of Schizophrenia.

The Goodenough drawings of schizophrenic patients during the awakening from the effects of metrazol seizure or insulin coma show decided signs of organic confusion in gestalt perception and representation. However, these apparent primitive form elements are used by the schizophrenic individuals in the schizophrenic integration which remains incomplete in the first stages of confusion. This schizophrenic integration soon gets the upper hand when the organic confusion expressed in the drawings subsides. The treatment, therefore, introduces a completely new element, organic confusion, into the schizophrenic picture. This corresponds in clinical observations to the aphasic signs and to investigations with Gestalt tests by Orenstein and Schilder.

The effect of the insulin and metrazol therapy lies, therefore, not in a direct attack on the schizophrenic structures. It is an attack on the deeper seated structures. In the process of reorganization of the organic function, finally a reconstruction and reorganization takes place in the deeper layers. This may, in the long run, lead to a reorganization of the schizophrenic process which, although organic, is not of the same massive organic type as the disturbance provoked by the shock therapy. If this reorganization of the schizophrenic process takes place, it reflects in the gradual loosening of the schizophrenic characteristics of the drawings. (Authors' abstr.)

Intelligence in Man after Large Removals of Cerebral Tissue: Defects following Right Temporal Lobectomy.

A case is reported in which an extensive removal from the right temporal lobe was followed by a disturbance of non-language capacities, with an apparently good retention of language capacities. It is thought that the defect as determined psychometrically is one of form perception, visual and non-visual, and that this is possibly accompanied by some disturbance of social comprehension. It is thought improbable that the defects are epileptoid in origin, and they appear at any rate to be related to the locus of the lesion.

The case shows that a good Binet score after cerebral injury is not sufficient evidence of good retention of other abilities, and throws light on the problem of the clinical estimate of intelligence, giving additional reason to regard normal intelligence as a complex whose components may be differently affected by cerebral lesions. (Author's abstr.)

J. GENET. PSYCHOL.

VOL. LV. SEPTEMBER, 1939.

A Longitudinal Study of the Occipital Alpha Rhythm in Normal Children : Frequency and Amplitude Standards.

A study of the frequency and amplitude of the occipital alpha rhythm in 132 children ranging in age from one month to sixteen years of age has been made, and the data grouped for use as standards. Frequency measurements are based on 369, and amplitude on 294 separate examinations at the various age-levels. Serial or longitudinal observations were made on most subjects, and show that the changes in frequency and amplitude with increasing age for individuals confirm those established for the group, cross-sectionally. The alpha rhythm, once established, increases rapidly in frequency during the first year, but more slowly thereafter until the adult average is first reached as an average by the 12-year-old group. Amplitude of the alpha waves increases during the first year or two, but drops sharply during the third year, and more gradually thereafter until the adult average is reached at about 15 to 16 years of age. The changes in frequency and amplitude of the alpha waves as a function of age are not directly related.

(Author's abstr.)

J. NERV. MENT. DIS.

VOL. XC. JULY, 1939.

A Specific Motility Psychosis in Negro Alcoholics.

Seven cases of a specific syndrome of alcoholic encephalopathy in negroes have been observed. The cases are characterized by confusion and threatening auditory hallucinations in the psychic sphere. The motility imitates the "Ganser-syndrome" of schizophrenia and appears in a playful and manneristic fashion. Nevertheless, the definite organic signs of iteration, retropulsion, falling backwards, rigidity and turning about the longitudinal axis are woven into the pattern. The disease can lead to death or deterioration; milder cases may recover. Only one similar case was observed in a white man. S. M. COLEMAN.

Tumour of the Base of the Brain Simulating an Aneurysm of the Internal Carotid Artery.

A case is reported showing the clinical and rœntgenological signs of an aneurysm of the intracranial portion of the internal carotid artery. Post-mortem examination showed an adeno-carcinoma of the base of the brain, originating from the nasopharynx. S. M. COLEMAN.

Familial Lateral Sclerosis.

Report of a family of familial spastic paraplegia with the disease occurring in seven members of four generations, the condition being either spastic paraplegia in the pure form or in association with ataxia. S. M. COLEMAN.

AUGUST, 1939.

Cerebral Lesions due to Vasomotor Disturbances following Brain Trauma.

From a detailed study of post-mortem findings in 22 cases of brain trauma the following observations are drawn. Many lesions following brain trauma may be discovered only with detailed microscopical studies. Lesions may occur distant to the immediate traumatic zone, and may be differentiated from some of the effects of *contre-coup* destruction. The structure of the vessel wall in such lesions may be perfectly retained. Angio-necrosis in traumatic lesions is secondary to tissue destruction. Some pathological findings in brain trauma are functional (reversible) in nature, and due to a disturbance in the regulating influence of the vasomotor apparatus. S. M. COLEMAN.

Blood-pressure Changes during Insulin Shock Treatment.

Observations on blood-pressure changes in four patients undergoing insulin shock treatment were made. All graphs indicate that insulin in doses large enough to produce shock caused a rise in the mean systolic pressure, which occurred from 1 to 2 hours after the injection of insulin and which varied from 8 to 37 mm. of mercury. In two graphs this rise remained throughout the treatment; in two others the mean systolic pressure dropped from this high level, especially during the last half hour, but remained above the initial mean reading. In one graph the

drop in mean systolic pressure was continuous after the second hour and fell below the initial level at the end of treatment.

Variations in the mean diastolic pressure are much less in degree and slower in onset. In two graphs the diastolic remained relatively constant, and in two others there was a rise of 5 to 13 mm. of mercury, which began two hours after injection of insulin. In one graph the mean diastolic pressure fell gradually during the entire treatment. S. M. COLEMAN.

Physicochemical Mechanisms in Convulsive Reactivity.

The polarization and, indirectly, the permeability of the cellular surface films for ions were determined *in vivo* on the cerebral hemispheres and on subcortical areas by measuring the difference in conductivity (polarization index Δ) at a certain high and a certain low frequency of the alternating current (experiments on cats; a few measurements on the human cortex). A new method is described that makes the determination of Δ independent of changes in the conductivity.

Anoxæmia increases the cellular permeability in the cerebral hemispheres as well as in the subcortex. Cerebral anæmia diminishes the conductivity. In the majority of the experiments an initial drop of Δ also was observed; when the anæmia lasts several minutes the curve of Δ again may rise, probably due to coagulation necrosis of a number of cells. Increase of intracranial pressure also lowers the conductivity. This is associated in the majority of the experiments with the drop of Δ.

Increase in the state of hydration produces a reversible increase of the cellular permeability. Hyperventilation acts in a similar way, as does alkalosis. Acidosis has only a slight effect upon Δ. Anæsthetics and hypnotics increase Δ, indicating an increase in the density of the cellular films.

Epileptogenous agents may act upon the nervous system by either of the following two mechanisms (or by both): (*a*) Production of a change in ion concentration on the surface of the nerve-cells. If the change in concentration reaches the threshold, excitation (convulsion) occurs. (*b*) Diminution of the density of the cellular surface films. The increase in permeability of the cell surfaces that is an important part of the excitation process is facilitated, and the threshold of the cells for metabolic or other stimuli is thus lowered. S. M. COLEMAN.

Periodic Paralysis.

Two isolated cases of periodic paralysis are reported, in which death from respiratory paralysis occurred during the attack. The possibility of a fatal result is always present in each attack of this disorder. There are now 358 cases in the literature, of which 182 are reported in some detail. The sex was stated in 342, of which 242 were males, giving a ratio of 2·4 males to 1 female. An hereditary history was present in 78% of the cases reported. The most effective treatment is the administration of a potassium salt in large amounts during the attacks.

S. M. COLEMAN.

Prolonged Non-Hypoglycæmic Coma Occurring during Insulin Therapy.

Prolonged non-hypoglycæmic coma is an unusual occurrence incident to insulin shock therapy. Nine cases are reported. They have features in common which suggest a symptom-complex, viz., prolonged coma (12 to 72 hours), convulsions, hyperglycæmia, protracted period of confusion, and good prognosis both physically and mentally. The only abnormal chemical finding of any significance was the chloride depletion in the various body fluids—an exaggeration of what is observed during the course of the usual insulin shock and coma. The pathophysiology is one in which the vegetative centres about the hypothalamus are most involved, and in fatal cases hæmorrhages have been shown to occur.

S. M. COLEMAN.

SEPTEMBER, 1939.

The Reactions and Behaviour of Schizophrenic Patients Treated with Metrazol and Camphor.

The writers describe a series of phenomenological observations dealing with the mental reactions and behaviour of schizophrenic patients undergoing metrazol and camphor therapies. They also offer some tentative theoretical formulations concerning the nature of the psychodynamic processes underlying these phenomena. In their opinion, it is not yet possible to evaluate these therapeutic methods. They are of the opinion that in certain types of schizophrenics metrazol can serve to facilitate development in the direction of social recovery. The value of camphor is considered an uncertain one. It does occasionally appear to have a certain potentiality for forcing a transformation in the chronic, vegetative patient, but the change induced is usually a transitory one. Moreover, it is pointed out, camphor is toxic to a dangerous degree. S. M. COLEMAN.

Preliminary Observations on the Course of the Traumatic Psychoses.

If a patient who has organic brain disease suffers a trauma to the head and develops a psychosis, the prognosis is graver and the course more protracted. This is especially true in those organic conditions where there is impairment of cerebral circulation, as in senility and arteriosclerosis.

Admitting the importance of the severity of the trauma, the significance of the localization of the lesion and the role of other constellatory factors, it is the writers' opinion that the previous personality plays an important role in the course of the traumatic psychoses. This is particularly true in the introverted or schizoid types, who often show significant and peculiar features in their clinical picture.

S. M. COLEMAN.

A Death Associated with Metrazol Therapy.

A case of sudden death with metrazol therapy is presented. A woman, aged 30, suffering from schizophrenia, catatonic type, died following her tenth convulsion. It is pointed out that the effect of this drug when used clinically has not been explained satisfactorily. The clinical picture points towards a specific effect on the central nervous system. In the case presented specific lesions were found in the brain, particularly areas of degeneration in the basal ganglia. Attention is drawn to the possible toxic and even lethal effects of the drug.

S. M. COLEMAN.

J. NEUROPHYSIOL.

VOL. II. NOVEMBER, 1939.

Physiological Analysis of the General Cortex in Reptiles and Birds.

1. The cerebral cortex of the turtle, *Emys europea*, appears to be electrically inexcitable in the usual sense of the term, i.e., there is an absence of visible motor reaction attributable to the excitation of cortical neurons.

2. The electrical activity of low voltage which it is possible to record from the cerebral cortex of the unanæsthetized turtle is essentially subcortical (striatal) in origin. However, the ability to produce "strychnine spikes", which are rapidly abolished by superficial cocainization, suggests the existence of a cortical component.

3. The cerebral cortex of the pigeon is electrically excitable by a weak current. The reactions to a unilateral stimulation consist in a conjugate deviation of the head and eyes toward the opposite side, accompanied by a miosis and opening of the palpebral fissure. This response is the expression of the excitation of neurons of the cortical layers, because (i) the response is abolished almost instantaneously by the superficial cocainization of the excited region; and (ii) an animal which presented a congenital aplasia of the cortex on one side, as verified histologically, did not react to the application of strong stimulation applied to this side, while the opposite cortex, which appeared to be normal, gave the usual response to weak stimulation. These conclusions concerning the reality of motor reaction dependent upon the cerebral cortex of birds confirm and justify by new evidence the studies made by older workers, particularly those of Ferrier and Kalischer. The negative results reported more recently are possibly explained by the use of light anæsthesia, or by the inhibition resulting from failure to apply cocaine to the borders of the wound in the unanæsthetized animal.

4. The simultaneous excitation of two symmetrical points on the right and the left cortex of the pigeon with currents of equal intensity results in rhythmic movements of the head in the vertical plane, suggestive of pecking movements in the intact animal.

5. The spontaneous electrical activity derived from the cerebral cortex of the unanæsthetized pigeon resembles closely that of the rabbit when awake. The partial resistance of this activity to superficial cocainization indicates that it includes a subcortical component. The superficial strychninization of the cortex causes the appearance of the large "strychnine spikes", which are abolished rapidly by superficial cocainization. A brief cortical faradization releases a short after-discharge of epileptiform type.

6. The cerebral cortex of the pigeon reacts to the illumination of the contralateral eye by a large initial wave (effect "on"). The cessation of the illumination does not provoke a distinct "off" effect.

7. The general conclusion derived from an analysis of the excitability and the

electrical activity of the cerebral " cortex " of the turtle and the pigeon indicates that, in the pigeon at least, the superficial layers of neurons covering the striatum dorsally and posteriorly have physiological properties and a functional significance—the latter being essentially opto-kinetic—much like those of the neo-pallium of mammals. (Authors' abstr.)

Studies in the Physiology of the Embryonic Nervous System. IV. Development of Acetylcholine in the Chick Embryo.

1. Tissues of chick embryos were ground and assayed for acetylcholine (ACh).

2. ACh increases from 2½ to 4 days of incubation and then shows random fluctuations until the 12th day.

3. There was no indication of a positive correlation between the development of ACh in the chick and the development of reflexes and of the nervous system.

In view of discrepancies between anatomical maturation and the concentration of ACh in relation to the appearance of reflexes, it is tempting to conclude that ACh, as it is found in a mixture of embryonic tissues, is not concerned with transmission of nerve impulse in the embryo. Such a conclusion does not preclude the possibility that the choline ester liberated at a particular moment of nervous excitation may act as a transmitter at synapses or at neuromuscular junctions. Such a possibility, however, remains to be proved. The mere presence of ACh or even an increase in its output at nerve terminals or synapses at the time of excitation is no sure evidence that the ester is actually concerned in transmission. The fact that ACh exists in most animal tissues, including such nerveless structure as human placenta, and can be detected when hydrolysis of the substance is prevented, has not been given satisfactory explanation by the proponents of chemical transmission.

The present results create a more difficult drawback which cannot be lightly dismissed as irrelevant to the theory. They lend support to the demand for better evidence that accumulation of ACh is not merely a result of increased metabolic activity or injury or other pathological process. The claims made by MacIntosh (1938) and by Bacq and Coppée (1938), that in degeneration experiments there is a time at which both the preganglionic fibres and ganglion-cells appear to be still functionally intact, whereas transmission across the synapses no longer occurs (which event coincides with the disappearance of ACh from the ganglion), are important in this connection, but they must be more thoroughly and systematically reinvestigated before they can be fully evaluated. The view that liberation of ACh is a general phenomenon associated with metabolic activities and is not in any way peculiar to nervous excitation also lacks decisive proof. The results of Lorente de Nó (1938) are significant, but not conclusive, and have been contradicted by a more recent investigation (MacIntosh, 1938). The evidence from the chick embryo here reported strengthens the metabolistic point of view, but does not disprove the transmission theory. (Author's abstr.)

Effects of Acoustic Stimuli on the Waking Human Brain.

Acoustic stimuli cause electrical on-effects and off-effects in the waking human brain. Though tones did not always produce visible responses, there appeared to be no difference between alpha and non-alpha types of subjects.

The on-effect, composed of a diphasic and sometimes triphasic wave, was most prominent at the vertex. The first phase was negative. Its latency was about 30 to 40 msec. The total duration of the on-effect was approximately 0·3 sec. or less. The voltage measured from peak to trough ranged from just visible to 100 μV. Frequently there was an off-effect similar to the on-effect, but never prominent.

A checking of the alpha rhythm was sometimes the only visible response. Fast frequencies were checked in two non-alpha subjects, and caused to appear in a third.

"Anticipatory" on-effects or off-effects appeared at an appropriate interval when a regularly-spaced sequence of tones was unexpectedly stopped or prolonged. If a subject was not aware that random sequences of different tones were to be given, or that regular sequences were going to follow irregular sequences, the "anticipatory" on- and off-effects would become more unpredictable. If the "psychological set" remained unaltered in relation to the experiment, but the physiological condition progressed from alertness to sleep, the on-effect would always become more predictable and more prominent. (Author's abstr.)

Electrical Reactions of the Human Brain to Auditory Stimulation during Sleep.

The electric response of the human brain to auditory stimuli during sleep, previously described and designated as the "K-complex", has been investigated in more detail. It is a multiple, diffuse, delayed, non-specific response to external sensory stimulation. Usually a fast component, consisting of a series of more or less regular waves at frequencies of 8 to 16 per sec., is superimposed on a series of slow (delta) waves, but either component may appear independently of the other. No shift of electrical base-line ("D.C. component") is associated with the K-complex.

Light and electric shocks may elicit K-complexes, but less effectively than do sounds. Typical K-complexes may appear "spontaneously" without assignable external cause.

The latency of the K-complex is usually of the order of 100 msec., and may be half a second or more. Both fast and slow components are more prominent in the central and frontal than in the occipital and temporal regions. The patterns are simultaneous and broadly similar over all these regions, but characteristic differences between central and frontal types of the slow component are described.

The fast component is often identical with the trains ("spindles") of 14-per-sec. waves, which are characteristic of the C and D stages of sleep. The appearance of the fast component seems to represent a partial arousal of the sleeper. The slow component develops progressively from the waking "on-effect", and increases in amplitude and duration as the subject becomes drowsy and goes to sleep. Both components vary systematically with the stage of sleep. The waves become slower as sleep deepens, and do not appear in the E stage of sleep. The characteristics of the spontaneous K-complexes are the chief criteria by which the B, C and D stages were originally identified.

A sound within 3 or 4 sec. after a previous stimulus usually fails to evoke a second slow component. If it succeeds, the second response is delayed and reduced in amplitude. The fast component, on the contrary, appears full-sized at all intervals of stimulation and merges with the fast component of the previous complex.

Forbes and his collaborators have described a "secondary discharge" which appears in the cerebral cortex of the cat under barbiturate anæsthesia following electrical stimulation of the sciatic nerve. The slow component of the K-complex shows the same characteristics as, and is probably strictly analogous to, this secondary discharge. (Authors' abstr.)

Conditioning of Afferent Impulses by Reflex Discharges over the Dorsal Roots.

When the action potential of the sensory impulses conducted through the saphenous nerve of the cat following a gentle tap on the skin is recorded from the side of the nerve, it is found that a deficit in the total number of impulses occurs if the train is immediately preceded by a reflex discharge through the nerve from the spinal cord.

The experiments conducted in the course of the present investigation permit the mention of a number of characteristics of the reflex discharge by the way of the dorsal roots, not included in the previous report:

(*a*) The reflex discharge into the individual fibres is repetitive.

(*b*) The reflex can be evoked by physiologically selected afferent impulses, as those set up by a tap on the skin or to the patellar tendon.

(*c*) As shown by Barron and Matthews, the size of the reflex is greatly augmented if the cord is cooled. However, well-defined reflexes are regularly present when the cord is at a normal temperature. (Author's abstr.)

Vagal Inhibition of Inspiration, and Accompanying Changes in Respiratory Rhythm.

1. In dogs anæsthetized with sodium barbital, and with both vagi sectioned, one vagus was stimulated centrally during inspiration. Adequate stimulation cuts short the current inspiration. This requires a certain threshold number of afferent volleys (voltage and frequency of stimuli being constant). The threshold number becomes less as inspiration advances.

2. Certain effects of a near-threshold series of volleys are described.

3. Graded reduction of inspiratory amplitude can be effected by varying the time at which the vagus is stimulated, but not by grading the number of inhibitory volleys. Vagal inhibition affects the respiratory centre in an all-or-none manner.

4. Increase of the respiratory dead space does not raise the " inhibitory threshold " of the centre. Inspiration becomes deeper, but this can be accounted for by a more rapid inspiratory movement, and by the time required for inhibition to be built up to an effective level.

5. The cutting short of inspiration, by the procedure described is accompanied by an acceleration of rhythm. The amplitude and rate effects are related in the following ways:

(*a*) The voltage threshold of the vagus is the same for both.

(*b*) Both effects require temporal summation of a series of vagal volleys. The minimum number of volleys required to accelerate is also the threshold number for inhibition of inspiration.

(*c*) Both effects are simultaneously lost when a cold block of the vagus is gradually induced.

(*d*) The acceleration varies in degree according to the stage at which the inspirations are cut short.

6. It is concluded that the effects upon rate and amplitude are probably due to a common afferent mechanism, the acceleration being dependent upon the reduced motor discharge.

7. A stimulating circuit is described. It permits uniform tetanization for controllable short periods (0·01 to 1·5 sec.), frequency and stimulus strength being independently variable. The circuit can be automatically governed by respiratory changes of intrapleural pressure. (Authors' abstr.)

Cerebellar Action Potentials in Response to Stimulation of Various Afferent Connections.

1. Single shock electrical stimulation of afferent connections to the cerebellum results in a response of the neurons of the cortex in the lobes with which the respective afferent system has connections.

2. Stimulation of the eighth nerve in the unanæsthetized decerebrated cat results in an electrical response in the cerebellum, limited to the flocculo-nodular lobe, the lingula, uvula and the fastigial nucleus.

3. Stimulation of the spinal nerves, or of the spinocerebellar tract in the mid-thoracic cord, produces cerebellar action potentials limited to the anterior lobe, the lobulus simplex, pyramis, and occasionally the lobulus paramedianus. No difference in location of the response depending upon the site of stimulation was seen, except for a response of greater amplitude on the homolateral side.

4. Stimulation of the pons sets up cerebellar action potentials limited to the middle lobe of the vermis (Ingvar), the lobulus ansiformis, lobulus paramedianus, paraflocculus and pyramis. Occasionally potentials are found also in the dorsal part of the culmen.

5. A stimulus in the region of the inferior olivary nuclei excites synaptically the olivocerebellar connections and produces cerebellar action potentials in all the lobes of the cerebellum. The responses of greatest amplitude are found when leading from the contralateral lobulus ansiformis.

6. In similar afferent systems, such as the nerves of the upper and the lower extremities, the responses led from an identical point may be strikingly similar. With dissimilar afferent systems, such as the inferior olive and the spinal system, potentials of different sign and shape may be led from the same point. The question is raised whether this dissimilarity of potential depending upon the source of the afferent stimulation may not be attributable to a difference in the anatomical connections within the cerebellar cortex.

7. It is thought that these action potentials are due to activity of the neurons of the cerebellar cortex and that they are not potentials of the axons or endings of the afferent fibres. In most instances the activity resulting from single shocks changes to a remarkably small degree the background activity which is characteristic of the cerebellar cortex. Under certain conditions, however, this activity may be initiated or increased by a response to an afferent stimulation. In no instance has a decrease been observed. (Author's abstr.)

Changes in Retinal Excitability due to Polarization and Some Observations on the Relation between the Processes in Retina and Nerve.

The electro-retinogram and the impulses from the optic nerve have been recorded during the passage of a galvanic current across the retina.

" Inside cathode " greatly enhances the discharge in the optic nerve and " inside anode " depresses it.

The complex retinal electrical response is also enhanced by " inside cathode " and depressed by " inside anode ".

After removal of the positive component, P II, of the electro-retinogram the remaining negative, P III, reacts to the polarizing current just as the whole response.

Antidromic impulses through the optic nerve have no effect whatsoever on the electro-retinogram.

Simultaneous records of the retinal and optic nerve responses illustrate the practically negligible nerve-retinal interval at cessation of illumination.

The off-discharge through the nerve is preceded by a small initial retinal positivity passing on into the large retinal off-effect, the main part of which follows a few milliseconds after the discharge in the nerve.

A brief discussion of the localization of the components of the retinal electrical response concludes the paper. (Authors' abstr.)

The Effect of Eserine on Spinal Reflexes in the Dog.

(1) Studies have been made of the effect of eserine on the knee-jerk, tibialis anticus reflex, and the crossed quadriceps reflex in chloralosed and in barbitalized dogs.

(2) Eserine, administered by perfusion through the lumbar subarachnoid space in the intact or spinal animal (cord transected at T10), depresses the knee-jerk and augments the flexion reflex in almost all cases. The crossed extension reflex is augmented in the extremity in which the knee-jerk is depressed.

(3) Eserine given intravenously is predominantly depressant to the knee-jerk, and augmentary to the flexion reflex and the crossed extension reflex.

(Authors' abstr.)

J. NEUROL. PSYCHIAT.

VOL. II (N.S.). OCTOBER, 1939.

The Functional Responses of the Sympathetic Nervous System of Man following Hemidecortication.

The authors found, after complete hemidecortication in a girl, that there was equality of sympathetic responses from both sides of the body and from cutaneous stimulation. This suggests that the reflex arcs used in these responses have no cortical cell station in man. G. W. T. H. FLEMING.

J. PHYS. U.S.S.R.

VOL. XXVI. Nos. 3 and 4. 1939.

On Localization of Cortical Processes Originated by Visual Stimuli.

Experiments were carried out on puppies and rabbits. Their behaviour at the initial stage of formation of the alimentary motor habit was directed by psychoneural activity, involving the simultaneous functioning of both halves of the brain acting as a whole. G. W. T. H. FLEMING.

The Effect of Minimal Stimulation upon the Chronaxie and Refractory Phase of Muscle.

The largest values of chronaxie were found in the proximal nerveless part of the muscle, ranging from ·7 to 5 σ. At a distance of from 2–4 mm. from the spot where the nerve enters the muscle the value of the muscular chronaxie is almost identical with that of the nerve's chronaxie, i.e., ·2–·3 σ. The absolute refractory phase of this proximal part of the muscle at rest is longer than that determined by stimulation through the nerve. The absolute refractory phase is increased at minimal stimulation. The chronaxie exhibits most marked alterations in the middle sections of the muscle and near the place of entry of the nerve.

The inhibitory effect depends upon alterations of the lability of the nerve-endings, and does not involve the development of heterochronism between nerve and muscle. G. W. T. H. FLEMING.

PART 4.

On Peculiar Features of Conditioned Defensive Motor Reflexes in Dogs with Unilaterally Transected Spinal Cord.

1. Soon after Brown-Sequard's unilateral severance of the spinal cord the unconditioned defensive motor reflexes exhibit the following peculiarities: (*a*) elevation of the threshold for stimulation with induction current, (*b*) tonic type of movements of the extremity, and (*c*) inversion of reflex response—extension instead of flexion.

2. Conditioned motor reflexes previously worked out disappear after unilateral spinal section and can be restored in the course of several days of training.

3. The re-establishing of motor conditioned reflexes from the extremity affected after section of the spinal cord means the elaboration of new conditioned reflexes, the function of which takes place at other points of the cerebral cortex and over other conducting paths.

4. A characteristic feature of conditioned motor reflexes after hemisection of the spinal cord is their rapid transition into the chronic inhibitory state.

5. This progressing inhibition of conditioned motor reflexes is based on the rapid exhaustion of the cortical elements assuming the role of the central link of reflex arc in those reflexes.

6. Decortication of the brain hemisphere homonymous to the sectioned side of the spinal cord causes all previously trained conditioned reflexes from the affected extremity to disappear.

7. Formation anew of defensive conditioned reflexes in dogs with hemisection following upon decortication of the homonymous hemisphere is exceedingly difficult; conditioned reflexes appear and rapidly vanish instead of becoming stable. As opposed to this, conditioned reflexes of fair stability are very easily developed from the anterior extremity homonymous to the decorticated hemisphere. This justifies the opinion that, in conditioned motor reflexes from the affected extremity worked out after hemisection, the central link of the reflex arc is situated in the hemisphere homonymous to the sectioned side of the spinal cord.

(Authors' abstr.)

The Localization of the Processes of General Inhibition of Antagonistic Muscles, and of Isolated Facilitation of the Agonist in the Neuronic Elements of the Spinal Cord.

In the spinal frog a single induction shock, inefficient with regard to the production of an outward reflex response, calls forth when applied to the receptive field of extension (skin of the calf) a general inhibition of the contraction of the antagonistic muscles of the knee which has produced stimulation of the plantar skin—this inhibition involves both the extensor and the flexor muscles.

The same inefficient stimulation of the flexor field results in facilitation, but not in inhibition of the extensor's contraction when this reflex contraction has been elicited from the extensor area, and not from the flexor field as in the former case.

Considering that one and the same stimulus may at the same time inhibit and facilitate the reflex contraction of one and the same muscle, it must be admitted that inhibition is localized in one set of neurones and facilitation in another.

The conclusion is drawn from the analysis of the experimental data that the general inhibition of the antagonistic muscles is due to development of an inhibitory process chiefly in the motoneurones, whereas the isolated facilitation of the agonist is based upon the development of a process of facilitation in the intraspinal neurone of the agonist. (Author's abstr.)

Sleep Produced by Electrical Stimulation of Sub-Cortical Ganglia.

The authors, using the method of Hess, easily obtained sleep by stimulating the subcortical ganglia with an intermittent current and an induction current. Sleep resulting from a feeble stimulus was not interrupted by a stronger stimulus, but on the contrary the sleep was deepened.

After repeated stimulations, conditioned sleep appeared where the cat went to sleep without stimulation when it was placed on the apparatus. Electrical hypothalamic sleep does not agree with the localization of sleep put forward by Hess nor with the "sleep centre" of von Economo. G. W. T. H. FLEMING.

The Role of the Sympathetic Nervous System in Sleep Phenomena following Electrical Stimulation of the Sub-cortical Ganglia.

Hypothalamic sleep does not occur in cats which have been deprived of their inferior cervical ganglia, stellar ganglia, abdominal sympathetic trunk and the innervation of their adrenals. It does not occur in cats deprived of their stellar and inferior cervical ganglia. In cats which only had their superior cervical sympathetic ganglia removed or section of the cervical sympathetic performed, electrical stimulation of the hypothalamus produced a condition of somnolence. Stimulation of the cranial end of the cervical sympathetic gave rise to very definite somnolence. These observations do not accord with those of Hess.

G. W. T. H. FLEMING.

J. PSYCHOL.

VOL. VIII. OCTOBER, 1939.

Temporary Changes in Affect and Attitude following Ingestion of Various Amounts of Benzedrine Sulfate (Amphetamine Sulfate).

1. When measured by a newly standardized optimism-pessimism scale, optimism of a personal and general nature is increased by ingestion of benzedrine sulfate. Larger doses operate especially to prolong the effects.

2. As indicated by 9-point, self-rating scales, the generally more desirable kinds and degrees of affect and attitude appear to be produced by smaller doses of

benzedrine. Larger doses tend to exaggerate some of these feelings, and to produce the undesirable opposites of others.

3. As indicated by other 9-point, self-rating scales, more favourable self-estimates of antecedent work accomplished tend to be produced by ingestion of benzedrine sulfate. These more optimistic evaluations are not completely generalized, in part apparently because the chemical also produces a greater indifference toward inferior performances.

4. The foregoing findings are true only " on the average ". Individual differences in affective response to the drug are profound. Some of these differences are related to initial, or prior, affective states. For others there is at the present stage of the analysis no explanation.

5. Ingestion of benzedrine sulfate appears not to affect the common personality traits measured by the Bernreuter personality inventory in any particular way. If this inventory has some general validity, the findings in the present study might appear to support the contention that personality traits remain unaffected by benzedrine ingestion. It seems to the present writers that the chemical does produce changes in behaviour of a temporary nature that would give the impression of (temporary) changes in personality traits. Since the response to benzedrine tends to be as individualized as it is, and since the Bernreuter inventory appears to have rather severe shortcomings in validity with individual cases and fails to depict individual traits and their inter-relationships, the inventory as originally scored and interpreted does not seem a promising tool for ascertaining at least the more crucial effects of benzedrine on personality. The problem definitely needs further clarification, and, very likely, experimentation along ideographic lines.

6. In general, it is reasonably clear that in a majority of individuals benzedrine sulfate produces a definite heightening of mood, a fairly—but not completely—generalized optimism and interest, together with an increased willingness to work for extended periods of time. In other individuals the same dosages appear to have none of these effects; in still others, opposite effects. With the present state of knowledge regarding benzedrine, a dosage optimal in any sense for given individuals can be determined only by experimentation. (Authors' abstr.)

J. SOC. PSYCHOL.

VOL. X. AUGUST, 1939.

MIND.

VOL. XLVIII. OCTOBER, 1939.

PSYCHIAT. QUART.
VOL. XIII. OCTOBER, 1939.

The Blood-Cerebro-spinal Fluid Barrier of Normal Children as Determined by the Bromide Permeability Quotient.

1. The " normal " bromide P–Q for white children lies between 3·0–3·5.

2. After the second year of age there are among white children fewer P–Q's below 3·1 than above it.

3. The " normal " bromide P–Q for negro children (and adults as well) presents a different abscissa distribution from that for the white.

4. The P–Q of the negro child lies between 2·5–3·0.

5. After the second year of age there are fewer P–Q's among negro children below 2·6 than between 2·6–3·0.

6. Very young children have P–Q's somewhat below the normal " low " figures for all age-groups of their particular race.

7. Febrility tends to lower the bromide P–Q independently of any correlation with changes in body-fluid chloride content.

8. Minor variations in time of fluid withdrawal, bloody contamination of the spinal fluid or hæmolysis of serum exert no perceptible effect upon the accuracy of the determination.

9. There is no perceptible difference between the chloride P–Q's of negroes and whites.

10. Withdrawal of successive samples of cerebro-spinal fluid from the lumbar cisterna results in a decided but gradual rise of the bromide P–Q figure.

11. Among epileptics there is a tendency for the P–Q to decrease rather than increase (as is the case in normal individuals with age). (Authors' abstr.)

A Method for Differentiating Manic-depressive Depressions from Other Depressions by Means of Parotid Secretions.

1. Parotid gland-rate determinations were made on a series of undifferentiated depressions before they were clinically studied. If the reading were below an average of ·01 c.c. per five minutes over a test of one-half hour duration the depression was recorded tentatively in the experimental records as a " manic-depressive depression ". If the average reading was above ·01 c.c. per five minutes the case was recorded as " not a manic-depressive depression ".

2. The clinical diagnosis in each instance was later made by two psychiatrists

working independently. The diagnoses of the two psychiatrists were then compared. Only when these agreed was the case included for report in this communication. These clinical diagnoses were then compared with the laboratory diagnoses based on the parotid secretory rate.

3. It was found that the laboratory diagnosis based on the parotid gland determinations agreed with the clinical diagnoses in 47 of 50 cases. Specifically out of 25 clinically determined manic-depressive depressions the parotid index agreed in 23 instances. Of the total of 25 other depressions not clinically diagnosed as manic-depressive, there was agreement with the parotid index in 24.

4. The parotid secretory rate is inhibited in the very early stages of the disorder before it is possible to make a definite diagnosis of manic-depressive depression by the usual psychiatric procedures.

5. Secretory inhibition prevails during the daily mood fluctuations of the patient, but the rate does return to the normal range when the patient recovers from the depression.

6. The rise of the secretory rate when the depression abates may be very sudden.

7. The parotid secretory test can be accomplished within an hour with simple inexpensive apparatus, involving little technical training.

(Authors' abstr.)

The Value of Diphenyl Hydantoinate (Dilantin) in Psychoses with Convulsive Disorders.

1. In individuals in whom seizures are controlled or markedly reduced in number and severity by the administration of dilantin there is a concurrent improvement in the mental condition.

2. When treatment by dilantin is instituted the anti-convulsant drug in current use should be withdrawn gradually. A week or 10 days should elapse before dilantin alone is used.

3. All cases treated had *grand* and *petit mal* attacks and psychomotor equivalents, so that no differentiation was made in the type of reaction.

4. Dilantin in doses over 0·4 grm. daily was definitely toxic in 16 of the 17 cases treated.

5. In three patients who did not tolerate over 0·4 grm. of dilantin well, the administration of 5 to 10 mgrm. of benzedrine sulphate in conjunction with dilantin allowed a maximum dose of 0·6 grm. to be given without toxic symptoms.

6. In one case the use of benzedrine sulphate apparently produced twitching of the arms and hands. This disappeared when the drug was discontinued.

7. Nine individuals were much improved. Eight were unimproved.

8. In one case treatment had to be discontinued because of toxic symptoms, in three patients because of an increase in the number and severity of seizures. Ten are still receiving dilantin. Three died.

9. The use of dilantin should be restricted to that group of patients who do not respond to less toxic forms of therapy. (Author's abstr.)

A Contribution to the Problem of Alcoholic Deterioration.

1. All the cases diagnosed as alcoholic deterioration over a 10½-year period have been re-examined with a view to clarifying the syndrome of alcoholic deterioration. A critical evaluation of all case-records was made, and those patients still available were personally examined. The study includes 32 patients, that is, all cases so diagnosed in a total of 5,824 admissions. Two patients were excluded because they were unavailable.

2. It has been shown that most of the cases so diagnosed do not fulfil the requirements of the entity, but seem to belong in other diagnostic groupings—psychopathic personality, schizophrenia, cerebral arteriosclerosis and others.

3. Four illustrative cases have been described and discussed.

4. Only 3 cases of the 5,824 admissions, or 0·51%, seem to fulfil the criteria of alcoholic deterioration, and even in these there is an element of doubt present.

5. The diagnosis of alcoholic deterioration is difficult to make within the first few months after admission.

6. Alcoholic deterioration is a much rarer entity than it is commonly held to be. (Author's abstr.)

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VOL. IV. JULY, 1939.

AUGUST.

1. Physiology, Biochemistry and Pathology.*

Variations in the Cholesterol Level in Multiple Sclerosis. E. Pichler and H. Reisner. [*Wien. klin. Wochschr.*, **51**, 1304–9 (1938).]

A distinct increase in serum cholesterol occurred only in acute cases of multiple sclerosis, and returned to normal on clinical improvement. In cases which had become chronic or improved slowly, if therapy produced an improvement, then a marked hypercholesterolæmia occurred, either as an accompanying symptom or as part of the defence mechanism of the body.

JOSEPH S. HEPBURN (Chem. Abstr.).

The Role of the Hæmato-Encephalic Barrier and the Changes in the Composition and Characteristics of Cerebro-spinal Fluid in Shock and in Traumatism. L. S. Shtern. [*J. Physiol.* (*U.S.S.R.*), **24**, 413–22 (1938).]

Under conditions of traumatic, toxæmic or chemical (peptone or histamine injections) shock, the resistance of the hæmatoencephalic barrier is altered, allowing the passage of ferrocyanides and iodides. The permeability to glucose and Ca is increased, that to K is decreased. In some cases the K/Ca coefficient falls below 1. The concentration of K, which is very low during the depression stage, increases and often rises above normal during the excitation stage. General anæsthesia, applied simultaneously with the shock, prevents these changes from taking place.

S. A. KARJALA (Chem. Abstr.).

The Permeability of the Cerebro-spinal Barrier to Sugar and Lactic Acid. A. P. Fridman and R. Kh. Arkina. [*Arch. sci. biol.* (*U.S.S.R.*), **50**, Nos. 1–2, 129–37 (1938).]

The coefficient of permeability of the cerebro-spinal barrier to sugar is practically constant in dogs, horses, cows and rabbits, varying within the limits 1·0 to 1·81. The quantity of lactic acid (I) in the cerebro-spinal fluid is not constant and is independent of its concentration in the blood. Conclusion: I is most probably of local origin in the brain.

S. A. KARJALA (Chem. Abstr.).

Blood-brain Barrier in Shock. G. I. Chvoles. [*Proc. Shock Congress, Kiev*, 1937, 57–9.]

Peptone shock in cats and dogs is abolished by (subcutaneous) injection of atropine, followed by NaH_2PO_4, into the cerebro-spinal fluid; each of these

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measures alone improves the condition, but does not save the animal. Intravenous KCl aggravates the condition. B. C. P. A. (Chem. Abstr.).

Potassium Compounds in the Brain. I. B. Arenshain and B. L. Al'bitskii. [*Biochimiya*, **4**, 30–4 (1939).]

A ligroin extract of K compounds of the brain, after repeated washings with water, caused only a certain part of its K content to pass into the aqueous solutions. It is suggested that human brain matter contains organic K compounds besides K salts. HILMEYER COHEN (Chem. Abstr.).

Are there Action Substances in Nerve Excitation? Alexander von Muralt. [*Naturwissenschaften*, **27**, 265–70 (1939).]

A review of the present knowledge of transmission of excitation in the nerve itself and the transmission of excitation from nerve to muscle. The former is assumed to be predominantly electrical, although accompanied by chemical reactions of low heat effect. The latter takes place by means of acetylcholine or adrenaline depending on the type of nerve-fibre. As to the " action substances " formed inside the neuron during the transmission of excitation impulse, their isolation is difficult owing to the extremely short period of their existence. By fixation with liquid air indications have been found of an acetylcholine-like substance (*C. A.* **31**, 7504[7]). Besides this, separation of aneurin (vitamin B_1) from excited nerves has been found (Minz, *C. A.* **32**, 5887[5]).

N. J. C. VAN DER HOEVEN (Chem. Abstr.).

Role of the Cervical Sympathetics in the Regulation of Thyroid and Thyrotropic Function. Unto U. Uotila. [*Endocrinology*, **25**, 63–70 (1939).]

The anterior pituitary is the principal activator of the thyroid. Hypophysectomy in rats is followed by thyroid atrophy which cannot be compensated by sympathetic stimulation (cold). FELIX SAUNDERS (Chem. Abstr.).

A Vagus-post-pituitary Reflex. VI. Phenomena of Exhaustion and Recuperation. Hsi-Chun Chang, Jen-Jo Huang, R. K. S. Lim and Kun-Jen Wang. [*Chinese J. Physiol.*, **14**, 1–8 (1939).]

The phenomena of progressive diminution of the pressor response to repeated vagal stimulation is correlated with the gradual exhaustion of the secretory granules in the pituicytes of the pituitary gland. By allowing a suitable period of rest, the pressor response to vagal stimulation recurs with the reformation of secretory granules in the pituicytes. The vagal pressor response in the non-eserinized animal can therefore be taken as a physiological index of secretory reserve in the pituitary gland.

VII. Non-eserinized Vagus Response in Different Vertebrates. Yunming Lu. [*Ibid.*, 9–18.]

A pressor response has been elicited in the toad, turtle, chicken, duck, rabbit and cat. It disappears after hypophysectomy. It cannot be shown in the snake fish (*Ophiocephalus argus* Cantor), although its pituitary gland contains pituicytes and pressor principle. W. H. SEEGERS (Chem. Abstr.).

The Glucolytic Activity of Brain. I. Macerated Brain Tissue. Alexander Geiger and Jonathan Magnes. [*Biochem. J.*, **33**, 866–76 (1939).]

The glucolytic rate of brain was lower in adult than in young rats; it was increased by dilution of the tissue with isotonic solutions, and was greater in Ringer solution than in phosphate buffers at the same pH; the addition of adenosine triphosphate (I) increased the rate in phosphate to that in Ringer solution; glucolysis was prevented by extracting the brain with water, and was irregularly

activated by glutathione (II). Only small amounts of lactic acid (III) were formed by brain from glycogen. Brain extracts had the same glycogenolytic activity as brain tissue, but a low glucolytic activity. No III was formed from hexose diphosphate (IV) by brain, the small amount of III found being formed from triose phosphate. Brain pulp was partly inactivated by incubation in N or O at 37°, but the glucolytic activity was partly restored by I and II. I could be replaced by adenylic acid (V) plus IV. Brain inactivated at pH 8·0 could not be reactivated. I may be regarded as the co-enzyme of brain glucolysis. P was transferred by brain from IV to V but not from phosphopyruvic acid. No phosphoric esters were formed from inorganic phosphate by brain. The breakdown of glucose in the brain departs in every respect from the breakdown of glycogen in muscle.

II. Effect of Cytolysis, the Presence of a Glucolytic Inhibitor. Alexander Geiger. [*Ibid.*, 877–84.]

Cytolized brain tissue showed no glucolytic activity, a reduced ability to oxidize III and no reduction in its succinate-oxidizing power. A heat-labile glucolysis inhibitor was present in cytolized brain tissue.

E. W. Scott (Chem. Abstr.).

Lactic Acid Oxidation in the Brain of B_1-Avitaminous Animals. Localization of the Chemical Lesion in Mammals and Birds. P. E. Galvao and J. Pereira. [*Arquivos inst. biol. (Sao Paulo)*, **9**, No. 3, 25–37 (1938).]

Extra O uptake in presence of lactate (with minced tissue) is decreased in the cerebrum (motor region) of rats and optic lobes of fowls showing nervous symptoms; in rats without symptoms a decrease was found in the mid-brain.

B. C. P. A. (Chem. Abstr.).

The Metabolism of Cerebral Tissue. A. K. M. Noyons and H. van Goor. Nederland. Tijdschrift Geneeskunde, **83**, II, 2527–9 (1939).

The O_2 consumption and CO_2 production of brain tissue *in vitro* differs in various animals, being larger in rats than rabbits or guinea-pigs.

R. Beutner (Chem. Abstr.).

Glucolytic Capacity of Various Parts of the Nervous System in Relation to the Substrate. E. B. Skvirs'ka. [*Biochem. J. (Ukraine)*, **12**, 5–14, *in English*, 16–17 (1938).]

Minced grey matter, white matter and sciatic nerve from rabbits were incubated in a M/15 phosphate medium at 37° for 1½ hours. Lactic acid production was measured, without any additional substrate and with the addition of glucose, fructose, galactose and glycogen. The highest glucolytic capacity was exhibited by grey matter in the presence of glucose. White matter and sciatic nerve showed almost identical glucolytic capacity in the presence of all substrates. In relation to their capacity to form lactic acid with all types of nerve tissue, the substrates can be classified in the following descending order: glucose, fructose, galactose and glycogen.

R. Levine (Chem. Abstr.).

The Effect of Darkness and Illumination on the Oxidation Reduction Potential of the Visual Zone of the Cerebral Cortex. A. I. Safarov. [*Biochem. J. (Ukraine)*, **12**, 177–85 (*in English*, 185–7) (1938).]

The visual zone of the cerebral cortex has a definite E_h value of about 370 mv., differing from the E_h value of other tissues. After an animal (rabbit) has been blindfolded for 5–15 days, the E_h value decreases in the area striata. Strong illumination of the eyes after temporary blindfolding leads to an increase in the E_h value. The oxidation-reduction potentials were determined potentiometrically *in vivo* and *in situ*, by exposing the occipital area of the brain.

R. Levine (Chem. Abstr.).

Arginine in Individual Brain Areas of Various Animals. *Yu. V. Lakhno.* *Biochem. J. (Ukraine)*, **12**, 19–28 (*in English*, 29–30) (1938).]

The arginine content of the brain of rabbits, cats and pigeons is distributed as follows: highest in the cerebellum, lowest in the spinal cord, with the cerebral hemispheres exhibiting intermediate values. The whole brain of carp and frog shows a higher concentration of arginine than does the cerebellum of mammals and birds. Conclusion: There is a tendency toward a decrease of brain arginine with the ascent in the phylogenetic scale. R. LEVINE (Chem. Abstr.).

Brain Creatine During the Embryonic Development of Vertebrates. *A. V. Palladin and E. Ya. Rashba.* [*J. Physiol. (U.S.S.R.)*, **24**, 265–76 (1938).]

The content of creatine (I), total N and H_2O in the brains of rabbit and guinea-pig embryos is higher during the second half of embryonic development than in mature animals. During development these values decrease until they reach those characteristic of mature animals during the 1st month of post-embryonic growth. The content of these substances in the hemispheres, cerebellum and medulla oblongata of cow embryos from the 3rd to the 8th month of growth is highest during the earlier stages, and reaches the maturity level in the 6th or 7th month of embryogenesis. Beginning with the 3rd month I is highest in the cerebellum, while the medulla oblongata is richest in total N and H_2O.

S. A. KARJALA (Chem. Abstr.).

Age Variations in the Reduction Capacity of the Brain and other Animal Tissues. *G. G. Ivanov.* [*Bull. biol. med. exptl. U.S.S.R.*, **7**, 216–18 (1939).]

The brain tissue, cardiac and striated muscle, spleen and testicles of white rats show three stages in the reduction of methylene-blue (I) during the course of animal life. In the 1st stage, at ages from 2 weeks to sexual maturity (3 months), a high reducing capacity is shown by rapid decolorization of I. The 2nd stage (3 months to 2 years) is characterized by a slow reduction of I, while in the 3rd stage a comparatively rapid decolorization of I again occurs. The liver and kidneys, however, in the 1st stage show a minimum with extremely slow decolorization of I. During the 2nd stage the reduction capacity increases markedly, followed by a new decrease in the 3rd stage. An electrometric study showed the brain tissues of young and old animals to have similar E_h values, while that of adult animals was considerably lower. S. A. KARJALA (Chem. Abstr.).

Factors Influencing the Oxygen Supply of the Brain at Birth. *J. Barcroft, D. H. Barron, K. Kramer and G. A. Millikan.* [*J. Physiol. (U.S.S.R.)*, **24**, 43–55 (1938).]

The O_2 saturation of the blood of sheep was determined by projection of a beam of light through the blood and through a colour-filter of suitable wave-length on to a photo-electric cell. The extent of obscurity as a result of hæmoglobin reduction gave a measure of the O_2 content. Pulmonary respiration increases the O_2 saturation of the carotid blood from 40–50 to 90%. During this respiration period the respiratory efforts seem to be connected with a rise in arterial blood-pressure of approximately 40 mm. of Hg., which increases the O_2 supply of the brain by increasing the rate of circulation of the blood, which has become more highly saturated with O_2 through respiration.

S. A. KARJALA (Chem. Abstr.).

Nature of the Reducing Substances of Brain. *A. Baudouin and J. Lewin.* [*Compt. rend. soc. biol.*, **131**, 730–2 (1939).]

Fresh rabbit brain contains reducing substances equivalent to about 0·1% of glucose. About 50% of the reducing action is due to creatine and creatinine and 20–25% to fermentable sugar. L. E. GILSON (Chem. Abstr.)

Pyruvate Oxidation System in Brain. I. Banga, S. Ochoa and R. A. Peters. [*Nature*, **144**, 74–5 (1939).]

Cocarboxylase, fumarate, inorganic phosphate, adenylic acid and cozymase are components of the pyruvate oxidation system in brain.

E. D. WALTER (Chem. Abstr.).

Pyruvic Acid Exchange in the Brain. P. E. Simola and Hella Alapeuso. [*Suomen Kemistilehti*, **12***b*, 9–10 (1939).]

Buffered brain tissue *in vitro* at 37°, when treated with pyruvic acid (I), gives rise to 50% of the amount of I destroyed as lactic acid (II) in an O_2 atmosphere and 33% of II in a N_2 atmosphere. In each case 10–12% alanine is formed. A rather large increase in α-ketoglutaric acid (III) and a small increase in succinic acid was observed. Little citric acid (IV) was formed in O_2 and none in N_2. No differences in malic and fumaric acid formation and no appreciable formation of AcOH were observed. The direct formation of AcOH from I in the animal organism is questioned. It is suggested that III is formed from glutamic acid. The formation of III from IV in liver tissue has been observed, but in the case of brain tissue, although a distinct consumption of IV is observed, little formation of III takes place. Studies of the action of tissues on AcOH and I do not support the theory that III is formed from these two compounds. S. A. KARJALA (Chem. Abstr.).

Pyruvate Oxidation in the Brain. V. Evidence Derived from the Metabolism of α-Ketobutyric Acid. Cyril Long and Rudolph A. Peters. [*Biochem. J.*, **33**, 759–73 (1939).]

Cocarboxylase is essential for the decarboxylation by yeast of α-ketovaleric acid (I) as well as for pyruvic (II) and α-ketobutyric (III) acids. Vitamin B_1 increases the rate of decarboxylation of I and III only in the presence of cocarboxylase. II and III are equally reactive with the pyruvate dehydrogenase system in brain under anaërobic conditions in the presence of methylene-blue. I is much less reactive. The Krebs' dismutation proceeds to the same extent with II and III, but I is less affected. Washed brain tissue causes oxidative decarboxylation of III, presumably to form propionic acid. I is oxidized only slightly. The purity of the acids used is essential. I and II enter into competitive inhibition with III in both normal and avitaminotic brains respiring *in vitro*. There is no inhibition of the indophenol oxidase system. II and III are oxidized at exactly the same rate under identical conditions. In the first case most of the initial oxidation product undergoes complete combustion to CO_2 and water. This indicates that there is a common initial path (A) for oxidative decarboxylation, and that in the case of II a further system (B) causes complete oxidation of part of the intermediate.

Appendix. R. W. Wąkelin. [*Ibid.*, 773.]

The residual substrates in pigeon brain tissue are almost completely removed by washing with Ringer phosphate, pH 7·3, and then with either 0·2 or 0·3% KCl followed by the former solution to reduce swelling. The tissue still contains succinic acid oxidase and pyruvic acid dehydrogenase.

E. W. SCOTT (Chem. Abstr.).

Experimental Studies on the Sugar Puncture. II. Origin of the Hyperglucæmia occurring after the Sugar Puncture. Mikio Miyake. [*Arb. med. Fakultat Okayama*, **6**, 265–78 (1939).]

Adrenaline produced hyperglucæmia in normal rabbits, but not in splanchnectomized rabbits. Ergotoxine (I) had no effect on the blood sugar in normal rabbits, but those treated with I and then subjected to sugar puncture (by Eckhard's method) showed no difference in blood sugar as compared with controls. Electrical stimulation of the base of the brain of rabbits treated with I did not

cause hyperglucæmia, but it did in normal animals. Adrenaline, added to the perfusion liquid of the toad liver, caused an increased percentage discharge of the sugar in the perfusate, but the absolute quantity was reduced on account of reduction in the amount of perfusate due to contraction of blood-vessels. Previous perfusion with I checked adrenaline reaction by paralysing the sympathetic nerve-endings of the blood-vessels so that the absolute quantity of sugar neither decreased nor increased. These experiments show that the sugar-puncture hyperglucæmia is adrenaline hyperglucæmia, which, however, results from a mechanical rather than a chemical action on a mother substance of sugar, such as glycogen. Increasing the circulation of blood by contraction of the blood-vessels in the skin and muscles washes out the reserve of sugar in the liver.

MAURICE M. RATH (Chem. Abstr.).

Changes in Lactic Acid, pH and Gases Produced in the Blood of Normal and Schizophrenic Subjects by Exercise. Joseph M. Looney. [*Am. J. Med. Sci.*, **198**, 57–66 (1939).]

The gases, pH and lactic acid were determined in the venous blood of 35 schizophrenic subjects and 35 normal subjects (living in the same environment) before and after running for 10 minutes up and down stairs. For the normal and schizophrenic subjects, respectively, the mean of work performed was 690 ± 24·6 and 812 ± 19·5 kg./m./min., the increase of lactic acid content was 65 ± 4·2 and 56 ± 4·7 mg./100 c.c., and the lactic acid production per kg./m./min. was 0·097 ± 0·007 and 0·065 ± 0·005 mg. These results indicate marked muscular inefficiency of the schizophrenic patients in regard to lactic acid production per work done. Before exercise, 4 minutes after exercise and 2 hours after exercise respectively the normal subjects showed blood pH values of 7·44, 7·36 and 7·47, O_2 contents of 10·5, 15·5 and 11·2 volume %, and CO_2 values of 57·8, 42·5 and 56·2 volume %; the corresponding values for the schizophrenic patients were pH 7·44, 7·35 and 7·46, O_2 contents of 11·5, 11·9 and 11·2 volume %, and CO_2 contents of 57·2, 41·1 and 56·3 volume %. The rate of disappearance of lactic acid was the same for both groups and dependent only on the blood level. As a result of the stress from exercise, the CO_2 mechanisms of the schizophrenic patients tended to approach more nearly that of the normal subjects. MARION HORN (Chem. Abstr.).

The Influence of Polyneuritis on the Lactic Acid and Glycogen Content of Pigeon Muscles Subjected to Different Types of Fatigue. L. I. Palladina and L. A. Dubovtseva. [*Biochem. J.* (*Ukraine*), **12**, 41–53 (in *English*, 57–61) (1938).]

Rhythmic stimulation of normal pigeon muscle causes a constant increase in lactic acid and a decrease in glycogen. Tetanic stimulation of the same muscles causes, instead, a decrease in lactic acid, although the glycogen content falls. The same results are obtained with muscles from polyneuritic pigeons except that the rate of glycogen decrease is considerably greater than in normal muscles. The differences in respect to lactic acid production after rhythmic and tetanic stimulation is being investigated. R. LEVINE (Chem. Abstr.).

Changes in the Blood of Neuropaths during Fatigue. I. M. Turovets. [*J. Med. Ukraine*, **8**, 807–18 (*in French*, 817–18) (1938).]

Aside from certain paradoxic reactions, no differences were observed in biochemical and neurovegetative reactions between neurotic and healthy subjects as a result of muscular fatigue. S. A. KARJALA (Chem. Abstr.).

Vitamin B_1 in Cerebro-spinal Fluid. Gilberto Guimarães Villela. [*Science*, **89**, 251 (1939).]

Acidify 10–15 c.c. samples to pH 4.L and adsorb on frankonite. Wash the adsorbate and dry at 100°. Divide the powder into two portions. Add graduated

amounts of one portion to a synthetic medium and inoculate with spores of *Phycomyces blakesleeanus* (Schopfer and Jung, *C. A.*, **32**, 6298[8]). Determine thiamine in the other portion by the thiochrome method. The *Phycomyces* test gave higher values than the thiochrome method. Catatonia and depressive state showed the highest values. In myxœdema and epilepsy with cretinism no trace of thiamine could be found by either test. FELIX SAUNDERS (Chem. Abstr.).

Vitamin B_1 Content of Spinal Fluid. Gilberto Guimarães Villela. [*Compt. rend. soc. Biol.*, **130**, 1493–4 (1939).]

In 36 samples of spinal fluid from normal subjects and patients with chronic mental and other diseases the vitamin B_1 content was close to 2γ per 100 c.c. After intravenous injection of 10 mgrm. of vitamin B_1 a transient increase occurred in the spinal fluid 30–60 minutes after the injection. Three hours later the original level was regained. L. E. GILSON (Chem. Abstr.).

Chemical Method for Vitamin C Determination in the Cerebral Fluid. A. P. Fridman. [*Lab. Prakt.* (*U.S.S.R.*), 1939, No. 4, 9–11.]

Into a 50 c.c. Erlenmeyer flask is introduced 7 volumes of distilled water, 1 volume of cerebral fluid, 1 volume of 10% $Na_2WO_4\,2H_2O$ solution, and 1 volume of $\frac{1}{3}$ NH_2SO_4. After the mixture is shaken and filtered, the clear filtrate is titrated with Tillman's reagent (2, 6-dichlorophenol-indophenol) until a light pink colour is obtained. The end-point must be carefully watched. Two methods for the preparation of Tillman's reagent and the calculation method are given. The amounts of vitamin C found in different fluids are: Rabbits 2–3 mgrm. %, dogs 3–6 mgrm. %, horse 2–4 mgrm. %, cow 3–5 mgrm. %, human 0·5–2·5 mgrm. %. W. R. HENN (Chem. Abstr.).

The Vitamin C Content of the Cerebro-spinal Fluid. J. W. Camerer. [*Monatsschr. Kinderheilk.*, **77**, 240–58 (1939).]

The average concentration of ascorbic acid in the cerebro-spinal fluids of healthy breast-fed infants is 4·2 mgrm. %; that of rachitic and of healthy artificially-fed infants was only slightly lower. Spasmophilia caused a marked decrease, to 0·85 mgrm. %. Findings were inconstant with inflammatory diseases and digestive disturbances of brief duration, but chronic illness tended to lower the concentration. In older children the average concentration was 2·13 mgrm. %. The concentration is quickly influenced by low or high intake of vitamin C. The maximum concentration obtained by giving ascorbic acid was 5·5 mgrm. %.
ELEANOR M. HUMPHREYS (Chem. Abstr.).

Estimation of the Alkaline Phosphatase in the Cerebro-spinal Fluid. H. H. Fleischhacker. [*Ensymologia*, **6**, 144 (1939).]

The phosphatase activity of normal cerebro-spinal fluid is 0·1–0·2 Bodansky units for β-glycerophosphate and less for α-glycerophosphate. The values are higher in some cases of brain tumour. FELIX SAUNDERS (Chem. Abstr.).

Crystal Formations Obtained by Evaporation of Mixtures of 0·85 % Sodium Chloride Solutions with Serum. I. Normal Human Serum, Serum Deprived of Complement by Heat, Serum Extracted with Ether and Serum from Patients in Insulin Shock. Mario Coppo and Mario Levi. [*Sperimentale*, **93**, 68–85 (1939).]

Characteristic patterns of crystallization were obtained with each type of serum. Twenty-six different normal human serums gave only three different types of crystallization. A. E. MEYER (Chem. Abstr.).

The Urea Content of Cerebro-spinal Fluid at Different Stages of Insufficient Blood Circulation. M. L. Aviosor. [*J. med., Ukraine*, **8**, 1159–68 (*in French*, 1168) (1938).]

The urea content of cerebro-spinal fluid (I) is generally lower than that of the blood. During insufficient circulation of the blood the urea content of I rises, together with the rise in urea in the blood. A greater increase in the urea content of I than is observed in the blood indicates an increased permeability of the hæmato-encephalic barrier. S. A. KARJALA (Chem. Abstr.).

Estimation of Tryptophane in the Cerebro-spinal Fluid. M. Kraus and K. Mezey. [*Schweiz. Arch. Psychiat. Neurol.*, **42**, 77–87 (1938).]

A simple method of estimating tryptophane in the cerebro-spinal fluid is described. Tryptophane was found in the fluid in cases of syphilitic diseases of the central nervous system. It was found only in those cases in which other signs of syphilis were present in the fluid. B. C. P. A. (Chem. Abstr.).

The Passage of Tryptophane into the Cerebro-spinal Fluid. Mitio Kasahara and Ituo Gammo. [*Klin. Wochschr.*, **18**, 686 (1939).]

The amount of tryptophane in the cerebro-spinal fluid is increased after intravenous injection of tryptophane. H. L. MASON (Chem. Abstr.).

The Role of the Nervous Factor in Chronic Intoxication by Industrial Poisons. P. Ya. Mytnik. [*J. Physiol. (U.S.S.R.)*, **26**, 120–7 (*in English*, 127) (1939).]

The experimental injury of the nervous system of animals results in visceral hæmorrhage, trophic ulcers and leucocytosis. Poisoning by subcutaneous injections of C_6H_6 results in leucopenia and visceral hæmorrhages. With preliminary subjection to nervous trauma, C_6H_6 causes only a slight reduction in the number of leucocytes, followed by leucocytosis. S. A. KARJALA (Chem. Abstr.).

The Content of Labile Phosphorus Compounds in the Brains of Cats. S. F. Epshtein. *Bull. biol. med. exptl. U.S.S.R.*, **7**, 94–97 (1939) (*in German*).]

The contents of easily hydrolysable H_3PO_4 phosphorus (7 minutes at 100° with N HCl) and creatinephosphoric acid P in the brains of cats under chloral hydrate narcosis are 19·3–22·7 and 5·1–8·7 mgrm.% respectively. Under somnifen narcosis the values are 14·3–16·2 and 6·0–7·4 mgrm.% respectively, and under urethane (I) narcosis 9·6–14·5 and 3·8–5·0 mgrm.% respectively. Under I narcosis the Ba fraction of the P compounds yielded 2·3–4·3 mgrm.% of amino N from the desaminase splitting of adenylic acid and 1·7–18·8 mgrm.% of H_3PO_4 phosphorus. The molar P/N ratio was 1·9–2·1. S. A. KARJALA (Chem. Abstr.).

A Method for Shortening the Duration of Lower Motor Neurone Paralysis by Cholinergic Facilitation: A Preliminary Report. Alexander Wolf and Abner Wolf. [*Trans. Amer. Neurol. Assoc.*, **64**, 205–7 (1938).]

Daily feeding of acetyl-β-methylcholine, KCl or prostigmine led to recovery from paralysis induced in cats by injection of alcohol into the sciatic nerve, or by section and resuture of the nerve. No recovery occurred in paralysed control cats not treated with the above compounds. The medicated cats showed better appetite, vigour and general health than the controls. The beneficial effect of prostigmine in promoting recovery from paralysis has also been observed in a clinical series now under investigation. In the single case cited, daily administration of 75–90 mgrm. prostigmine orally for 2 weeks led to considerable recovery from a postmastoidectomy facial palsy that had previously shown little improvement during the past 9 years. The beneficial effects of cholinergic drugs in paralysis

are attributed to their facilitation of the passage of impulses through the lower motor neurone by preservation of acetylcholine bombardment at the dendrites of the anterior horn-cells. This constant stimulation apparently maintains the tone and body of the denervated muscles against atrophy and hastens neural regeneration. The cholinergic drugs may prove useful not only in traumatic nerve lesions but also in other types of lower motor neurone lesions, perhaps even in amyotrophic lateral sclerosis, progressive spinal muscular atrophy or chronic poliomyelitis.

MARION HORN (Chem. Abstr.).

Does a Diabetic Polyneuritis Exist? F. Rathery and Pierre Klotz. [*Bull. mém. soc. méd. hôp. Paris*, **54**, 574–80 (1938).]

Daily subcutaneous injections of 1 mgrm. (500 I.U.) crystallized vitamin B_1 and the ingestion of several vitamin B_1 tablets daily produced a rapid improvement in the polyneuritis in a diabetic patient. Vitamin B_1 caused a distinct increase in the carbohydrate tolerance, which remained high after discontinuation of the treatment. The parallel regression of the nervous symptoms and of the glucosuria apparently favours the theory of the diabetic nature of the nervous disturbances. Diabetic polyneuritis is probably of an avitaminotic character.

J. Haguenau. Ibid., 644–5.

Haugenau does not believe that the data of Rathery and Klotz justify the conclusion of the existence of a specially diabetic polyneuritis.

R. BERGGREN (Chem. Abstr.).

Blood Proteins in Delirium Tremens. J. M. Thomas, E. V. Semrad and R. M. Schwab. [*Amer. J. Med. Sci.*, **195**, 820–3 (1938).]

The serum albumin of 18 patients with delirium tremens during the acute phase was below 4 grm.%. In 12 of 22 cases serum albumen was lower after the acute phase had subsided. There was no significant alteration in serum globulin.

B. C. P. A. (Chem. Abstr.).

The Blood and Spinal Fluid Sugar and Chloride Content in Meningitis. Esther Hendry. [*Arch. Disease Childhood*, **14**, 159–72 (1939).]

Sugar concentrations in non-meningitic cerebro-spinal fluids were 50–83 mgrm.% (average 64), in tuberculous fluids 5–86 mgrm.% (below 50 in 25 of 28 cases), and in purulent fluids 0–52 mgrm.% (below 35 in 11 of 15 cases). The ratio of cerebro-spinal fluid sugar to blood sugar was above 0·6 in non-meningitic fluids, was lowered in tuberculous fluids usually to less than half, and further lowered in the purulent fluids of meningococcus menigitis, etc. Values above the normal minimum for concentration and ratio were found in poliomyelitis, benign lymphocytic meningitis, and non-meningeal tuberculosis. Cl concentrations of tuberculous cerebro-spinal fluids were substantially reduced from the normal values of 635–770 mgrm.% as NaCl, those of purulent fluids somewhat less, while no change in ratio to blood Cl was observed. Apparently blood Cl level determines that of the cerebro-spinal fluid, while other factors also operate on the sugar concentration. As diagnostic aids, cerebro-spinal fluid sugar and its ratio to blood sugar are considered more satisfactory than Cl values.

KATHRYN KNOWLTON (Chem. Abstr.).

Effects of Sorbitol and Sucrose on Cerebro-spinal Fluid Pressure and Urine Output. Henry G. Schwartz and Robert Elman. [*Proc. Soc. Exptl. Biol. Med.*, **39**, 506–8 (1938).]

In dogs, 50% sorbitol solution, 2·5 c.c. kgrm. injected intravenously causes a more marked and protracted fall in spinal fluid pressure, and a greater diuresis than does an equivalent amount of sucrose. Sorbitol is non-toxic.

L. E. GILSON (Chem. Abstr.).

The Arsenical Content of the Brain in Cases of Encephalitis, Inflammatory Occlusion of the Aqueduct, and Acrodynia. A. D. Ecker. [*Proc. Staff Meetings Mayo Clinic*, **14**, 43–8 (1939).]

Brain As concentrations of 0·10–0·83 mgrm.% (similar to the concentrations found in acute arsenical poisoning or arsphenamine hæmorrhagic encephalitis), in 2 of 4 cases of non-neoplastic occlusion of the aqueduct of Sylvius and in 1 of 2 cases of acrodynia. It is suggested that As may play an ætiologic role in these diseases. MARION HORN (Chem. Abstr.).

Symmetrical Cerebral Calcification Associated with Parathyroid Insufficiency. L. M. Eaton. [*Proc. Staff Meetings Mayo Clinic*, **14**, 48 (1939).]

Of 8 patients with symmetrical cerebral calcification, 3 had parathyroid insufficiency. Treatment of the parathyroid insufficiency in 2 patients followed was successful in stopping the convulsive seizures and improving the mental status. Dihydrotachysterol (A.T. 10) was used in 1 patient.

MARION, HORN (Chem. Abstr.).

Presence of Acetone in the Cerebro-spinal Fluid in Meningitis. J. Fournier and L. Feissolle. [*Compt. rend. soc. biol.*, **131**, 566–8 (1939).]

Acetone was found in the spinal fluid in meningitis due to various types of infection. It is ascribed solely to malnutrition. This is in harmony with its high frequency in tuberculous meningitis. L. E. GILSON (Chem. Abstr.).

Apparent Relation between Hypophyseal Tumours and Benzopyrene Injected into the Cerebrum of the Rat. C. Oberling, C. Sannie, P. Guerin and M. Guerin. [*Compt. rend. soc. biol.*, **131**, 455–7 (1939).]

In a new series of experiments the injection of crude or pure benzopyrene or methylcholanthrene into rat brains did not produce tumours of hypophysis; hence the cases previously reported (*C.A.*, **31**, 3134[1]) should be ascribed to coincidence. Spontaneous hypophyseal tumours are not uncommon in rats more than 20 months old. L. E. GILSON (Chem. Abstr.).

The Variations of Cholinesterase in the Brain and Spinal Cord of Tetanized Animals. Giacomo Pighini. [*Biochim. terap. sper.*, **26**, 226–7 (1939).]

The cholinesterase in the cord and still more in the cerebral cortex is increased in animals poisoned with tetanus toxin. A. E. MEYER (Chem. Abstr.).

Method for Comparative Determination of Cholinesterase in Various Sectors of the Nervous System. Giacomo Pighini. [*Biochem. terap. sper.*, **26**, 157–9 (1939); *cf. C.A.*, **33**, 7393[3].]

Triturate a 0·2-grm. sample with quartz sand and emulsify in 50 c.c. physiological NaCl solution. Neutralize with 0·01 N NaOH (phenolphthalein) and add 2·5 c.c. of a solution containing 1 grm. acetylcholine in 10·5 c.c. Keep at 37° and titrate with NaOH every 5 minutes to a total of 6 titrations. The optimum pH for the action of the enzyme is 8·2–8·4, which corresponds to a pink colour of phenolphthalein. By repeated titration a considerable shift from the optimal condition is prevented. A. E. MEYER (Chem. Abstr.).

Synthesis of Acetylcholine by Brain Tissue. E. R. Trethewie. [*Australian J. Exptl. Biol. Med. Sci.*, **16**, 343–6 (1938).]

Synthesis of acetylcholine in the presence of glucose was demonstrated for guinea-pig brain. EDWARD EAGLE (Chem. Abstr.).

Chemical Transmission Agents in Nerves : Acetylaneurin. Richard Kuhn, Theodor Wieland and Heinrich Huenschmann. [*Z. physiol. Chem.*, **259**, 48–52 (1939).]

Heating 2-methyl-4-amino-5-bromomethylpyrimidine-diHBr with 4-methyl-5-acetoxyethylthiazole gave 4-methyl-5-β-acetoxyethyl-N-(2-methyl 4-aminopyrimidyl(5)methyl)-thiazolium bromide-HBr (acetylaneurin), m. 235·5–6° (decomp.). This substance is as active on intestinal strips as choline. Aneurin itself has no action. MILTON LEVY (Chem. Abstr.).

Acetylcholine Metabolism in the Central Nervous System. The Effects of Potassium and Other Cations on Acetylcholine Liberation. P. J. G. Mann, M. Tennenbaum and J. H. Quastel. [*Biochem. J.*, **33**, 822–35 (1939).]

The addition of K ions (0·027 M) to an eserine-containing medium in which intact brain slices were respiring caused a large increase in the rate of formation of acetylcholine (I). High concentrations of K ions inhibited the synthesis of I. The effect of K ions did not occur in a substrate-free medium. The additional I formed by K ions was all in the free form. The accelerating action of K ions was neutralized by the addition of Ca or Mg ions. Rb and Cs ions had an effect similar to, but smaller than, that of K. The addition of K ions to minced brain tissue did not cause as great an increase in the formation of I. The addition of K ions to brain slices or mince, when I was not being formed, caused a fall in the amount of " combined " I and a correspondingly equal increase in the amount of free I. The effect of K ions was less in a phosphate medium than in a bicarbonate medium. The direct effect of the K ions was to increase the permeability of the nerve-cells, so that I diffused from the cells at a greater rate. The addition of I to a medium containing brain slices depressed the formation of I. NH_4 ions acted like K ions in causing a breakdown of " combined " I with an increase in free I.
E. W. SCOTT (Chem. Abstr.).

The Mechanism of the Biological Synthesis of Acetylcholine. II. Edgar Stedman and Ellen Stedman. [*Biochem. J.*, **33**, 811–21 (1939).]

A study was made of the formation of acetylcholine (I) brain tissue *in vitro* under various conditions. The amount of I formed when minced ox brain in eserinized Ringer solution was shaken at 37° was approximately equal to that produced by grinding the minced tissue with $CHCl_3$-eserine and keeping it at room temperature for the same period, 2 hours. Et_2O resembled $CHCl_3$ in its ability to promote the formation of I in brain tissue, but was more efficient. The effect of Et_2O was greater at 37° than at room temperature, but the reverse held for $CHCl_3$. The amount of I formed at 0° with $CHCl_3$ was very small compared to the amount formed at 37°—a finding contrary to that of Mann *et al.* (*C.A.*, **32**, 4645[1]). The addition of Na acetoacetate to the $CHCl_3$ or Et_2O preparations increased the yield of I. The addition of glucose to the eserinized Ringer preparation did not appreciably increase the amount of I formed, contrary to Mann's finding. Stedman and Stedman suggest that acetoacetic acid is the precursor of I and that the " preformed-precursor " of Mann does not exist. E. W. SCOTT (Chem. Abstr.)

Function-testing the Vegetative Nervous System with Acetylcholine. I. Tests on the Healthy. Ryuzō Tanahasi. [*Nagoya Igakkai Zasshi*, **48**, 195 (1938).]

As a result of pharmacological tests, 22 healthy subjects were classified in 4 types; their vegetative nervous systems were vagotonic, sympatheticotonic, stable or labile. The injection of 10–30 mg. acetylcholine per kgrm. of body-weight into subjects having labile or vagotonic nervous systems caused reductions in the leucocyte and erythrocyte counts, hæmoglobin, blood sugar, pulse-rate and blood-pressure. Miosis also occurred. The body temperature tended to fall. In subjects with stable or sympatheticotonic vegetative nervous systems, the effects

were slight and appeared only with 30-mgrm. doses. Since there is no discomfort or unfavourable after-effects from its use, acetylcholine is preferable to pilocarpine in pharmacological function-tests on the vegetative nervous system.

II. Test in Various Diseases. [*Ibid.*, 257.]

The acetylcholine method was applied to 36 patients with various diseases involving abnormal tonus of the vegetative nervous system. Of 32 subjects with vagotony or lability, 31 were positive to both the acetylcholine and the pilocarpine tests. Results on 4 sympatheticotonic patients were negative in both tests. In two cases the use of acetylcholine caused asthmatic symptoms, as did also the ingestion of the acetylcholine-containing foods, yams (*Dioscorea*) and taro (*Colocasi antiquorum*). In various disease conditions also, acetylcholine is preferable to pilocarpine in testing the vegetative nervous system.

W. C. TOBIE (Chem. Abstr.).

Tissue Acetylcholine. VI. The Liberation of Acetylcholine from Nerve Trunks during Stimulation. H. C. Chang, W. M. Hsieh, T. H. Li and R. K. S. Lim. [*Chinese J. Physiol.*, **14**, 19–26 (1939).]

Electrical stimulation of the nerve-trunk, isolated from the body or *in situ* mobilizes free acetylcholine (I) from the nerve-trunk into the saline solution (containing 0·1 mgrm. eserine per c.c.) in which it is immersed and increases the amount of free I as revealed by subsequent saline extraction. The total amount of alcohol-extractable acetylcholine may not be changed appreciably. A nerve-trunk previously incubated at 37° for 2 hours contains more total alcohol-extractable acetylcholine and liberates more I when stimulated than non-incubated nerves.

WALTER H. SEEGERS (Chem. Abstr.).

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2. Pharmacology and Treatment.

A Paradoxical Phenomenon of Insulin Shock Treatment. S. Lups. [*Klin. Wochschr.*, **18**, 813–16 (1939).]

The coma of 3 patients deepened when sugar was given by stomach-tube. This coma was prolonged, and restoration was effected only by intravenous administration of glucose. Adrenaline had no effect on the blood-sugar.

H. L. MASON (Chem. Abstr.).

Blood Sugar and Cerebro-spinal-Fluid Sugar during Insulin Shock Treatment of Schizophrenia. V. Schretzenmayr. [*Arch. Psychiat. Nervenkrankh.*, **108**, 680–93 (1938).]

Three patients with schizophrenia, already under insulin treatment for some time, showed high readings of blood sugar and cerebro-spinal fluid sugar before breakfast and while not under treatment. After insulin coma the blood sugar returned more quickly than the fluid sugar to normal.

B. C. P. A. (Chem. Abstr.).

Changes in Blood Lipides during Insulin Treatment of Schizophrenia. L. O. Randall, D. E. Cameron and J. M. Looney. [*Amer. J. Med. Sci.*, **195**, 802–9 (1938).]

Five schizophrenic patients who showed a good remission during insulin treatment developed a significant rise in whole blood phospholipide, total cholesterol, and total lipide. In 9 of 11 patients who failed to respond to treatment a transitory mild lipæmia occurred. Insulin did not significantly affect the post-absorptive level of the blood lipides.

B. C. P. A. (Chem. Abstr.).

Physiological Studies in Insulin Treatment of Acute Schizophrenia. Serum Lipides. Lowell O. Randall and E. M. Jellinek. [*Endocrinology*, **25**, 105–10 (1939).]

Twenty-two patients in the acute stage of schizophrenia were tested for serum lipides (phospho-lipides, total cholesterol, free cholesterol, cholesterol ester and total lipides) in the 2 weeks preceding and the 2 weeks following insulin treatment. All the mean lipide values, except free cholesterol, were initially significantly lower than the values obtained in normal controls. After medication the levels of all the lipides, except free cholesterol, were increased significantly and reached the normal level in the " recovered " as well as in the " not recovered " patients. The increase in lipide values was maintained by the " recovered " patients during the 2 weeks after termination of the insulin treatment, but the " not recovered " patients tended to drop back toward the initial level. The cholesterol ester/free cholesterol ratio became stabilized in " recovered " patients, but instability was increased in the " not recovered " group after insulin treatment.

F. SAUNDERS (Chem. Abstr.).

Serum Potassium and Serum Calcium in Insulin Shock Therapy. J. L. Clegg. [*Lancet*, **1**, 871–2 (1939).]

The serum Ca was usually normal and the K higher than normal in patients under treatment with hypoglucæmic shock. During the shock the concentration of serum K became lower than the initial concentration, while that of Ca remained the same. E. R. MAIN (Chem. Abstr.).

Changes in the Oxidation-Reduction Potential of the Blood of Schizophrenic Patients under the Influence of Insulin. M. Merezhins'kiĭ. [*Biochem. J. (Ukraine)*, **12**, 189–205 (*in English*, 207–8) (1938).]

Venous blood was used for measurements. The administration of insulin leads to an increase in the E_h value of the blood. This rise may be nullified by the administration of glucose, to counteract the insulin effect. Glucose alone will not change the E_h value in any direction. There is no correlation between the changes in the E_h of the blood and its content of O, glutathione and reduced ascorbic acid. No prognostic significance can be attached to the changes in E_h. The oxidation-reduction potential of the blood merely indicates a tendency in metabolic processes, but is not of absolute significance.

R. LEVINE (Chem. Abstr.).

Changes in the Glucose-Tolerance Test Occurring During and After Insulin Shock Therapy for Schizophrenia. H. Freed, S. De W. Ludlum and E. A. Strecker. [*Amer. J. Med. Sci.*, **196**, 36–44 (1938).]

The glucose-tolerance curve was abnormal in 41% of 22 cases of schizophrenia. During and after insulin shock therapy a biphasic change in the character of the glucose-tolerance curve was found. The immediate effect was to produce a hyperglucæmic (diminished tolerance) type of curve. In 10 of 12 patients followed 2–10 months after their last treatment a hypoglucæmic (increased tolerance) curve occurred. B. C. P. A. (Chem. Abstr.).

Physiological Studies in Insulin Treatment of Acute Schizophrenia. The Choline Esterase Activity of the Blood Serum. Lowell O. Randall and E. M. Jellinek.]*Endocrinology*, **25**, 278–81 (1939).]

The choline esterase activity of the blood-serum of 22 schizophrenic patients in the acute stage was determined by the gasometric method (Ammon, *C.A.*, **28**, 1734[9]). The choline esterase level of the patients was initially somewhat lower than that of the normal controls, but the difference was not significant. After insulin treatment the choline esterase level increased significantly whether the patients recovered or not. In the 2nd week after medication the esterase level tended to decrease to the normal level. FELIX SAUNDERS (Chem. Abstr.).

Blood Minerals. *J. M. Looney, E. M. Jellinek and Cora G. Dyer.* [*Ibid.*, 282–5.]

K, Ca and P of the blood were determined on 22 schizophrenic patients 4 times in the 2 weeks preceding and 4 times in the 2 weeks following insulin treatment. K and Ca showed no significant changes after medication. The mean level of the inorganic P of the blood was initially significantly higher than in normal controls. The P level of the 10 patients who recovered dropped after treatment to the normal level.

The " not-recovered " patients showed only an insignificant decrease.

FELIX SAUNDERS (Chem. Abstr.).

Intensifying the Effect of Insulin with Acetylcholine. *E. E. Gorodetskii.* [*Problemy Endokrinol.*, **2**, No. 1, 69–76 (1937).]

The simultaneous injection of acetylcholine along with insulin considerably increases the action of the latter ; this effect is regularly observed in rabbits, while with diabetic individuals the results are less uniform. The blood sugar was determined only for the first 2 hours of the insulin's action. Conclusion : Through the effect on the vegetative nervous system conditions affecting the action of insulin can be influenced in either the positive or negative direction.

M. G. MOORE (Chem. Abstr.).

Effects of Insulin Treatment on the Cerebro-spinal Fluid of Schizophrenics. *Mona Spiegel-Adolf and Herbert Freed.* [*Proc. Soc. Exptl. Biol. Med.*, **40**, 398–400 (1939).]

The non-electrolyte/electrolyte ratios were measured by combined methods on spinal fluids of schizophrenics treated with insulin. A marked parallelism was found between increases in this ratio and the occurrence, frequency and severity of the convulsions. These findings confirm previous observations in epileptics and in metrazole-treated schizophrenics (*cf. Confinia Neurol.*, **2**, 1 (1939).

L. E. GILSON (Chem. Abstr.).

Heart Action of Camphor, Metrazole and Coramine. *G. Kahlson.* [*Skand. Arch. Physiol.*, **80**, 209–13 (1938).]

Rhythmical activity of frog ventricle after a Stannius ligature was maintained by electrical stimulation ; the electrocardiogram was recorded from the base and the apex. Local administration of therapeutic concentrations of metrazole and coramine on the apex electrode does not alter the monophasic action current. Camphor (1 : 10,000–1 : 25,000) diminishes the size and duration of the action potential.

B. C. P. A. (Chem. Abstr.).

A Comparative Study of the Stimulant Analeptics Picrotoxin, Metrazole and Coramine. *H. W. Werner and A. L. Atum.* [*J. Pharmacol.*, **66**, 260–78 (1939).]

Picrotoxin is a somewhat more effective analeptic agent than metrazole against severe depression produced in rabbits by intraperitoneally injected nembutal. Coramine is relatively ineffective. Coramine is sometimes depressant, picrotoxin and metrazole are not. Of the three compounds, metrazole has the highest factor of safety when convulsions *per se* are desired in normal rabbits. It is safest when given by rapid intravenous injection. Metrazole and picrotoxin are inactivated at about the same rate *in vivo* ; coramine is inactivated much more slowly.

L. E. GILSON (Chem. Abstr.).

Micro-identification of Metrazole in Mixed Aqueous Solutions. *Vincent E. Stewart.* [*Ind. Eng. Chem., Anal. Ed.*, **11**, 345–6 (1939).]

A modification of Wollner and Matchett's method (*C.A.*, **32**, 1520[2]) is used to separate metrazole from alkaloids and other drugs in body fluids. The sensitivity

of the test is 1 part in 10,000, the smallest amount of metrazole that can be extracted and identified is about 0·1 mgrm. per 100 ml. of sample.

T. H. DUNKELBERGER (Chem. Abstr.).

The Pharmacologic Antagonism of Metrazole and Sodium Amytal as Seen in Human Individuals (Schizophrenic Patients). Louis H. Cohen. [*J. Lab. Clin. Med.*, **24**, 681–4 (1939).]

Rapid, simultaneous injections of both drugs result in the inhibition of the hypnotic effects of Na amytal by metrazole and the rise in the convulsant threshold of metrazole by Na amytal, so that certain combinations of drugs produce no effects. The convulsant threshold of metrazole seems to bear a direct relationship to the amount of Na amytal. HOWARD W. ROBINSON (Chem. Abstr.).

The Analeptic Action of Synephrine-Azoman and Metrazoleveritol in Poisoning by Hypnotics. F. Hildebrandt and J. Bruns. [*Schmerz, Narkose-Anesthesie*, **11**, 112–19 (1938).]

In rats under the influence of various hypnotics, a combination of metrazole with veritol exerted greater analeptic action than a combination of synephrine with azoman. The analeptic effects were greatest against soluble barbital and avertin, weaker against chloral hydrate, paraldehyde and pernocton and weakest against urethan. The analeptic effects of the combination of metrazole with veritol were no greater than those of metrazole alone.

MARION HORN (Chem. Abstr.).

Cerebro-spinal Fluid During Convulsions due to Cardiazole. [*B. Niketic and Z. Susic. Arch. Psychiat. Nervenkrankh.*, **108**, 562–71 (1938).]

In 15 patients treated with cardiazole (metrazole), lumbar puncture was performed during the convulsion. The lumbar cerebro-spinal fluid pressure increases during the initial " myoclonic " phase, reaches its peak of over 100 cm. of water during the tonic phase and decreases again. The cerebro-spinal fluid is chemically normal. B. C. P. A. (Chem. Abstr.).

The Colorimetric Identification of Barbiturates in the Urine and other Organic Fluids with Cobalt, as Described by W. Parri. M. Aiazzi Mancini and E. Pecciarini. [*Biochem. terap. sper.*, **26**, 119–22 (1939); *cf. C.A.*, **19**, 1176.]

Extract 10 c.c. of urine 3 times with 5 c.c. $CHCl_3$ and dry the solutions thoroughly with Na_2SO_4. Mix 1 c.c. of the $CHCl_3$ solution with 10 drops of a 0·2% solution of Co acetate in MeOH and add carefully 4–6 drops of a 2% solution of NaOH in MeOH. A violet ring at the surface indicates the presence of moderate quantities of barbiturates. The reaction appears if the $CHCl_3$ contains at least 0·5 mgrm. veronal. Concentration of the solution by evaporation increases the sensitivity. The reaction is rendered more sensitive if the urine is treated with $KMnO_4$ in presence of H_2SO_4 until no more $KMnO_4$ is reduced.

A. E. MEYER (Chem. Abstr.).

The Effect of Certain Barbiturates upon the Oxygen Uptake and Anaërobic Reduction of Methylene-blue by Rat Liver and Brain. Carla M. Zorn, Edward Muntwyler and O. W. Barlow. [*J. Pharmacol.*, **66**, 326–35 (1939).]

The O uptake of rat liver slices without added substrates was inhibited more or less by 0·01% of the following Na barbiturates, listed in decreasing order of effectiveness: amytal, pentobarbital, neonal, ortal, phenobarbital, evipan, alurate and dial. Within the concentration range 0·001–0·1% inhibition increased with the concentration. Na barbital did not inhibit O uptake even when increased to

0·5%. The order of O effectiveness in producing narcosis in rats is—pentobarbital, alurate, amytal, dial, neonal, evipal, phenobarbital, ortal and barbital. The anaërobic reduction of methylene-blue by liver tissue without added substrates was markedly decreased by 0·1% of the above Na barbiturates excepting barbital. In rat brain the anaërobic reduction of methylene-blue was less affected by the barbiturates than in liver. L. E. GILSON (Chem. Abstr.).

Detoxication of Barbiturates and the Influence of the Method of Administration. Demonstrated with Nembutal and Pentothal. Richard Kohn-Richards and Clyde Grimes. [*Anesthesia and Analgesia*, **18**, 139–45 (1939).]

The detoxication of these two barbiturates was studied in rabbits by giving a single intravenous dose or a slow intravenous infusion. After this, the degree of detoxication was measured by the determination of the supplementary dose after certain time intervals which were necessary to cause respiratory paralysis. A mathematical formula has been worked out by which the rate of destruction of the drugs can be calculated during a constant infusion from the results obtained from single-injection experiments. G. H. W. LUCAS (Chem. Abstr.).

Picrotoxin-Barbiturate Antagonism in Decorticated Animals. H. R. Miller and E. A. Spiegel. [*Yale J. Biol. Med.*, **11**, 497–500 (1939).]

In 15 animals (9 incomplete and 6 complete decortications) the intraperitoneal injection of picrotoxin awakened the animals from barbiturate sleep.
G. H. W. LUCAS (Chem. Abstr.).

Formation of Acetylcholine in Brain in vitro in the Presence of Methylene-blue and Cobra Venom. Elisabeth Corteggiani. [*Compt. rend. soc. biol.*, **131**, 883–7 (1939).]

The addition of a little methylene-blue greatly increases the amount of acetylcholine liberated by cobra venom under the conditions previously described (*C.A.*, **32**, 9292[3]). L. E. GILSON (Chem. Abstr.).

Comparative Study of the Liberation of Acetylcholine from Brain Tissue in vitro by Cobra and Vipera aspis *Venoms, Lysocythin and Saponin. J. Gautrelet and E. Corteggiani.* [*Ibid.*, 951–4; *cf. C.A.*, **32**, 9292[3].]

Viper venom has a weaker action than cobra venom, and lysocythin and saponin have a much weaker action than either venom.
L. E. GILSON (Chem. Abstr.).

Acetylcholine and Cholesterol. Fritz Zinnitz. [*Arch. exptl. Path. Pharmakol.*, **190**, 594–604 (1938).]

The effect of cholesterol acetate (I) on the action of acetylcholine (II) was studied on the hearts of intact and spinal frogs. In small doses I increases the effect of II; in large doses I causes a reversal of II action leading to systolic contracture of the heart. The effect of I is reversible.
EDWARD EAGLE (Chem. Abstr.).

Action of Toxic Doses of Atropine on the Central Nervous System. Theodore Koppanyi. [*Proc. Soc. Exptl. Biol. Med.*, **40**, 244–8 (1939).]

The effects of large and near lethal doses in frogs, dogs and cats are described. Atropine, like morphine, has a two-fold action on the central nervous system, depressing and stimulating. The mechanism of the action is not clear. Whether or not the actions can be explained by the acetylcholine-blocking effect still remains to be determined. L. E. GILSON (Chem. Abstr.).

Concentration of Sulphanilamide in Human Spinal Fluid and Blood after a Single Intrathecal Injection. E. Neter, D. H. Weintraub and A. L. Dayman. [*Proc. Soc. Exptl. Biol. Med.*, **40**, 164–6 (1939).]

Four hours after a single intrathecal injection of 80 mgrm. sulphanilamide in patients free of meningitis concentrations of 10–16 mgrm.% were found in the spinal fluid. All was eliminated in 18–24 hours. The maximum found in the blood at any time was 0·7 mgrm.%. L. E. GILSON (Chem. Abstr.).

Disturbances of Excitability in Narcosis. A. Richard. [*Anesthésie et analgésie*, **4**, 472–6 (1938).]

Evidence is cited from the literature to demonstrate that the influence of cerebral cortical centres on peripheral excitability is abolished completely by $CHCl_3$ (I) and gardenal (II), but not by chloralose (III) or morphine (IV). Thus disturbances in peripheral excitability due to centrally acting toxins, e.g., alcohol, ether, Pb, Mn or As are abolished by I and II, but not by III or IV. In addition, III does not suppress subordination reflex mechanisms, such as the reflex influence of the labyrinth on peripheral neuromuscular excitability.

MARION HORN (Chem. Abstr.).

Action of Asphyxia on Nervous Excitability. A. Richard. [*Anesthésie et analgésie*, **4**, 477–82 (1938).]

Asphyxia, produced in dogs mechanically (by prevention of inspiration) or chemically (by administration of CO or HCN), first causes disturbances in peripheral excitability via both the local effect of the asphyxiated blood on the neuromuscular appearance and the central effect of disturbances of subordination. Later the asphyxia produces a disappearance of cortical excitability, which can be counteracted by convulsants, e.g., caffeine, coramine or camphorated oil. However, such analeptics are of use in asphyxia only if the neurocirculatory excitability is still functioning. Coramine gives good results in asphyxia when injected intraspinally, since this avoids the cardiovascular depression (due to carotid sinus excitation) which occurs on intravenous administration.

MARION HORN (Chem. Abstr.).

The Influence of "Animal Hypnosis" on the Course of Narcosis in Cold-blooded Animals. Josef Stroder. [*Schmerz, Narkose-Anæsthesie*, **11**, 82–4 (1938).]

The time required for a frog to reach deep narcosis after injection of 25% urethan solution into the dorsal lymph-sac was reduced 50% by "hypnosis".

MARION HORN (Chem. Abstr.).

The Mode of Action of Narcotics with Brief Action. I. Comparison of the Activity of Evipan and Eunarcon in Animals. Heinz W. Voigt. [*Schmerz, Narkose-Anæsthesie*, **11**, 44–50 (1938).]

The average lethal doses for mice of the various narcotics, injected as their Na salts, were as follows (in mgrm./kgrm.): evipan (I) 298, eunarcon (II) 176, phanodorn 302, numal 200 and noctal 104. The rates of elimination in rabbits were 0·8–0·9 and 0·65–0·7 mgrm./kgrm./min. for I and II respectively. II increased the Co-combining power of the blood when injected into rabbits. The greater toxicity and narcotic power of II, as compared with I, is attributed to the presence of Br in II.

II. Attempts to Localize the Point of Action of the Side Reactions. [*Ibid.*, 50–6.]

Repeated injection of narcotic doses of I in rabbits causes anatomical alterations in the brain ganglion cells, possibly related to the functional central nervous side effects of I. MARION HORN (Chem. Abstr.).

The Action of 1, 2-Benzopyrene on the Central Nervous System. Ivan Bertrand and Jean Cruner. [*Bull. assoc. franç. étude cancer*, **27**, 697–705 (1938).]

Introduction of crystals of 1, 2-benzopyrene suspended in lanolin or paraffin oil into the brain of rabbits led sometimes to a glial reaction resembling hepatolenticular syndromes, but never to tumour production.

MARION HORN (Chem. Abstr.).

Influence of Mescaline (Trimethoxy-3-Phenyl-Ethylamine) and of Dimethoxy-β-Phenylethylamine on Arterial Tension. A. Geesink and W. A. den Hartog Jager. [*Arch. neerland. physiol.*, **24**, 79–82 (1939).]

Mescaline does not have any effect on arterial pressure. In the cat 100 mgrm. of dimethoxy-β-phenyl-ethylamine increases the arterial pressure 20%. The effect on the pressure is not the cause of the experimental catatonia.

FELIX SAUNDERS (Chem. Abstr.).

The Effect of Acetyl-β-Methylcholine (Mecholyl) on the Gastric Secretion in Animals and in Man. James Flexner and Irving S. Wright. [*Amer. J. Digestive Diseases Nutrition*, **5**, 736–9 (1939).]

In rabbits subcutaneous injections of 2 and 4 mgrm. mecholyl chloride caused no outpouring of mucinous alcoholic gastric secretion and no change in the free and total acid of the gastric contents; in cats no free HCl was present in the fasting gastric specimen and none appeared after injection of 2, 4 and 10 mgrm.; in man subcutaneous injection of 25 mgrm. caused no marked change in the character of the gastric secretions and a slight rise in flow of mucinous and alchoholic saliva; accidental swallowing of this neutralizes the rise in gastric acidity.

E. EAGLE (Chem. Abstr.).

Human Autonomic Pharmacology. XVII. The Effect of Acetyl-3-Methylcholine Chloride on the Gall-bladder. Purcell G. Schube, Abraham Myerson and Ruth Lambert. [*Amer. J. Digestive Diseases Nutrition*, **5**, 687–90 (1938).]

Acetyl-3-methylcholine (mecholyl) has practically no effect on the size and shape of the gall-bladder, but definitely inhibits the emptying of the gall-bladder after ingestion of a fat meal. EDWARD EAGLE (Chem. Abstr.).

Autonomic Drugs and the Biliary System. II. Changes in Liver Secretion and their Relation to Alterations in Respiration, Arterial Pressure and Portal Pressure Produced by Acetyl-β-Methylcholine Chloride, Adrenaline and some Related Compounds. James Flexner and Irving S. Wright. [*J. Pharmacol.*, **66**, 171–81 (1939).]

Acetyl-β-methylcholine, histamine, benzedrine and adrenaline do not directly affect the rate of bile flow; the changes in liver secretion noted are apparently related to sudden arterial blood-pressure changes. The response to all the effective drugs is diminished when they are injected into the portal vein.

L. E. GILSON (Chem. Abstr.).

Comparative Pressor Efficiency of Sympathomimetic Amines in the Normal State and in Decerebrate Shock. Cathrine A. Crismon and M. L. Tainter. [*J. Pharmacol.*, **66**, 146–70 (1939).]

The maintenance of pressor efficiency in the circulatory depression of decerebrated cats was studied with cobefrine, adrenaline, *m*-hydroxyephedrine, propadrine, 3, 4-dihydroxy-ephedrine, phenylethanolamine, epinine, *m*-hydroxynorephedrine, arterenol, tyramine, paredrine, benzedrine, neo-adrenaline. The efficiency of the compounds decreased in the order named. The last three were effective only in very large doses. In general, greater absolute and percentage responses to given doses

of the amines were noted after destruction of the central vasomotor mechanisms ; hence these amines do not produce their usual circulatory stimulation through central nervous mechanisms. L. E. GILSON (Chem. Abstr.).

"Anencephalic Blood Picture" or "Contra-striatal Blood Picture" Produced Pharmacologically. A Second Possibility of Topical Diagnosis of Brain from Blood Picture Alone. Akira Sato and Saburo Kuribayasi. [*Tôhoku J. Exptl. Med.*, **35**, 522–36 (1939) (*in English*).]

Rabbits were given subcutaneous injections of 210–400 mgrm. morphine-HCl per kgrm. of body-weight frequently enough to keep them in a paralysed state for about 5 days. The number of large and small peroxidase granules in the pseudo-eosinophilic leucocytes was increased 3 hours after the first injection and continued to increase for about 2 days, then declined in numbers but not always to normal values. Smaller amounts of morphine had almost no effect. Conclusions : The " peroxidase centres " discovered by Sato are located in the diencephalon or mesencephalon. Normally the telencephalon regulates the action of these centres in stimulating the production of peroxidase (which appears as granules in the pseudo-eosinophiles), but its regulatory effect may be inhibited by heavy doses of morphine. Increased numbers of peroxidase granules in human cases would be of diagnostic significance, indicating some injury to the telencephalon (cerebrum).
W. C. TOBIE (Chem. Abstr.).

Effect of Sulphanilamide on the Viability of Meningococci in Spinal Fluid. Erwin Neter. [*Proc. Soc. Exptl. Biol. Med.*, **39**, 84–6 (1938).]

Cerebro-spinal fluid from patients with meningococcal meningitis was mixed with sulphanilamide and incubated. Subcultures made from these mixtures were delayed or inhibited in growth in dependence on the concentration of sulphanilamide and the duration of the original incubation. B. C. P. A. (Chem. Abstr.).

Experimental Rabies, with Special Attention to the Vitamin C (Reducing Compound) of the Brain as well as that of the Aqueous Humour and of the Cerebro-spinal Fluid. Toziro Uno. [*Orient. J. Diseases Infants*, **21**, 79–80 (1937); *Chem. Zentr.*, **1**, 1819 (1938).]

Rabbits which were infected with five different strains of rabies showed in most cases no reduction in the vitamin C content of the brain and cerebro-spinal fluid. Thus vitamin C was retained in the most vital organs. A decrease, however, was frequently observed in the aqueous humour. M. G. MOORE (Chem. Abstr.).

Alcohol in the Cerebro-spinal Fluid. F. N. Riklin. [*Schweiz. Arch. Neurol. Psychiat.*, **41**, 173–92 (1938).]

Alcohol was given by mouth and its concentration determined at intervals of 10–20 minutes in the blood and the lumbar and cisternal fluid. The alcoholic concentration in cisternal fluid more closely parallels that in the blood than the concentration in the lumbar fluid. The first symptoms of intoxication (the tested persons were patients with general paralysis or schizophrenia) were observed after 43 minutes, when the concentration in the blood was 0·099%, in the cisternal fluid 0·085, and in the lumbar fluid 0·045 ; the symptoms disappeared after 160 minutes, when the respective concentrations were 0·080%, 0·099% and 0·095%.
B. C. P. A. (Chem. Abstr.).

Effect of Percaine on the Myelinated Fibres of the Sympathetic Nervous System. A. Donaggio. [*Boll. soc. ital. biol. sper.*, **13**, 241–3 (1938).]

Percaine (nupercaine) in rabbits causes modifications of the cervical sympathetic nerves, appropriate staining methods indicating a spiciform structure.
B. C. P. A. (Chem. Abstr.).

The Pharmacology of Bismuth: Its Effect on the Reactions of the Vegetative Nervous System. I. A. Storozhev. [*Arch. sci. biol.*, No. 2, 29–42 (*in English*, 41–2) (1937).]

The intravenous injection of 0·1–1 mgrm. of Bi tartrate produces a noticeable increase in the excitability of the sympathetic nerve-endings of the nictitating membrane of the cat, and increases its reaction to adrenaline. Only a slight effect in diluted solution was observed on the surviving vessels of isolated organs. A depressor effect was observed on the isolated heart of warm-blooded animals, and the injection of 2–4 mgrm., or repeated small doses, produces a momentary stoppage of the heart which is not checked by preliminary atropinization. Diluted solutions have a depressing action on the isolated intestine. Mixed with calomel, Bi has a synergistic action on the secretory function of the small intestine.

S. A. KARJALA (Chem. Abstr.).

Absorption of Sulfonal in the Body Fluids. Ganassini. [*Boll. soc. ital. biol. sper.*, **14**, 234–5 (1939).]

Experiments *in vitro* showed that the solubility of sulfonal was increased by the presence of bile-salts and in conditions of alkalinity and temperature similar to those of intestinal juice. Administration of sulfonal to rabbits in pills and in keratin capsules indicated that sulfonal did not generally reach the intestinal juice intact. With dogs there was no difference in results of the two modes of introduction.

HELEN LEE GRUEHL (Chem. Abstr.).

The Prevention by Vitamin B_1 of Paralysis Caused by Feeding Uliron. W. Engelhardt and H. Hullstrung. [*Klin. Wochschr.*, **18**, 774–5 (1939); *cf. C.A.*, **33**, 234[9].]

The paralysis that results in 10–15 days when pigeons are fed 1·5 grm. per kgrm. of body-weight of uliron (4-amino-4[1]-(dimethylsulfamyl) benzenesulfonanilide) is entirely prevented by parenteral administration of 10 mgrm. of vitamin B_1. Paralysis of short duration is healed by vitamin B_1, but if it is stopped after a few days the symptoms return, possibly as the effect of uliron, which is stored in the body.

H. L. MASON (Chem. Abstr.).

The Concentration of Procaine in the Cerebro-spinal Fluid of the Human Being After Subarachnoid Injection. H. Koster, A. Shapiro and R. Warshaw. [*Arch. Surgery*, **39**, 97–103 (1939).]

The concentration of procaine at the site of injection, 3 mm. above the site of injection and at the cisterna magna, after the injection of 33 mgrm. of procaine-HCl in 7 c.c. of cerebro-spinal fluid parallels the findings previously described (*cf. Amer. J. Surgery*, **33**, 245–81 (1936); *C.A.*, **30**, 7608[5]; **33**, 237[6]), where 150 mgrm. of the anæsthetic dissolved in 3·5 c.c. of spinal fluid was injected. Procaine spreads rapidly away from the site of injection in a cephalad direction so that the concentration falls there and rises in the dorsal region. At no time does the concentration become as high as that found simultaneously in the lumbar region.

JOHN T. MYERS (Chem. Abstr.).

Caffeine and Cholinergic Nerves. H. Fredericq and Z. M. Bacq. [*Bull. acad. roy. med. Belg.*, **3**, 341–67 (1938).]

Caffeine (0·5%) increases the inotropic and chronotropic effects of vagal stimulation on the tortoise auricle. In higher concentrations (5%) it reduces these effects. These sensitizing and desensitizing effects are completely reversible. In the cat, caffeine increases the inhibiting action of excitation of vagal fibres. In the dog, the drug increases the vasodilator action of acetylcholine and the action of the *n. erigens*. Caffeine does not increase the response of frog skeletal muscle to

maximum indirect stimulation and delays relaxation ; it has only a slight potentiating action in the cat. In the cat, the drug transforms an acetylcholine contraction of muscle into a contracture, and this latter is succeeded by non-responsiveness to nerve stimulation. B. C. P. A. (Chem. Abstr.).

Quinine in Myotonia Congenita : Its Antagonism to Prostigmine. Grace Briscoe. [*Lancet*, 1939, i, 1151–2.]

The effect of quinine, injected intravenously, on normal skeletal muscle (cat quadriceps *in situ*) is antagonistic to prostigmine and synergistic with curarine. The effect of quinine is produced both by raising the threshold on the motor end-plates and by direct action on the muscle-fibre. It is suggested that in myotonia congenita there is hyperexcitability to normal amounts of acetylcholine.

E. R. Main (Chem. Abstr.).

Changes in Spleen Size, Blood-pressure and Erythrocyte Count After the Administration of Benzedrine Sulphate in Dogs. J. L. Pinkston and J. O. Pinkston. [*J. Lab. Clin. Med.*, **24**, 1038–45 (1939).]

Benzedrine sulphate (1 mgrm. per kgrm. of body-weight administered intravenously to anæsthetized dogs) caused a contraction of the exposed spleen, accompanied by promptly occurring erthyrocytosis and a definite, transitory rise in blood-pressure. A second injection of the same amount caused either no change in the blood-pressure or a slight transitory fall. These changes were also obtained in adrenalectomized dogs, but did not occur in splenectomized animals with intact adrenals. Howard W. Robinson (Chem. Abstr.).

Some Effects of Stimulation of Sympathetic Nerves and Injection of Pressor Drugs in Adrenalectomized Cats. C. W. J. Armstrong, R. A. Cleghorn, J. L. A. Fowler and G. A. McVicar. [*J. Physiol.*, **96**, 146–63 (1939).]

In the terminal stage of adrenal insufficiency, splanchnic nerve stimulation or the intravenous injection of nicotine had but negligible pressor effects. Adrenaline, on the contrary, elicited a very marked rise in blood-pressure, and dilatation of the pupil and strong and sustained contraction of the nictitating membrane. The injection of adrenaline in cats in adrenal insufficiency caused visible constriction of splanchnic vessels, and an immediate decrease in the volume of the intestine as determined by the plethysmograph. Animals kept in good condition by cortical extract treatment after adrenalectomy showed responses to brief stimuli and to drugs which compare favourably with results obtained on acutely adrenalectomized controls. E. D. Walter (Chem. Abstr.).

Ratio of Reduced Ascorbic Acid to Ascorbic Acid in the Clinic. Relation to the Autonomic Nervous System. G. Michetti, B. Bartoline and E. Roncallo. [*Minerva med.*, 1939, **1**, 549–53.]

Drugs which stimulated the sympathetic or inhibited the vagus (adrenaline, atropine) in general increase the ratio and the total elimination of ascorbic acid in the urine, while drugs which stimulated the vagus (pilocarpine, prostigmine) diminished the ratio and the elimination of ascorbic acid. The ratio of reduced/oxidized ascorbic acid was considered the expression of the oxidative-reductive processes of the tissues. H. L. Gruehl (Chem. Abstr.).

Nicotinic Acid in the Treatment of Atypical Psychotic States. H. M. Cleckley, V. P. Sydenstricker and L. E. Geeslin. [*J. Amer. Med. Assoc.*, **112**, 2107–10 (1939).]

In 19 patients the usual criteria for clinical diagnosis of pellagra were largely absent. Hebetude grading into profound stupor may be the only sign of severe acute pellagra, and administration of nicotinic acid is justified as being the only method for diagnosis of such cases. F. P. Griffiths (Chem. Abstr.).

The Effect of Circulatory Drugs on Narcosis. E. Werle and J. Lentzen. [*Arch. exptl. Path. Pharmakol.*, **190**, 328–40 (1938).]

Callicrein deepens and prolongs the anæsthesia, having the maximum effect with evipan and the least effect when urethan is used. Acetylcholine or adenylic acid has no effect on evipan (I), urethan (II), or eunarcon (III) narcosis. Histamine deepens and prolongs evipan narcosis. With small doses of I (10–25 mgrm./kgrm.) the maximum effect is obtained. Frequent injections of histamine do not increase the effect. The result obtained from subcutaneous injection of 500 γ of histamine at the beginning of narcosis is less than that caused by 200 γ injected intravenously. Vasopressin causes marked deepening and prolongation of narcosis. One-half unit of vasopressin causes death in a rabbit given 25 mgrm./kgrm. of III. With small doses of III the prolongation of narcosis declines more strongly than the deepening. Large doses of III cause a more rapid decline of depth of narcosis. Vasopressin affects I narcosis in the same manner as it affects III narcosis. Several injections at long intervals strengthen the effect, particularly at the middle and end of narcosis. When II is used only vasopressin in large doses (1·5 units per animal) is without effect. Adrenaline and sympathol have an effect similar to that of vasopressin, the former being the more effective. Both have their greatest effect against small doses of I, and frequent injections cause a more prolonged effect.

EDWARD EAGLE (Chem. Abstr.).

The Effect of Benzedrine Sulphate on Metabolism and the Cardiovascular System in Man. Karl H. Beyer. [*J. Pharmacol.*, **66**, 318–25 (1939).]

Benzedrine sulphate, 30 mgrm. orally, increased the normal metabolic rate an average of 15·4% within the first 2½ hours. Return to normal required more than 9 but less than 24 hours. The per minute volume of inspired air was not significantly altered owing to compensatory increase in tidal volume whenever the rate of respiration was reduced. Buccal temperature rose about 1° F. Blood-pressure rose about 30% in about 1½ hours and then slowly returned to normal in somewhat less than 24 hours. Pulse-rate was unaffected or very slightly increased.

L. E. GILSON (Chem. Abstr.).

The Electrical Impedance of Muscle During the Action of Narcotics and Other Agents. Rita Guttman. [*J. Gen. Physiol.*, **22**, 567–91 (1939).]

Na, K and Mg had little effect on the electrical impedance of sartorius muscle of *Rana pipiens*; but Ba and Ca caused it to fall. Physiologically unbalanced salt solution did not seem to affect impedance. When a sugar solution was permitted to circulate past both sides of the muscle, half the effect on impedance was over in ¾ minute; this indicates that inorganic cations and organic narcotics reach cell surfaces quickly, whereas their action on the muscle is much slower. Penetration of sugar into the intercellular spaces of muscle follows the diffusion law. Saponin, $CHCl_3$, Na taurocholate, BuOH, AmOH, isoamyl carbamate, chloral hydrate and Na salicylate depress 1,000-cycle resistance of muscle when used in sufficient quantity. A detailed study of isoamyl carbamate showed that low concentrations increase, high concentrations decrease, resistance. Over a wide frequency range, the resistance of the fibre membranes first increases, then decreases; at sufficiently great narcotic concentration, membrane resistance may disappear entirely. Membrane capacity is only slightly affected.

C. H. RICHARDSON (Chem. Abstr.).

Obituary Notices.

SIGMUND FREUD.

SIGMUND FREUD, the greatest psychologist the world has ever known, passed away on September 25. He belonged to the race which has been persecuted from time immemorial. His own ancestors, who had long settled on the Rhine, were hounded from Cologne to Lithuania in the fifteenth century. Thence they migrated through Galicia to Austria. Freud himself was born in Moravia on May 6, 1856. At the age of four he went to Vienna, which became his home for the remainder of his life, until—through the kindness of English friends—he was evacuated to this country from the Nazi persecution. He had always been an admirer of the English character. One obituary notice states that he was kindly treated by the Germans. He was not ; unless confiscation of half his money and property and the battering of his son by storm troopers are to be regarded as kindness !

At school he was at the top of his class for seven years. He was originally trained for the law, but then took to medicine, and was particularly interested in the physiology and anatomy of the nervous system. Indeed, he lectured on both these subjects, did valuable research and, so far as I know, his method of staining axis-cylinders has never been superseded.

Owing to financial considerations he had to abandon such non-lucrative work and became a physician, still maintaining his interest in the nervous system, and in due course he studied under Charcot at the Saltpetrière. Hence he took to hypnotism, which he practised among his patients in Vienna ; but he was dissatisfied with its results and by good fortune came into contact with Breuer, who had discerned in one of his hysterical patients an underlying mental mechanism. He discussed this patient with Freud, and gave him his first glimpse into unconscious processes of the mind.

After this he gradually gave up hypnotism and worked along psycho-analytical lines, but it was not until 1896 that he gave the name " psycho-analysis " to his method. He pursued his researches absolutely alone and in the face of the fiercest opposition until 1907, when a few disciples began to gather round him. The number grew, and in 1910 was large enough to found the International Psycho-analytical Association, which to-day has branches in Great Britain, France, Holland, Switzerland, Russia, Denmark, Norway, Palestine, America (5), and until recently in Germany, Austria and Hungary.

Nevertheless, opposition to psycho-analysis did not die down and probably

never will, owing to its truths being intrinsically of an unpleasant nature to most people, revealing as it does that man is not master of his own mind. Feeling along these lines has at times run very high. Indeed in 1917 the then President of our Association wrote a letter to the *British Medical Journal* denouncing psycho-analysis. Several resignations from our Association followed and even from the British Medical Association, so he wrote another letter stating that he was expressing merely his own views and not those of the Medico-Psychological Association, although, without doubt, he would have received overwhelming support had a plebiscite been taken. It will be remembered too that it was about this time that Mercier wrote accusing "Psycho-*analists*" of practising their profession in order to gratify their own sexual passions; also he deliberately spelt Freud's name "Fraud". Of course he did not know Freud, for he would have found him to be a man of the highest integrity, to whom anything approaching deception or ever insincerity was absolutely foreign and abhorrent, a scrupulous enthusiast for the truth, whose distinguishing trait was—as Dr. Ernest Jones justly pronounced in his funeral oration—"nobility of character".

Freud was a man who would listen patiently to informed criticism, but criticism based on ignorance he simply disregarded; for he discerned more clearly than the critic himself or any other man the unconscious motives which lay behind. Errant disciples have experienced the lash of his tongue probably more than others, but at the same time he had a sparkling wit.

To trace the history of psycho-analysis would be beyond the scope of this notice. Is it not written in the hundreds of lengthy papers and books by Freud himself? A brief account of his life and work is to be found in his *Autobiographical Study*, translated by James Strachey and published by the Hogarth Press.

Freud was a great linguist; he spoke many tongues fluently and his English was perfect. Indeed he was of the greatest assistance to some of his translators. He was familiar with all the literature that mattered in almost every language, and his general knowledge was encyclopædic.

He knew well enough that he was a great man, yet he was modest withal. Although he raised psychology from the rank of a purely academic study to a living science, pursuing its ramifications into every other branch of knowledge bearing on the study of man—history, anthropology, folk-lore, mythology, religion, education, everyday life, wit, literature, art and others—yet he writes: "The sphere of application of psycho-analysis extends as far as psychology, to which it forms a complement of the greatest moment. Looking over the patchwork of my life's labours I can say that I have made many beginnings and thrown out many suggestions. Something will come of them in future, though I cannot myself tell whether it will be much or little. I can, however, express a hope that I have opened up a pathway for an important advance in our knowledge."

Three years ago, on the occasion of his eightieth birthday, the Royal Medico-Psychological Association elected him to its Honorary Membership.

Freud had no fear of death, but those who loved him were relieved to know that at long last he was released from the dreadful pain of his fatal illness which had threatened him for years.

W. H. B. STODDART.

HENRY HAVELOCK ELLIS.

HENRY HAVELOCK ELLIS, who passed away in July, had been an Honorary Member of our Association for fifteen years, but he never attended a meeting, for he disliked public gatherings, and his retiring nature never allowed him to address one.

Born at Croydon in 1859, he came of sea-faring stock on both sides of the family, and his earliest years were spent at sea. Indeed he received his beginnings of education at sea. Up to the age of twelve he attended a private school near London. Thence he was transferred to Australia, where he soon became a schoolmaster, and at the age of nineteen he became headmaster of a private school there.

All this early travel, together with his wanderings in Australia, gave Ellis a sense of the world-as-a-spectacle, a desire for adjustment of the cosmos, and at the age of nineteen he decided to study medicine, not as a career, but as a biological foundation for his life's work.

He went to St. Thomas's Hospital and took the L.S.A., but his interests at the time were sociological. In 1882 he was instrumental in founding the Progressive Association for the Promotion of Intellectual and Social Well-being, but there soon came a split, the object of the minority of whom Ellis was one being "the subordination of material things to spiritual", while the majority formed the beginning of the Fabian Society.

Temperamentally he was an artist, regarding Living as the supreme art, and he used to write of such subordinate arts as The Art of Love, The Art of Thinking, The Art of Religion, The Art of Morals, The Art of Dancing and The Art of Writing. He found beauty in everything.

It was probably his sociological interests and activity that brought him into contact with many literary giants of the day, and in 1887–89 he edited the unexpurgated Mermaid Series of Elizabethan dramatists. Then he started the *Contemporary Science Series*, which continued until 1914. As we all know, many of these are classics.

But the monumental work of his life was of course his *Studies in the Psychology of Sex* (1897–1908). As a pioneer he approached this study, not with

curiosity or even in a cold scientific spirit, but with reverence for Love, which he regarded as the "condition of right seeing" and with admiration for its beauty. Other books have been written on the subject, yet paradoxically none has attained the same scientific purity. This great work was driven from this country to America by the Bedborough Trial, in which a bookseller was put up as a defendant instead of Ellis himself. Bedborough tactlessly pleaded guilty; but, surely, even the prejudiced prudery of the 'nineties did not justify the Recorder's abusive comments respecting the author, whom the College of Physicians honoured in 1936 by electing him under their very special rule to the Fellowship of the College.

This interest in sex is foreshadowed in many of his sonnets, written between the ages of 15 and 21, but not published until forty-four years later. His output was tremendous, for he wrote more than twenty books other than the *Studies in the Psychology of Sex*, to say nothing of numerous articles in magazines.

Ellis was a great admirer of Freud. Indeed the first full account in English of Breuer and Freud's *Studies of Hysteria* appeared in the first volume of the *Studies of the Psychology of Sex*. These two great men exchanged publications and letters, and Freud pays a tribute to Ellis in his *Interpretation of Dreams* and elsewhere Freud rejected Ellis's notion of him that he was an artist who arose in science, but we might well designate Ellis as a scientist who arose in art.

Æsthetic and mystic philosopher, artist, poet, musician, scientist, Ellis regarded himself as a spectator of the world, seeing with his own eyes, cultivating his own tastes, and having but little respect for authority; but he was never hostile and never bore ill-will. He was reclusive, living preferably in out of the way parts of England, but not seclusive; for, if one took the trouble to hunt him out, he was the most accessible of men.

He was a stately man with a majestic head, a luxuriant growth of hair, and a fine flowing beard. One photograph of him reminds me of Hughlings Jackson. Ellis once wrote "Without a clear-eyed vision there can be no sweetness in the world, and without sweetness there can be no true revelation of Light." Then again, "If I were ambitious I would desire no finer epitaph than that it should be said of me 'He added a little sweetness to the world and a little to its Light'". Without allowing him the self-accusation of ambition, we can surely allow him his modest epitaph—and a great deal more.

W. H. B. STODDART.

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CORRIGENDUM.

In our last issue of January, 1940, p. 90, in the paper by R. Freudenberg, M.D., and J. Fine, M.D., the figures are incorrectly placed over the legends.

The existing legend,	Fig. 1, p. 90,	concerns	Fig. 4, p. 92,	which is to be read as	Fig. 1.
„	„	Fig. 2, p. 90,	„	Fig. 1, p. 90,	„	„	Fig. 2.
„	„	Fig. 3, p. 91,	„	Fig. 2, p. 90,	„	„	Fig. 3.
„	„	Fig. 4, p. 92,	„	Fig. 3, p. 91,	„	„	Fig. 4.

Part I.—Original Articles.

STUDIES OF WATER METABOLISM IN ESSENTIAL EPILEPSY.

I. THE WATER BALANCE.

II. WATER CONTENT OF THE BLOOD.

By Guy D. Greville, M.A.Cantab., Ph.D.,

and

Tudor S. G. Jones, B.Sc., Ph.D.Wales, A.I.C.,

with the technical assistance of

W. F. G. Hughes.

From the Biochemical Department, Runwell Hospital, near Wickford, Essex.

(Received January 10, 1940.)

I. The Water Balance.

The comparatively old belief, that the epileptic patient shows a retention of water before the onset of a major seizure and an increase in the water excretion afterwards, achieved great importance from two findings of more recent date: on the one hand, the frequency of the seizures may be increased on hydration of the organism by administration of excessive amounts of water in combination with antidiuretics; on the other, the frequency may be decreased on dehydration either by restriction of the water intake or by other means (see for example Fay, 1929, 1930; McQuarrie, 1929; McQuarrie and Peeler, 1931; McQuarrie *et al.*, 1932; Engel *et al.*, 1934; Clegg and Thorpe, 1935; Stubbe Teglbjaerg, 1936; Ziskind *et al.*, 1939; Hagenmeyer and Langelüddeke, 1939; but contrast Cameron, 1931; Fetterman and Kumin,

1933; Wilson and Limberger, 1933; Stone and Chor, 1937; Pette and Janzen, 1938). It is therefore most desirable that the value of the evidence connecting water balance and the occurrence of spontaneous seizures should be assessed.

Attention has been concentrated mostly upon urine volume and body-weight changes. Rohde (1908) (see also Allers, 1910) found that in one patient, but not in others, there was an increased urine secretion at the time of the seizures. Changes in body weight usually accompany changes in the water content of the organism, and the earlier observations (from 1881 to 1922) on their relation to the incidence of fits are reviewed by Wuth (1928). Frisch (Frisch and Walter, 1922; Frisch and Weinberger, 1922; Frisch, 1937; but contrast Wildermuth, 1925) observed a gradual or rapid rise in body weight before the fit with a rapid fall afterwards, and regarded the latter as secondary to the former. He stated that the weight changes were so large (up to 2 kgm. in 24 hours) that they could only be ascribed to changes in the water content of the organism, and that his findings brought him into accordance with Rohde and Allers, who drew attention to a preparoxysmal oliguria which found its compensation in a postparoxysmal polyuria.

In 1927 Gamble and Hamilton (see also Gamble, 1930) studied an epileptic child who regularly had frequent and severe seizures during two days, followed by complete freedom for a week, after which the cycle was repeated. From measurements of fixed base excretion in the urine they concluded that the child showed an alternating retention and release of body fluid, the latter occurring during the periods of seizures. There was a "rough but definitely corresponding fluctuation in the daily volume of urine," which reached a maximum in the first day of each period. Gamble however admitted the possibility that his findings might be simply products of the convulsive state and therefore without pathogenic significance, although he regarded this as improbable.

Geller (1936), after observing 37 epileptics, claimed that before the fits there was regularly a retention of water, which was excreted afterwards. This was particularly clear with patients who had infrequent fits, less so with those with frequent seizures; but when the latter were given luminal, they too showed the alternation of the preparoxysmal retention and postparoxysmal diuresis. The water intake of the patients was unlimited, and the existence of retention was apparently judged from the urine volume and the changes in body weight.

In contrast to the above-mentioned workers, Stubbe Teglbjaerg (1936), in a careful study of ten epileptics, could find from body weight and urine volume measurements no connection between the water balance and the onset of spontaneous seizures. No more definite results were obtained by Pette and Janzen (1937) with a "large number of epileptics," whilst Albrecht (1938) calculated the "daily balance" from the fluid intake and output in six epileptics and found that it was unconnected with the incidence of fits.

It must be pointed out that the water intake, urine volume and change in body weight are together not sufficient for an estimation of the water balance; the loss of water through skin and lungs must be known as well. Apparently none of the above authors made any allowance for this when they assessed the state of hydration of their patients. Stubbe Teglbjaerg (1936) did indeed measure the "insensible perspiration," which includes the water loss through skin and lungs; he found that it had normal values in epileptics; but he does not seem to have used these values in the calculation of water balances.

Complete water balances have however been calculated by McQuarrie and his collaborators in their experiments with epileptic children; and so far as can be seen there is no connection between water retention and the incidence of spontaneous seizures during the control periods when no agents were being administered (cf. Engel *et al.*, 1934).

In view of the conflict of evidence, we have studied the water exchange as completely as possible in three typical cases of essential epilepsy, in order to determine the state of the water balance before, at the time of, and after the occurrence of *grand mal* seizures. At the same time, to control the technique, measurements have been made on a non-epileptic patient.

Experimental Section.

Patients investigated.

Case 1.—Male, aged 52. Labourer. Admitted to Runwell Hospital 2.ii.39. Certified patient.

History.—The father suffered from epilepsy. The patient himself suffered from epilepsy since later childhood, having fits at varying intervals. He left school at the age of 14 years from the top standard. The first signs of psychosis appeared nine years previous to admission.

Physical condition.—Examination showed no evidence of organic disease in any of the systems. Radiography of the skull revealed no abnormality. Kahn test of blood and C.S.F.: negative. Other tests of C.S.F.: normal.

Mental condition.—He suffered from epileptic psychosis. He was egocentric, irritable and extremely circumstantial. He displayed the typical epileptic temperament and showed a fair degree of intellectual deterioration, reasoning and judgment being much impaired. Perseveration was a marked feature, and he was totally lacking in insight into his condition.

Seizures.—Prominal medication was started soon after admission. He had four *grand mal* seizures during March and one in April. On April 30 prominal was discontinued: he had four *grand mal* seizures in May and eight in June.

Case 2.—Male, aged 46. Labourer. Admitted to Runwell Hospital 2.viii.37.

History.—He had previously been in another hospital since 1928, suffering from epileptic psychosis. His age at the onset of seizures is believed to have been between 25 and 30 years. He left school at the age of 14 from Standard ex-7.

Physical condition.—Examination on admission showed no evidence of organic disease in any of the systems. Radiography of the skull revealed no abnormality. Kahn test of blood: negative. Tests of C.S.F.: normal.

Mental condition.—He suffered from epileptic psychosis. Unstable and irritable, he displayed the typical epileptic temperament. He was confused and retarded in

thought, and expressed various somato-psychic delusions. He was frequently querulous and hypochondriacal, and after fits tended to become violent.

Seizures.—Under luminal therapy his seizures, which consisted both of *grand mal* and *petit mal* attacks, numbered on the average six to eight per month.

CASE 3.—Male, aged 48. Admitted to Runwell Hospital 18.xii.36.

History.—He had been in other institutions since 1927, suffering from imbecility with epilepsy.

Physical condition.—Examination showed no evidence of organic disease in any of the systems. Radiography of the skull revealed no abnormality. Kahn test of blood: negative. Tests of C.S.F.: normal.

Mental condition.—He suffered from imbecility with epilepsy. He was simple and childish and of poor intellectual make-up. He showed a fair degree of confusion and his memory was much impaired; at times he was irritable, quarrelsome and excited.

Seizures.—During his stay in this Hospital his fits were well controlled by prominal therapy, and their number varied greatly from month to month. He had 50 fits in 1937, but only four in 1938.

CASE 4 (control patient).—Male, aged 27.

Physical condition.—He showed no evidence of organic disease in any of the systems. Kahn test of blood negative.

Mental condition.—He suffered from hysteria.

Seizures.—He had no hysterical fits.

The Determination of the Water Balance.

The method used by us for the determination of water balance is based on the principles laid down by Isenschmid (1918), Newburgh *et al.* (1931), Wiley and Newburgh (1931), and Peters *et al.* (1933).

If we consider the ways in which the human organism exchanges water with its environment, we see that it receives the water contained in the foods eaten and the fluids drunk, and in addition that produced in the body by oxidation of the hydrogen of the foodstuffs, which is known as the "water of oxidation" or "metabolic water." It loses water in the urine and the faeces, and by means of the "insensible water loss," which is the water lost through skin and lungs. That the water of oxidation and insensible water loss are very important factors is shown by the figures given in Table I for a typical 24-hour water exchange in one of the patients. In particular, measurements of water exchange which do not take into account the insensible water loss may lead to incorrect conclusions.

The insensible water loss is calculated from the "insensible *weight* loss," which is the nett loss of body weight after allowance has been made for the loss in weight due to the urine and faeces and the gain in weight due to the ingesta. It is calculated over any given period from the relation:

$$\text{Insensible weight loss} = \text{weight of ingesta} - \text{weight of excreta} - \text{gain in body weight} \quad (1)$$

The insensible *water* loss is then calculated by using the fact that the insensible weight loss is composed of three quantities: (1) loss in weight due to the

insensible water loss, (2) gain in weight due to oxygen absorbed in respiration, and (3) loss in weight due to carbon dioxide eliminated.

Insensible water loss = insensible weight loss — $(CO_2 - O_2)$. (2)

The quantity $(CO_2 - O_2)$ and the metabolic water are both determined by the amounts of protein, fat and carbohydrate oxidized by the organism in the period in question and are calculated from the equations:

Weight of $(CO_2 - O_2)$ = 0·08 protein — 0·08 fat + 0·41 carbohydrate (as hexose) . . . . . (3)

Weight of metabolic water = 0·41 protein + 1·07 fat + 0·58 disaccharide + 0·556 polysaccharide . . . . . (4)

The method of estimating the quantities of protein, fat and carbohydrate oxidized from the known composition of the diet is given below (see p. 202). Insensible water loss and metabolic water having been estimated, the water balance, *which is the difference between the water gained by the body and that lost*,* is calculated from the equation (cf. Table I):

Water balance = water of ingesta + metabolic water — water of excreta — insensible water loss . . . . . (5)

The following data are therefore necessary for the calculation of the water balance by this method: change in weight of subject; weight and water contents of food, fluids, faeces and urine; weight of protein, fat and carbohydrate oxidized.

TABLE I.—*Water Balance.*

Water gained.		Water lost.	
Water of food . .	471	Water of urine . .	1,968
Water as fluid . .	2,302	Water of faeces . .	74
Metabolic water . .	273	Insensible water loss .	1,287
	3,046 gm.		3,329 gm.

Water balance = water gained — water lost = 3,046 — 3,329 = —283 gm.

Insensible water loss = insensible weight loss — $(CO_2 - O_2)$

1,287 1,428 — 141 gm.

Insensible weight loss = weight of ingesta — weight of excreta — gain in body weight.

1,428 = 3,332 — 2,116 — (—212) gm.

* We distinguish between the nett gain in water by the body (the water balance) and the nett gain in water by the body from its environment. The two differ by the amount of water formed in the organism, i.e. the metabolic water (equation 7).

An alternative formulation :

A simplified equation for the calculation of the water balance may be derived directly as follows :

Gain in body weight = gain in water from environment + solids of ingesta — solids of excreta + O_2 — CO_2 . . . . . (6)

also

Water balance = gain in water from environment + metabolic water . . . . . (7)

hence

Water balance = gain in body weight — solids of ingesta + solids of excreta + (metabolic water + CO_2 — O_2) . . . (8)

Equation (8) has been derived by Peters *et al.* (1933) from Newburgh's equations (equations 1, 2 and 5 above), the last term being calculated according to the following equation :

Metabolic water + CO_2 — O_2 = carbohydrate burned + 0·49 × protein burned + fat burned . . . . . (9)

In spite of the simplicity of these equations, we have preferred the original procedure, which has the advantage that the total amounts of water gained and lost, and also the water lost through skin and lungs, are found separately in the calculations. However, for the sake of convenience the principles of equations 8 and 9 have been used in Table II and equation 10.

Diet.

The patients were given an ordinary mixed diet of fixed amount and composition. Breakfast and tea were the same from day to day, but three different menus were devised for dinner and were given in rotation. The composition of the daily diets was as follows :

	Diet 1.	Diet 2.	Diet 3.
Protein (gm.)	104	104	103
Fat (gm.)	96	82	81
Carbohydrate as hexose (gm.) .	312	364	346
Calories	2,528	2,610	2,525

The protein intake was equalized in the three diets in order to minimize day-to-day variations in the excretion of urea and hence in the diuresis caused by this substance.

Water intake.—It was decided that the patients should have the same water intake each day. As the water contents of the three diets differed, amounts of fluid were given which were calculated to bring the total water

intake up to approximately the same amount on each diet. Unavoidable variations in the water contents of the cooked foods caused variations in the daily total water intake, but the actual value of the latter was always known with accuracy (see below).

Salt intake.—The foods were cooked without the addition of salt, and the NaCl intake was brought up to a fixed value by the addition to each day's diet of a weighed amount of table salt. The intake of NaCl, except for one period with patient 2, was 13·3 gm. per day.

Iron medication.—To avoid possible anaemia due to the repeated removal of small quantities of blood for analysis, the patients were given iron and ammonium citrate gr. 45 *t.d.s.*, or ferrous sulphate (Fersolate Glaxo) tabs. 2 *t.d.s.*

Food Analyses.

Water.—Representative food samples were weighed out in aluminium milk-bottle caps and their water content determined by drying to constant weight at 104° C. As it was necessary to calculate the total amount of water in the diet every day, the water contents of the cooked foods (meat, vegetables, pudding) of each meal were determined; but for the other constituents of the diet, which were less variable (bread, butter, milk, marmalade and cake), average figures were taken from a series of analyses of representative samples.

Protein.—The nitrogen was determined by the Kjeldahl method and multiplied by 6·25.

Fat was determined as described by McCance and Shipp (1933). Fat in butter was estimated by petroleum ether extraction of the dried substance. Milk fat values were taken from figures supplied by the Essex Milk Recording Society.

Carbohydrates.—Figures for the carbohydrate content of vegetables, orange juice and bread were taken from the tables of Nixon and Nixon (1938). No attempt was made to analyse the cooked puddings and cake for monosaccharide, disaccharide and polysaccharide, but the figures used were calculated from the quantities and carbohydrate contents of the raw materials, the puddings being steamed in closed vessels. Lactose in milk was determined by the method of Jones (1936). The carbohydrate in marmalade was determined as hexose after $HgSO_4 - BaCO_3$ precipitation (West, Scharles and Peterson, 1929) and inversion according to Jackson and Gillis (1920).

Chloride was estimated by Volhard titration (1) after wet ashing in the presence of $AgNO_3$ and HNO_3, and (2) after leaching with dilute HNO_3 (Plimmer, 1938). Chloride in butter was determined by an application of the method of Davies (1932).

Precautions for ensuring constancy of composition of the diet included: use of lean meat, bulk samples of morning milk from the Hospital farm, and the " crumb " only of specially baked and carefully wrapped bread and cake.

Analyses of Urine and Faeces.

The water contents of faeces and urine were determined by drying to constant weight at 104° known weights and volumes respectively. Nitrogen in urine was determined by the alcohol Kjeldahl method of Cole (1933); for this purpose the urine was collected in Winchesters containing 60 ml. of 2 N. H_2SO_4.

Experimental Procedure.

Routine.—The patients were kept under as constant a routine as possible. The mornings they spent in bed, and every afternoon unless it was raining they went for a short walk for the same time and at approximately the same speed. Measures were taken to avoid visible sweating.

Collection of excreta.—Each specimen of urine was passed into a separate stoppered bottle containing 1 ml. toluene, except when, for a short period, urinary nitrogen was being determined as previously described. The specimens for each 12 hours were mixed and their weight and volume measured. A sample was taken for determination of water content.

The faeces were passed into tared metal bed-pans, which were immediately covered. After weighing, a sample was taken for determination of water content.

Weighing of the patients was carried out twice daily, at 7 a.m. and 7 p.m., on a machine sensitive to ½ oz. (14 gm.). The patients were weighed unclothed, after emptying the bladder. At the morning weighing they were in the fasting condition.

Diet.—The patients were encouraged to eat their diet completely. If a small quantity were left, it was weighed, and allowance made for it in the calculation of water intake, ($CO_2 - O_2$) and metabolic water.

Bleeding.—For the determinations described in Part II, 5 or 8 ml. of blood were removed immediately before breakfast.

Calculation of the Water Balance.

The metabolic mixture.—The amounts of protein, fat and carbohydrate oxidized by the organism (the "metabolic mixture") differ somewhat from the amounts in the diet. These three constituents will be considered in turn.

The amount of *protein* oxidized is commonly obtained by multiplying the urinary nitrogen by 6·25 (Loewy). It was not possible to determine the nitrogen excretion of all four patients every day, but the measurement was made on Patients 2 and 3 for three to four weeks. In calculating the metabolic mixture for Patients 2 and 3 the mean values 89 and 96 respectively (Table II) for protein oxidized have been used. For the other two patients the figure 93 has arbitrarily been chosen.

TABLE II.

	Patient 2.	Patient 3.
Number of days	23	27
Protein oxidized per day (gm.):		
(1) Mean	88·9	95·7
(2) Standard deviation	±7·3	±6·0
(3) 3 × standard deviation	±21·8	±18·1
(4) Water equivalent to (3) (protein oxidized × 0·49)	11	9

The values of the standard deviation (Table II) signify that only once in 370 days would the amount of protein oxidized be expected to differ from the mean by more than ±21·8 gm. for Patient 2 and ±18·1 gm. for Patient 3. The values of the term in the expression (metabolic water + CO_2 − O_2) corresponding to these amounts of protein oxidized (equation 9) are 11 and 9 gm. respectively. Hence when the mean, rather than the individual, values of protein oxidized are used in the calculation of the water balance, errors of 11 and 9 gm. respectively will be exceeded only once in 370 days. These errors are for all practical purposes negligible.

The amount of *fat* oxidized may be calculated from the amount of fat in the diet and the amount deposited in the body. The patients were on a supermaintenance diet and gained in weight. As adipose tissue contains 10 per cent. of water, 90 per cent. of the gain in weight is assumed to be due to fat deposition (Newburgh *et al.*, 1931). Accordingly the gain in body weight over the whole period is reduced to a daily average, and 90 per cent. of this is subtracted from the dietary fat to obtain the fat of the metabolic mixture. Owing to the variations in the state of hydration of the organism, it is clearly inaccurate to calculate the gain in weight over a period merely by subtracting the initial from the final weight. A graph was constructed for each patient (see curves at bottom of Figs. 1–4) showing the fasting weight for each day over the period of the experiment, and a straight line fitted to the points. The slope of this line is the best representation of the daily gain in weight, 90 per cent. of which is accordingly subtracted from the dietary fat. Newburgh and his associates do not mention having taken this precaution.

Estimated as above, the rate of gain of weight of Patient 2 was 38 gm. per day, corresponding to 34 gm. of fat deposited, the figures for Patient 3 being 48 and 43 and for Patient 4, 26 and 23 gm. respectively. After six weeks, during which time his weight increased by 51 gm. per day (46 gm. fat deposited), Patient 1 was given 8 gm. of protein, 22 gm. of fat and 47 gm. of carbohydrate less than the standard diet. After a period of adjustment his weight became almost constant, falling by 7 gm. per day (6 gm. of fat lost per day) (Fig. 1).

FIGS. 1–4.—Urine volumes are given in litres ; body weight, water balance and insensible water loss in kgm. Each water balance value is for a period of 48 hours. Vertical broken lines denote *grand mal* seizures. The white rectangles in the urine volume histogram indicate reductions in the water intake (by 280 ml. and 570 ml.). Each 24-hour period is from 7 a.m. to 7 a.m., except for Patients 2 and 3 after July 29.

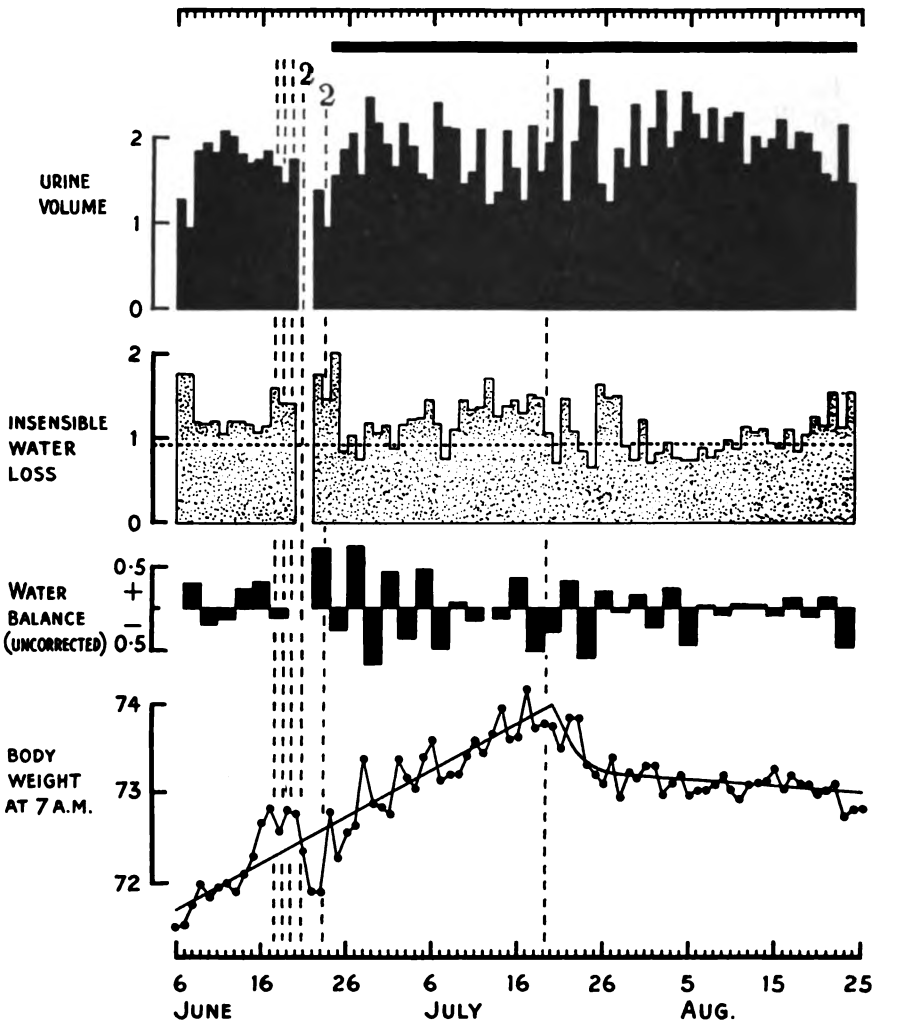

FIG. 1.—Patient 1. Horizontal bar indicates luminal 1 gr. per diem. Horizontal broken line shows value of the insensible water loss at which 25 per cent. of the average total heat production is lost by vaporization of water.

In addition to the correction for fat deposited, a small deduction (4 gm. per day) was made for the fat lost in the faeces.

As regards *carbohydrate*, it has been shown that, after time has been allowed for equilibrium to be attained on a diet which approaches the requirements of the individual, the amount of carbohydrate burned is equal to that supplied by the diet (Newburgh *et al.*, 1937, *a*).

Thus for each patient, by the methods outlined above, we were able to estimate the average amounts of protein, fat and carbohydrate oxidized on each of the three daily diets. These data were then sufficient for the calculation of the metabolic water and the term $(CO_2 - O_2)$ by equations 3 and 4. The water balance for each 24-hour period could now be calculated in the manner already described.

The diagrams.—Figs. 1–4 show data for the patients with the corresponding numbers. At the bottom of each figure is a curve showing the body weight at 7 a.m. each day. The straight line through the curve, which has been fitted by the method of successive averages, indicates for each day the value of the body weight which would be expected if the rate of change were constant. The straight lines in the right-hand parts of Figs. 2 and 3 are continuations of those on the left-hand parts, but have together with the curves been displaced for economy of space. The difference between the actual values of the body weight and the corresponding values given by the straight line represent daily variations from the average in the exchange between the organism and its environment, resulting from variations in the amount of body water, energy metabolism, and the intake and output of solids. Curves showing these daily differences between the actual and predicted values of the body weight are given in Fig. 6 (Part II).

Above the weight curves in Figs. 1–4 water balances are shown; these are considered later. Above these come in turn the 24-hour values of the insensible water loss and those of the urine volume, both in histogram (step diagram) form. The former are obtained by subtracting from the insensible weight loss the average daily values of the term $(CO_2 - O_2)$ estimated in the way described in the previous section. Water balance, insensible water loss and urine volume values are calculated for the 24-hour period, 7 a.m. to 7 a.m.; for a short time, however, from July 29 to the end, the values for Patients 2 and 3 are for the period 7 p.m.–7 p.m. It may be noted that the scales for all the above-mentioned quantities are the same, so that ready comparison can be made of the magnitude of interesting changes.

Corrections for the daily variations in energy metabolism.—In the method for estimating the metabolic water and the term $(CO_2 - O_2)$ described above, the values used for the amount of protein, fat and carbohydrate burned each day are average ones. This means that in the estimation of the water balance it has been assumed that the total energy metabolism does not vary each day from the value which has been deduced from the composition of the diet, the

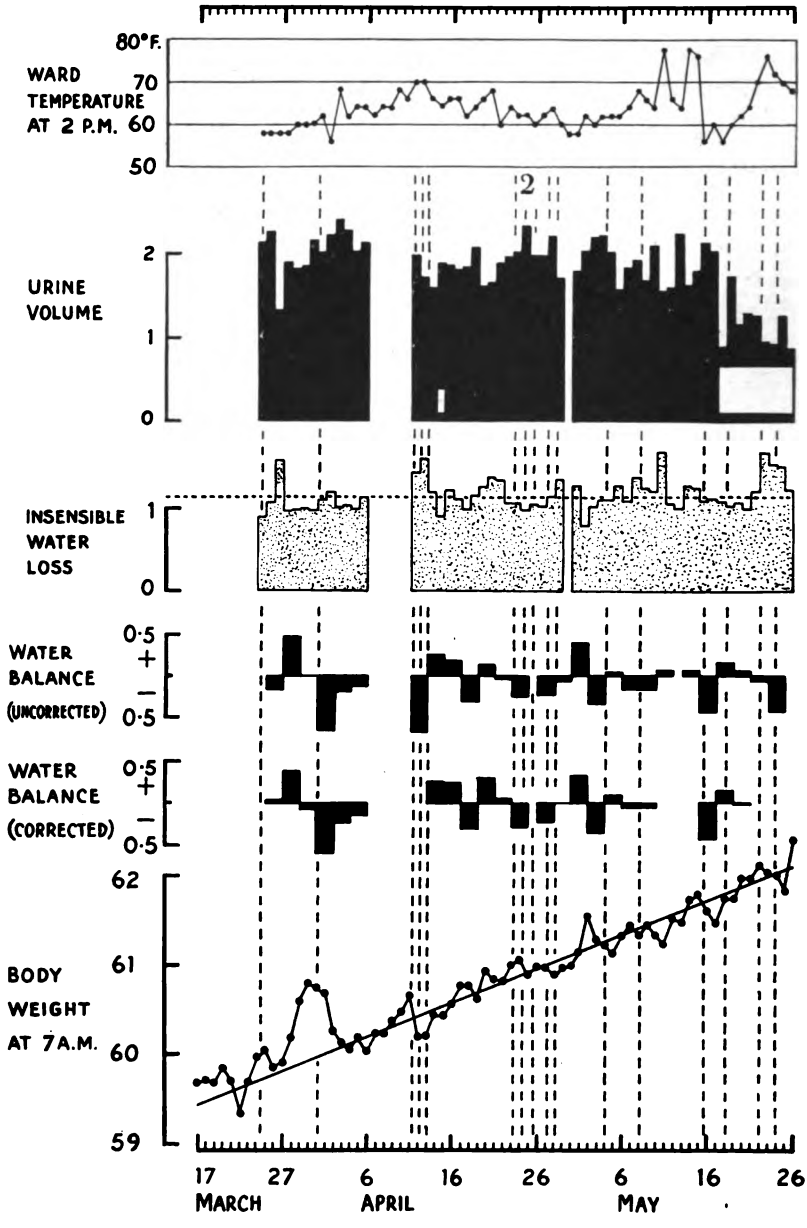

FIG. 2.—Patient 2. Horizontal bar indicates luminal 1 gr. per diem. Horizontal broken line shows value of insensible water loss at which 29 per cent. of the average total heat production is lost by vaporization of water.

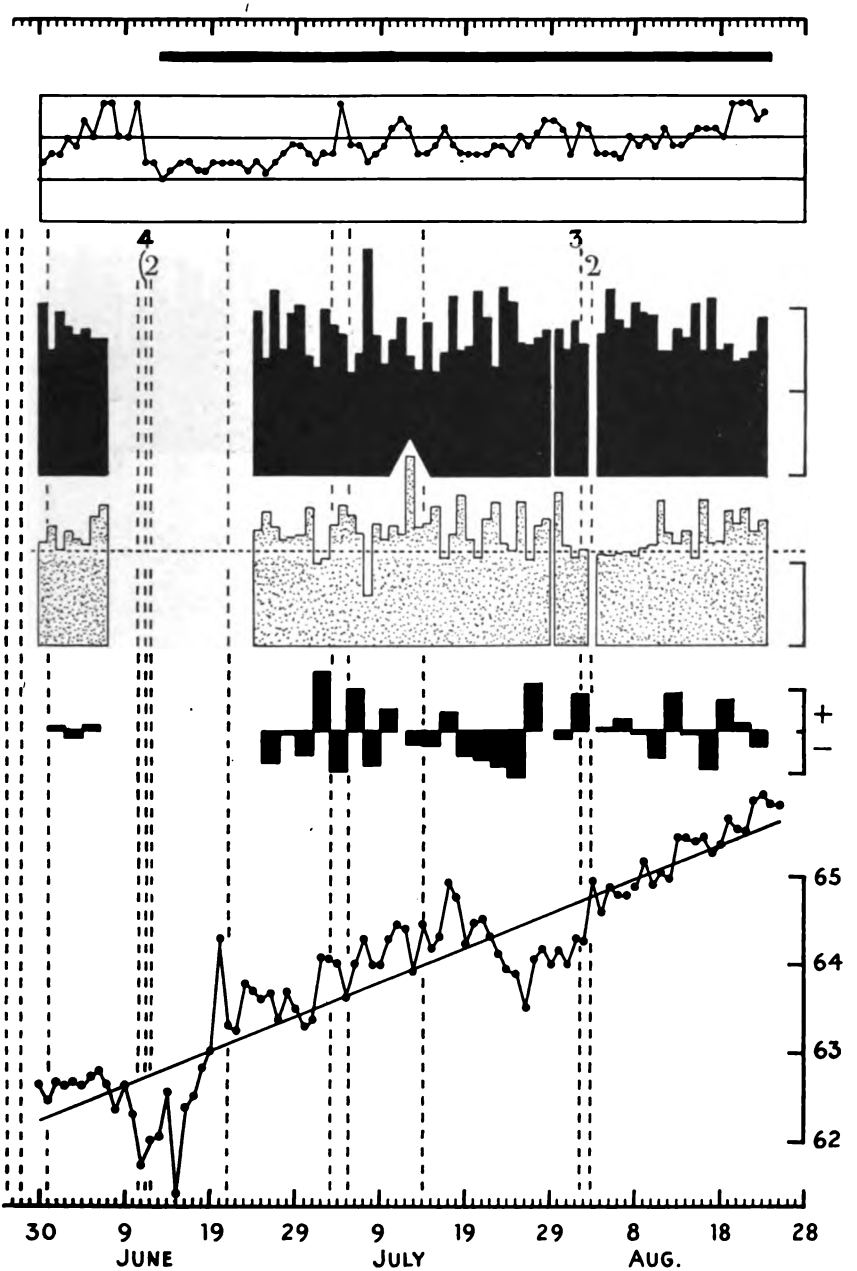

FIG. 2—*continued.*

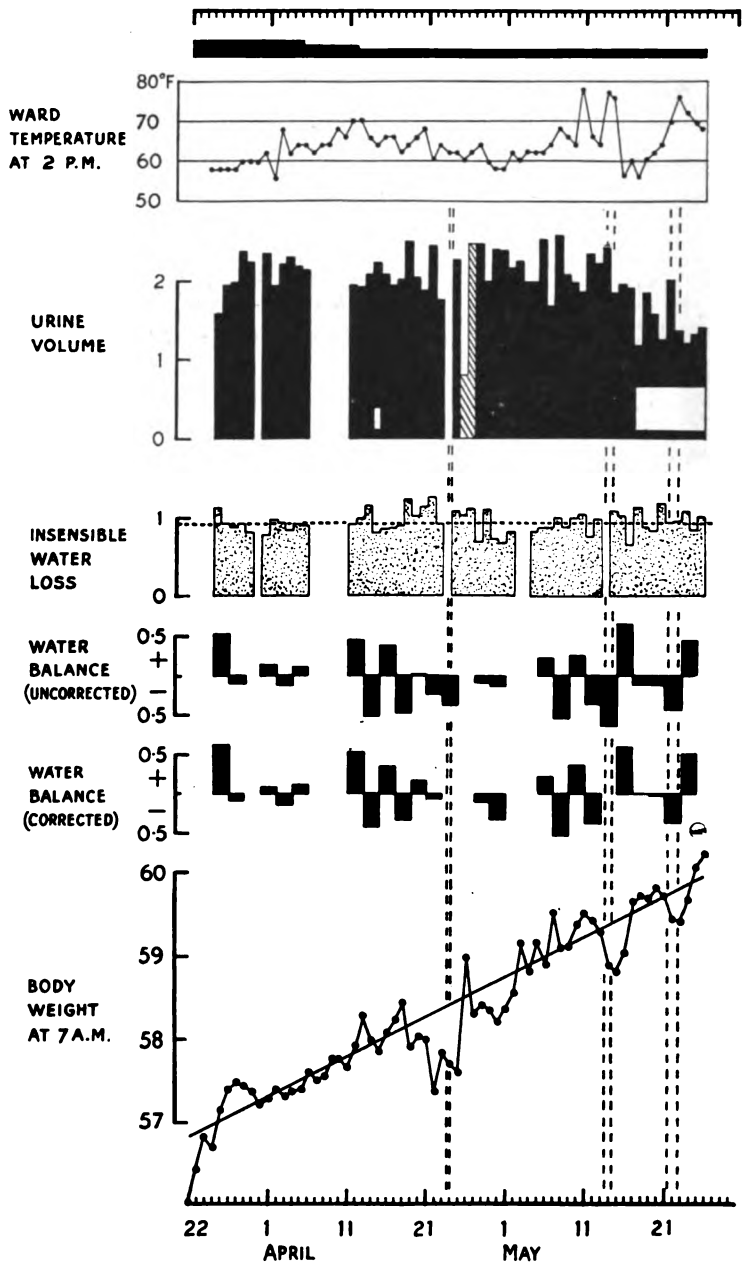

FIG. 3.—Patient 3. Horizontal bars indicate proninal 9 gr. reduced to 7·5 gr. and finally to 6 gr. per diem. Horizontal broken line shows value of insensible water loss at which 25 per cent. of the average total heat production is lost by vaporization of water.

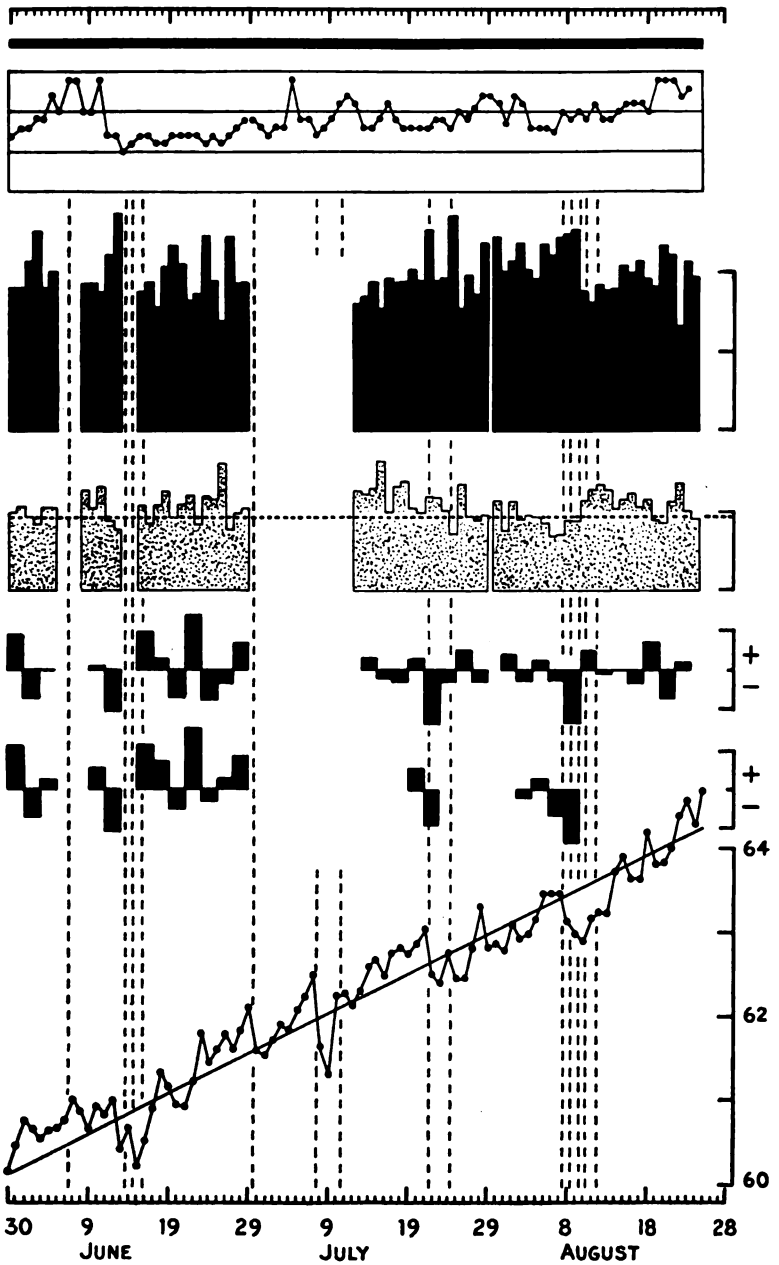

FIG. 3—*continued.*

probable average fat deposition and the average nitrogen excretion. There is reason to believe, however, that normally despite constant conditions there are considerable daily variations in the total metabolism; and the

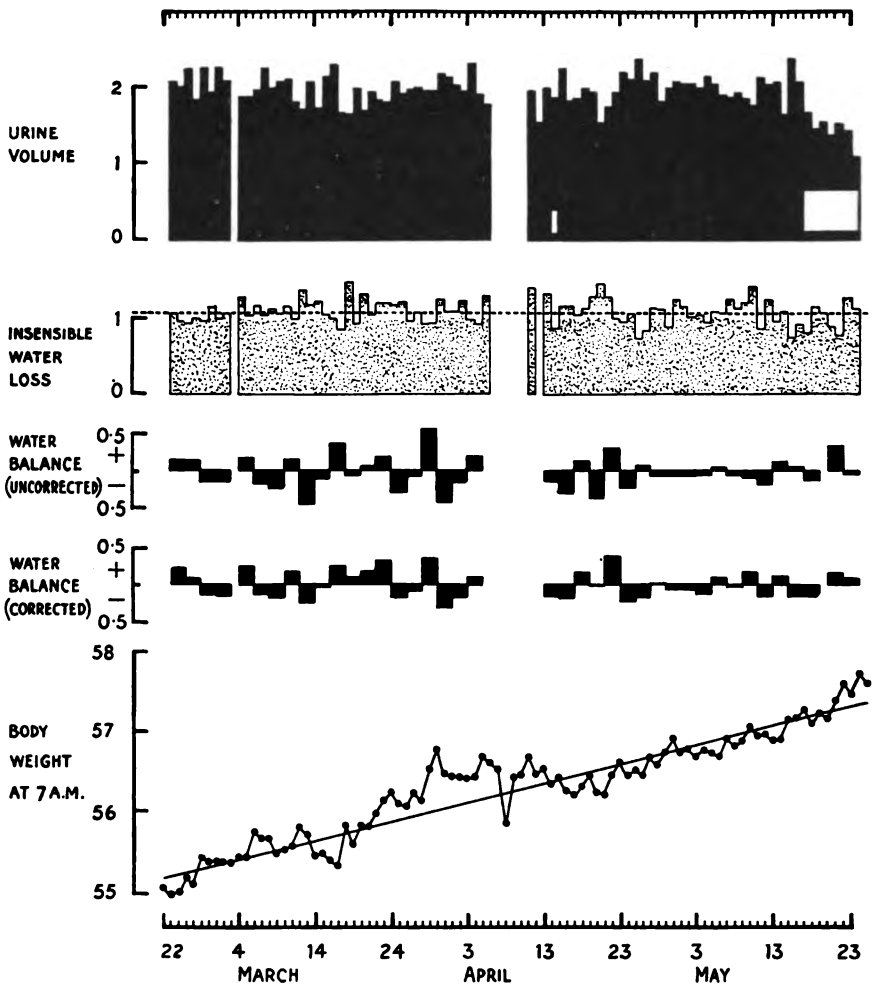

FIG. 4.—Patient 4 (non-epileptic). Horizontal broken line shows value of insensible water loss at which 26 per cent. of the total heat production is lost by vaporization of water.

importance of this is seen from the following consideration: From equations 8 and 9 we may derive the relationship:

$$\text{Water balance} = \text{gain in body weight} - (\text{solids of ingesta} - \text{solids of excreta}) + (C + 0{\cdot}49\,P + F) + (C' + 0{\cdot}49\,P' + F') \quad (10)$$

where C, P and F are the average values of carbohydrate, protein and fat

oxidized, calculated as described above, and C′, P′ and F′ are the differences between C, P and F and the amounts actually oxidized in the period under consideration. The longer the period, the smaller will C′, P′ and F′ become. Now since the second and third terms on the right-hand side roughly cancel each other under constant conditions, large changes in the body weight (say ½ kgm. or more in 24 hours) must be due largely to changes in the water balance, but may also be due in part to the assumption of values of importance by the last term of the equation. Thus for example a large fall in body weight may be due to an increase of metabolism as well as to a release of body water. It is therefore important that in the estimation of water balance an allowance be made whenever possible for daily changes in the total metabolism. The only way in which energy metabolism can be accurately measured over periods longer than a few minutes lies in the use of direct or indirect calorimetry in the respiration chamber (see DuBois, 1936; Newburgh *et al.*, 1937, *b*); but it is very doubtful whether this apparatus, even if available, could be used with epileptic patients in an extended research like the present one. Newburgh and his associates have, however, devised an indirect method whereby the total metabolism can, under the right conditions, be estimated over very long periods of time.

In the calculation of the metabolic mixture given above the chief simplifying assumptions are that for each period (1) the carbohydrate oxidized is equal to the carbohydrate ingested, and (2) the fat oxidized is equal to the fat absorbed less the average amount of fat deposited. The second of these assumptions was not used by Newburgh in the calculation of water balance, although it was used by him in a somewhat different connection. His calculations involved a principle which, following an observation of Benedict and Root (1926), was established by Newburgh *et al.* (1931; 1937, *a*). This was that in subjects who avoid sensible perspiration the heat dissipated by the vaporization of water from skin and lungs is a constant proportion (25 per cent.) of the total heat production. The latter could therefore be calculated from the insensible water loss: the evaporation of 1 gm. of water requires 0·58 Calories. The heat produced by oxidation of protein was calculated from the urinary nitrogen, and that produced by oxidation of carbohydrate from the known composition of the diet, according to assumption (1) above. Subtraction of these two quantities from the total heat production gave the heat produced by oxidation of fat and hence the fat oxidized. The calculation is most conveniently performed in one stage from the insensible *weight* loss (I.L.) by the equation of Lavietes (1935):

$$\text{Fat oxidized (F)} = \frac{\text{I.L.} - 2{\cdot}18\ \text{C} - 1{\cdot}96\ \text{P}}{3{\cdot}93} \qquad . \quad . \quad . \quad . \quad (11)$$

where C is the carbohydrate of the diet and P is the protein oxidized (urinary nitrogen × 6·25). Its derivation is as follows:

By Newburgh's principle,

$$0{\cdot}58 \times \text{insensible water loss (gm.)} = 0{\cdot}25 \times \text{total heat production (Cals.)},$$

or

$$\text{insensible water loss} = \text{total heat production} / 2{\cdot}32.$$

We have:

$$\text{Total heat production} = 4{\cdot}1\ C + 4{\cdot}25\ P + 9{\cdot}3\ F,$$

$$\text{I.L.} = \text{insensible water loss} + (CO_2 - O_2). \quad . \quad \text{from equation 2,}$$

$$\text{and } (CO_2 - O_2) = 0{\cdot}41\ C + 0{\cdot}13\ P - 0{\cdot}08\ F \quad . \quad . \quad \text{from equation 3.}$$

$$\text{Hence I.L.} = \frac{4{\cdot}1\ C + 4{\cdot}25\ P + 9{\cdot}3\ F}{2{\cdot}32} + (0{\cdot}41\ C + 0{\cdot}13\ P - 0{\cdot}08\ F),$$

$$\text{whence I.L.} = 2{\cdot}18\ C + 1{\cdot}96\ P + 3{\cdot}93\ F \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

It is necessary to consider the applicability of this method of correction to the data in the present research. The 25 per cent. proportionality has been demonstrated by Newburgh and his associates both for short periods under the restricted conditions of the respiration chamber and for longer periods under the conditions of normal life. The constancy of this ratio in disease or disturbed physiological states, however, has been doubted by Lavietes (1935); and it would certainly be unwise to assume without experimental proof that it holds for epileptics. Also since any extra loss of water, e.g. by visible perspiration, invalidates the principle, the external environment of the subject assumes great importance. The long-term measurements of Newburgh *et al.* (1931) were made in the winter time, but our own observations extend into the hottest months of the year. The ratios between the heat of vaporization and the average total heat production (the latter calculated from the diet and the weight changes) in our experiments are given in the last column of Table III. With the non-epileptic patient (4) and with Patient 3 in the cooler months the ratio does not differ greatly from Newburgh's figure, especially as there is the possibility of some error in the estimation of the total heat production. The increase in the ratio in June and July is very marked, but even in the colder months Patient 2 shows a high value. Patient 1 was observed in the hot months only.

Without necessarily being convinced that Newburgh's principle applies to epileptics, we have used it to apply a correction for varying metabolism, but only when there was no reason to suspect excessive loss of water by vaporization. Reference to Figs. 1–4 will show why certain days must be excluded. Across each histogram for insensible water loss a horizontal broken line has been drawn. This represents the value of the insensible water loss at which a certain proportion (25 per cent. for Patient 1, 29 per cent. for Patient 2, 25 per cent. for Patient 3 and 26 per cent. for Patient 4) of the average total heat production is lost by the vaporization of water. The figures for the last three

TABLE III.—*Average Daily Values.*

Patient No.	Month and number of days.	Insensible water loss. (g.)	Heat dissipated by vaporization (1). (Cals.)	Total heat production (2). (Cals.)	Ratio $\frac{(1)}{(2)} \times 100$.
1	June (23)	1,271	738	2,113	34·9
	July (31)	1,191	692	,,	32·8
	August (23)	1,000	580	2,168	26·8
2	Feb.–Mar. (14)	1,120	650	2,224	29·2
	April (24)	1,137	658	,,	29·6
	May (27)	1,183	687	,,	30·9
	June (13)	1,375	798	,,	35·8
	July (28)	1,370	795	,,	35·8
	August (24)	1,278	740	,,	33·2
3	March (8)	917	532	2,140	24·8
	April (24)	953	553	,,	25·8
	May (24)	945	548	,,	25·6
	June (23)	1,048	607	,,	28·4
	July (17)	1,131	656	,,	30·6
	August (26)	1,023	594	,,	27·8
4*	Feb. (13)	1,021	592	2,340	25·3
	March (30)	1,095	635	,,	27·2
	April (24)	1,087	630	,,	26·9
	May (23)	1,037	601	,,	25·7

* Non-epileptic patient.

patients are based on the observations during the cooler months. The temperature of the ward at 2 p.m. each day is shown at the top of the diagrams. With Patient 2, high values of the insensible water loss often coincide with a rise in temperature to 70° F. or above, and it is supposed that there is an excessive vaporization of water on these occasions. Accordingly, corrected values of the water balance are given for this patient only when the temperature is below 70° F. (lowest histogram). Patient 3 was less sensitive to rises in the temperature of his surroundings, and fewer days have had to be omitted. No corrected values have been given for any patient after the end of June, except for two short periods in July and August when they are given for Patient 3, as his insensible water loss was apparently normal and the temperature was moderate.

Our method of correcting for variations in total metabolism differs slightly from that of Newburgh, who assumed that the amount of carbohydrate oxidized was constant and calculated for each period the amount of fat oxidized.

In the present research it was necessary to estimate the water balance over rather short periods ; and under these conditions there is no reason to suppose that the oxidation of carbohydrate is any more constant in amount than that of fat. Now from equation 12 it is just as possible to calculate C after assuming a value for F as it is, following Newburgh, to calculate F after assuming a value for C. It is seen from the equation that an increase of 100 gm. in the insensible weight loss might be due to an increase of 25 gm. in the oxidation of fat if P and C are constant, or of 46 gm. in the oxidation of carbohydrate if P and F are constant. Hence if the increased oxidation were assumed to be that of fat, the corrected water balance would increase by 25 gm., whereas if it were ascribed to carbohydrate the change would be 46 gm. (equation 10). It is likely that the proper figure would lie between these two ; so that in calculating the corrected water balance we have made the larger possible allowance for variations in the total metabolism by assuming the fat oxidation to be that previously deduced from the diet and the average gain in weight, and then calculating for each period the carbohydrate oxidation. Instead of using Newburgh's ratio 25 per cent. as was done in deriving equation 12, we have taken the figures 29 per cent., 25 per cent., 26 per cent., based as before on the observations in the colder months, for Patients 2, 3 and 4 respectively. The equations for calculating the amount of carbohydrate oxidized then became :

$$\text{Patient 2, } C = \frac{\text{I.L.} - 2{\cdot}26\,P - 4{\cdot}57\,F}{2{\cdot}46}$$

$$\text{Patient 3, } C = \frac{\text{I.L.} - 1{\cdot}96\,P - 3{\cdot}93\,F}{2{\cdot}18}$$

$$\text{Patient 4, } C = \frac{\text{I.L.} - 2{\cdot}04\,P - 4{\cdot}08\,F}{2{\cdot}25}.$$

We would emphasize that as it has not been proved that Newburgh's principle holds for epileptics, we have in addition calculated uncorrected values of the water balance throughout the whole experimental period. Histograms for these are given in the diagrams. However, corrected values have been given whenever possible ; and it should be remembered that, if Newburgh's principle does hold, the correction is probably too drastic, and the true figure probably lies between the corrected and uncorrected values.

Length of the experimental period.—The shorter the period over which the water exchange is measured, the greater is the error in the calculation of the metabolic mixture. Thus as regards the uncorrected water balance it is of importance that the subject will not necessarily be in carbohydrate balance when the period is less than one week (Newburgh *et al.*, 1937, *a*). Similarly for the corrected water balance it is of importance that according to the same authors " the percentage of heat removed by vaporization of water during a

single 24 hours was not sufficiently fixed to afford a reliable determination of the total heat." However, the changes in the weight curves are so rapid that a period of two days is considered to be the longest which would be of use in the present work, and the histograms give water balances calculated over 48 hours. It is realized that the shortness of the period must lead to some error, but this would seem to be unavoidable. The object of the experiments being to study the water metabolism in the few days preceding and succeeding fits, the periods were so chosen that one immediately preceded a seizure and the next started on the day on which the fit occurred.

One difficulty arose through working with epileptic patients. Sometimes during a *grand mal* seizure they were incontinent of urine, so that the data for the 24 hours had to be discarded. The discontinuities in the diagrams are largely attributable to these mishaps. Nevertheless on some of these occasions we have still been able to calculate the uncorrected water balance, for the contribution of the solids of the urine to the right-hand side of equation 8 is not great, and the error introduced into the water balance by the loss of 100 ml. is only about 2 gm.

Results.

Note 1.—In all the diagrams, *grand mal* seizures are represented by vertical broken lines. When several fits occurred within 24 hours they are indicated by a single line with a numeral at its head. *Petit mal* seizures are not shown.

Note 2.—Anticonvulsant drugs were given to the patients during the periods indicated by horizontal bars at the top of the diagrams. The dosage was as follows: Patients 1 and 2, luminal 1 gr. per diem; Patient 3, prominal 9 gr., reduced as shown to 7½ gr. and finally to 6 gr. per diem.

Note 3.—After June 7, Patient 2 became very unco-operative and refused some of his food. The data were therefore discarded until June 24 when he was judged to be in metabolic equilibrium again. For reasons of convenience, during the period June 29 to July 12 the excreta of Patient 3 were not measured, although his dietary and other conditions were maintained as before.

Note 4.—Part of the large rise in the weight of Patient 3 on April 25 was due to retention of urine in the bladder and it was necessary to catheterize the patient on the next day. The urine volume was not of great significance on these days and this is indicated by hatching in the histogram.

Note 5.—During period April 2 to May 26 the chloride intake of Patient 2 was reduced as an experiment to 5·5 gm. NaCl per day instead of the usual 13·3 gm.

Weight balance and water balance.—It will be seen from Figs. 1–3 that several of the *grand mal* seizures were preceded by a rise in the weight curve and followed by a fall. The most salient examples are the fits of June 17 (Patient 1), March 31 and April 11 (Patient 2), and June 29 and July 7 (Patient 3). The magnitude of the weight changes did not, however, approach the 2 kgm. in 24 hours mentioned by Frisch (1937), the largest observed being 0·9 kgm. (July 17, Patient 3). Also it is a matter of opinion whether the present curves show any examples of the " plötzlich einsetzende, sprunghafte Gewichtszunahme " which, according to Frisch, often precedes a fit. It is

worthy of note that the curve for Patient 4, the non-epileptic, shows oscillations about the straight line which are comparable in shape and magnitude with those seen in the curves of the epileptic patients.

In Tables IV and V changes in the body weight and water balance are related to the incidence of seizures. In these tables only the first fit of a series has been taken into account, a fit being regarded as one of a series if it was not separated by an interval of three days or more from the next fit; thus a seizure is not recorded unless there was a period of at least three fit-free days preceding it.

In section (i) of Table V are shown the number of seizures which were preceded by a rise in the weight curve, the number preceded by a fall in the curve, and so on. In making this assessment we have not restricted ourselves to any particular number of days before and after the fits, but have judged solely from the course of the curve. In the doubtful cases the thesis of Frisch, Geller, etc., has been favoured, that is, a rise in the curve before a fit or a fall after a fit has been recorded wherever possible. Nevertheless only 10 seizures out of 22 can be said to have been preceded by a rise in the curve and

TABLE IV.

Date of seizure.	Before seizure (2 days). Weight balance.	Water balance uncorrected.	Water balance corrected.†	After seizure (2 days).* Weight balance.	Water balance uncorrected.	Water balance corrected.†
PATIENT 1:						
June 17	+423	+308	..	−116	−97	..
July 19	−470	−502	..	..	..	..
PATIENT 2:						
March 24	+534	..	..	−189	−140	−214
,, 31	(+93)	(+1)	(−90)	−562	−630	−585
April 11	+208	..	..	−544	−647	..
,, 23	+66	−24	+54	−189	−164	−235
May 4	−416	−337	−348	+37	+29	+101
,, 8	−90	−155	−48	−76	−153	−37
,, 15	+236	+61	..	−416	−419	−422
,, 22	+80	+7	..	−175	−252	..
,, 31	..	..	..	+94	..	..
July 3	+606	+707	..	−415	−470	..
,, 14	−47	−161	..	−189	−181	..
August 1	+66	−102	..	+549	+431	..
PATIENT 3:						
April 23	−252	−235	−60	−323	−374	..
May 13	−323	−360	−370	−592	−645	..
,, 21	−67	−115	−29	−408	−434	−367
June 6	+31	+22	..	+17	..	..
,, 13	−494	−510	−529	−323	..	..
,, 29	+400	+344	+428	−650	..	..
July 7	+343	..	..	−1,286	..	..
,, 21	+187	+154	+267	−719	−678	−440
August 7	−96	−127	−322	−578	−662	−674

* This period includes the day of the seizure.
† i.e. corrected for variations in total metabolism (see text).

TABLE V.—*The Frequency of Seizures Accompanied by the Changes Indicated Below.*

(i) Changes in the body weight curve.

Patient No.	Before the seizure (2 days).			After the seizure (2 days).*		
	Rise.	Fall.	Indefinite.	Rise.	Fall.	Indefinite.
1	1	1	0	0	0	2
2	5	0	6	1	4	6
3	4	2	3	0	6	3
Total	10	3	9	1	10	11

(ii) Changes in body weight (weight balance).

	+.	−.	o.	+.	−.	o.
1	1	1	0	0	0	1
2	4	1	6	1	4	7
3	2	3	4	0	8	1
Total	7	5	10	1	12	9

(iii) Changes in body water (water balance), uncorrected.

	+.	−.	o.	+.	−.	o.
1	1	1	0	0	0	1
2	1	1	7	1	5	5
3	1	3	4	0	5	0
Total	3	5	11	1	10	6

(iv) Changes in body water (water balance), corrected.

	+.	−.	o.	+.	−.	o.
2	0	1	3	0	4	2
3	2	3	2	0	3	0
Total	2	4	5	0	7	2

* This period includes the day of the seizure.

again only 10 out of 22 to have been followed by a fall. Both Frisch (1937) and Geller (1936) insist that the fits must not be too frequent if the characteristic changes are to be observed. It is therefore of interest that with Patient 2 in the periods when the fits or series of fits were separated by considerable intervals (March 17–April 17 and July 1 to the end), five were preceded by a rise in the curve and only one was not. On the other hand, the

fits or series of fits of Patient 3 were well separated throughout, but only four out of nine were preceded by a rise in the curve. It is thus impossible to say that even under the most favourable circumstances a seizure is always preceded by a gain in body weight, or that conversely a marked rise in the weight curve is always followed by a seizure. Nevertheless a rise in the curve precedes a seizure often enough to prevent this phenomenon being dismissed as unimportant. This applies also to the fall in weight which may occur after the fit. We therefore proceed to consider whether the changes in the weight curve indicate corresponding changes in the amount of body water, and whether there is a relationship between water balance and the incidence of fits.

It is very difficult to devise a rigid yet completely satisfactory method for settling the latter question. Owing to possible systematic errors, discontinuities due to incontinences, etc., it is not possible to use the water balances to estimate the water content of the organism at any given time, even relative to an arbitrary zero. We can only give the change in water content, i.e. the water balance, over a given period; and this introduces a difficulty. It has been judged necessary to consider the water balance during the same time period before (or after) each fit, but the important change does not always occur at the same time in relation to the fit. Thus with Patient 2 the (corrected) water balance for the two days immediately before the fit of March 31 (see Fig. 2) was −90, whereas for the fourth and third days before the fit it was +389. More often however the increase in the body weight and the establishing of a positive water balance previous to the seizure occurs on the two days before the fit. We have therefore arbitrarily fixed our attention on the two days immediately before and after the fits, the latter period always including the day on which the fit occurred. The values on these days of the weight balance and the water balance, the latter with and without correction for variations in the total metabolism, are collected in Table IV. The weight balance is here the change in body weight in the two days, corrected for the steady change in weight as determined by the slope of the straight line fitted to the weight curve.

It will be seen from Table IV that under our experimental conditions there is good agreement within certain limits between weight balance, uncorrected water balance and corrected water balance. The degree of agreement is shown more exactly below. We have arbitrarily divided the values of the balance into three groups: values greater than +200 gm. in the two days are shown as "+", those more negative than −200 as "−", and those numerically smaller than 200 as "0." When on any occasion the values for corrected water balance and weight balance fall into the same group, agreement is recorded, when into different groups, disagreement. The same applies to the other two pairs. With this convention we show below the number of occasions on which there is agreement or disagreement between the different balances given in Table IV.

	Weight balance and water balance (uncorrected).		Weight balance and water balance (corrected).		Water balance (corrected) and water balance (uncorrected).	
	Agreement.	Disagreement.	Agreement.	Disagreement.	Agreement.	Disagreement.
Before fit	18	1	8	3	8	3
After fit	16	1	7	2	7	2
Total	34	2	15	5	15	5

It should be remarked that in eleven out of the twelve cases of disagreement the balances differ by less than 200 ; they can probably be regarded as borderline cases resulting from the arbitrary method of analysing the data.

The data of Table IV have been analysed in another way in sections (ii), (iii) and (iv) of Table V. Here the figures indicate the numbers of fits which were preceded or followed by values of the weight balance and the water balance which were (as before) greater than +200 (+), more negative than −200 (−), or numerically less than 200 (0) grams for the 48 hours. To the fits shown as having been preceded by a positive water balance should be added, for the reasons already given, the fit on March 31 (Patient 2, see Fig. 2). Further, certain inferences may be made from the data in the diagrams which cannot be put in the tables. Thus on June 20 and 21 (Patient 1) and May 13 and 14 (Patient 3) there was a fall in weight following a fit, but owing to incontinence the water balance is missing. However, it may be inferred that there was a large negative water balance on these days, as on the following two days there was in each case a large positive water balance which was probably compensatory.

It remains to summarize the observations shown in the diagrams and analysed in the tables. We have been able to estimate the water balance on certain of the occasions on which there was a large rise in weight during the two days before a fit or a large fall during the subsequent two days. On all these occasions save one there is agreement between water balance and weight balance, so that the changes in the weight may be considered with a high degree of probability to be due for the most part to changes in body water. The exception was the fit on May 15 (Patient 2), but here the weight increase was small. Now the agreement between the weight balance and the water balance is as good over the rest of the periods as it is for those just before and after the fits ; for example, with Patient 3 the weight balance and the corrected water balance differ by more than 200 gm. in only two 48-hour periods out of 34. This makes it likely that the large weight changes before and after fits for which we have no water balance figures were also largely due to corresponding release or retention of body water. Finally, on no occasion was a large positive water balance observed before a fit when there was no large increase in weight. Similarly no large negative water balance was found

after a fit when there was no large fall in weight. In analogy with the deductions from the weight curve, it is impossible to say that a seizure is always preceded by a retention or followed by a release of body water. Nevertheless, a negative water balance follows more than half the seizures shown in Table IV.

Urine volume and insensible water loss.—Changes in the water content of the body may result from variations in the secretion of water through the kidney or in the loss of water through the skin and lungs. It would be interesting to determine which is responsible for the changes which may accompany fits. It was mentioned in the introduction that several workers have found oliguria before the fit and polyuria afterwards. In the present work the changes in body water are relatively small, there is considerable variability in the urine volume and insensible weight loss despite the constant conditions, and incontinence reduces the amount of available data. The few seizures which are of interest are considered separately as follows :

Patient 1.—June 17 : No very marked changes in urine volume or insensible water loss (I.W.) accompanied the weight increase before the fit. During the series of fits I.W. was increased.

Patient 2.—March 31 : Both urine volume and I.W. were greater during the fall in weight after the fit than they were during the preceding rise in weight.

April 11 : I.W. was high during the series of fits, but on these two days the weather was very warm (see temperature curve).

April 23 : During this series of fits when there was a negative water balance, I.W. was below the average and the urine volume was rather high.

May 15 : After the fit when there was a fall in weight, I.W. was not raised but the urine volume was high.

May 18 : I.W. was not raised after the fit, but although the weight was steady the urine volume was high.

July 3 : Before the seizure, when there was a positive water balance, I.W. was below the rather high average for that month. The urine volume was probably average.

July 14 : The urine volume was high on the day of the fit.

Patient 3.—May 13. There was incontinence on this day, but the urine volume was probably high.

May 21 : The day before the fit I.W. was rather high. After the fit it was average, but the urine volume was high.

June 29 : Before the fit I.W. was average.

July 21 : I W. was somewhat higher after the fit than before it. The urine volume was high on the day of the fit. On the 24th, when there was another fit, I.W. was low and the urine volume high.

August 7 : I.W. was lower before than during the series of fits, when, however, the room temperature was somewhat higher.

It seems certain that the loss in body weight and water following a fit coincided with increased urine output. On three out of eight occasions on which judgment could be made, a fit was accompanied by increased insensible water loss. The latter would be expected from Newburgh's principle if the energy metabolism increases after a fit, as has occasionally been observed (e.g. Pette and Janzen, 1937). As we have seen, such possible alterations of metabolism were too small to affect our conclusions regarding the changes in

body water. We cannot draw any conclusions about the urine and the insensible water loss in the period before seizures. On the few suitable occasions almost every possibility has been fulfilled.

Note.—Variations in the water intake: On April 14 the intake was reduced by 280 ml. and from May 17–26 by 570 ml. This is shown in the diagrams by white spaces in the urine volume histogram. There were also daily variations in the water intake, due partly to the variability of the water content of the foodstuffs and partly to a systematic excess of about 150 ml. in the water content of diet 2 as compared with the other two diets. The extremes were: Patient 1, 2,607–2,923 ml.; Patient 2, 2,699–2,931 ml.; Patient 3, 2,692–2,934 ml. The day-to-day variations were usually much less than this, and definitely need not be considered in assessing the urine volume measurements.

Discussion.

Gross retention of body water is clearly not decisive for the onset of the major epileptic seizure. Nevertheless, a fit is quite often preceded by the establishment of a positive water balance. It seems possible from this that water retention may be one of the factors which precipitate a convulsion. It is, however, equally possible that the unknown set of conditions which determine the onset of a fit may on occasion influence the water exchange between the organism and its environment. We have at present no way of deciding between these alternatives.

The present work illustrates the great difficulty in obtaining adequate unequivocal evidence concerning the relation of water exchange to the incidence of fits, even where the investigations extend over long periods of time. We have been handicapped by the smallness of the changes in body water accompanying fits in the patients whom we have studied. This has made it particularly difficult to elucidate the occurrences immediately preceding a convulsion. We would suggest the necessity for further investigations after the manner of the present one. They should be carried out on patients who show at the time of the seizures changes in weight comparable with those which Frisch had the opportunity to observe.

II. Water Content of the Blood.

Object of the Experiments.

Any changes in the water content of the organism accompanying seizures may or may not involve changes in the blood volume. If the latter is altered, there will be corresponding changes in the concentrations of the blood constituents unless there are adequate compensatory mechanisms which lead to their maintenance at the original levels. In order to determine whether any such changes in the concentration of blood constituents do indeed occur, we have made daily measurements of the blood total solids and the plasma

nitrogen content. The latter is of particular interest in that the plasma proteins in the exertion of their colloid osmotic pressure provide a factor in the regulation of the distribution of water between the blood and the tissues.

It should be mentioned that it is not certain that there are changes in the volume of the circulating blood before and after seizures. Measurements of the blood volume in epileptic patients have been made by Hodskins *et al.* (1932) and Stone and Chor (1937). The design of their experiments, however, did not permit the certain detection of changes in the blood volume immediately before and after a seizure. On the other hand, Gamble (1930) considered that the body water thrown out during the periods of convulsions in the epileptic child studied by him was of interstitial origin.

Total solids of the blood in epilepsy have been determined by Albrecht (1938). She found that the variations in the water content of the blood, which were greater in patients who were having seizures than in those who were in a fit-free phase, bore no connection with the incidence of fits.

Protein fractions of the blood.—Using a refractometric method DeCrinis (1920) found that the serum albumin rose, often very quickly, before an epileptic fit and fell rapidly afterwards. On the other hand, a rise in the serum albumin did not always lead to a fit. Meyer and Brühl (1922) also made refractometric measurements. Whilst observing large fluctuations at the time of fits, they could find no correlation between high serum albumin values and the onset of seizures. Even in the same patient some fits were preceded by a rise, others by a fall. Frisch and Fried (1927) criticized the use of the refractometer in the determination of blood protein and employed a gravimetric method. They claimed an increase in the albumin/globulin ratio in the preparoxysmal phase, but there were no characteristic changes in the total serum protein. McKenzie and McChesney (1935) found no correlation between the total serum protein and the frequency or recentness of seizures. It was normal immediately after convulsions and remained normal. More positive findings were claimed by Contini (1936), who reported mean values obtained with 20 epileptics. Between fits the total protein was slightly increased from the normal value, the globulin was normal and the albumin decreased. After the fits the globulin remained unaltered, but the total protein and the albumin rose to higher values. Finally, Stone and Chor (1937) observed that the "blood protein" (presumably total plasma or serum protein) was somewhat higher after seizures than before them, but "the degree of the increase was too slight to be considered significant."

Non-protein nitrogen of the plasma (N.P.N.).—The literature is reviewed by Lennox and Cobb (1928) and by Wuth (1928). In the interval between seizures Wuth found normal values. After epileptic fits, according to Krainsky, Teeter, Rohde, Allers and Wuth, there is an increase in N.P.N. This was regarded by Wuth as a result of the muscle contractions, since he found it also after the convulsions of other disorders. In contrast, Frisch and Walter

observed in two epileptic patients a rise in N.P.N. before seizures and a fall afterwards. In a third patient the post-paroxysmal fall was again observed. Finally, Lennox and his collaborators, and also Pezzali, found no connection between the N.P.N. level and the incidence of fits.

METHODS.

The following were determined daily for various parts of the experimental period: total solids, haemoglobin and cell volume in whole blood; total nitrogen and non-protein nitrogen in plasma.

The patients were those whose histories are given in Part I. The blood was taken from them by venipuncture without stasis, at approximately the same time each day, while they were fasting and resting in bed. Clotting was prevented by the addition of 3 mgm. per ml. of potassium oxalate, crystallized in the sample tube by evaporation from a stock solution neutralized to pH 7 $\pm$ 0·2 (phenol red) by addition of oxalic acid. The analytical methods were as follows:

Total solids.—Duplicate 1 ml. portions of blood were pipetted into small aluminium milk bottle caps and dried to constant weight at 104° C. They were weighed after cooling for exactly ten minutes in a sulphuric acid desiccator: heat-dried protein slowly gains in weight over sulphuric acid. The difference between duplicates seldom exceeded 1 per cent. of their mean.

Haemoglobin was determined as carboxyhaemoglobin by dilution of the whole blood with ammonia solution and treatment with pure carbon monoxide (Palmer, 1918). The colour comparison was made photo-electrically with the Hilger Absorptiometer, which was calibrated accurately with haemoglobin solutions, the strengths of which were known on the Sahli scale. The haemoglobin contents of two blood specimens could be compared thus with an accuracy of 1 per cent., although the accuracy of the absolute figures was limited by that of the Sahli method. For our purpose, which was to investigate daily variations, absolute figures were unimportant.

Cell volume was determined using the Wintrobe tube, great care being taken to achieve complete sedimentation.

Total and non-protein nitrogen were determined in duplicate by the micro-Kjeldahl method, the former in a carefully made dilution of plasma, and the latter in the filtrate after precipitation of the plasma proteins with trichloracetic acid.

RESULTS.

Curves showing simultaneous measurements of plasma total nitrogen, non-protein nitrogen and blood total solids are given in Fig. 5. For short periods haemoglobin and, later, cell volume are compared with the blood total solids. As would be expected, there is good parallelism between the haemoglobin concentration and total solid content of the blood. Variations in the latter are also accompanied by similar changes in the cell volume. This is seen again in the correlation diagrams of Fig. 7, where in the bottom row the two quantities are plotted against one another. As the blood was removed from the patients while resting in bed, it is unlikely that the number of circulating red cells at the time of venipuncture varied much from day to day. Hence the approximate proportionality between total solids and cell volume probably indicates that the alterations in the number of red cells in a given

volume of the circulating blood are due to the entry and withdrawal of roughly isotonic fluid.

Grand mal seizures are indicated by vertical broken lines, and inspection shows no constant connection between the incidence of fits and the variations in plasma total and non-protein nitrogen and blood total solids. Consideration of the time of each seizure in relation to the time of the removal of the blood does not affect this conclusion. However, as will now be shown, the variations in blood total solids and plasma nitrogen are not entirely without significance.

From Fig. 5 it will be seen that, particularly with Patient 1, the curves for blood total solids and plasma nitrogen tend to run parallel to each other. That there is a fair degree of correlation between these two quantities is evident from the dot-diagrams, in which they are plotted one against the other (Fig. 7, top row). They are not of course totally unrelated, since the plasma proteins contribute to the whole blood total solids ; and if the concentrations of all the other blood constituents remained constant, there would be a linear relationship between the blood total solids and the plasma nitrogen. This is represented on the diagrams of Fig. 7 by the straight lines passing through the centroid of the scattered points. If the cell volume remained constant the solid lines would apply, but as we have seen, the cell volume increases with the total solids. When allowance has been made for this, the relationship is approximately represented by the broken lines. Clearly the rate of increase of blood total solids with plasma nitrogen is greater than that given by either the broken or the solid lines. Hence changes in the concentration of the proteins in the plasma tend to be accompanied by simultaneous changes in the same direction of other solid constituents of the blood. Haemoglobin is of course quantitatively by far the most important of the latter.

That the concentrations of protein in the plasma and of haemoglobin in the whole blood tend to undergo parallel changes strongly suggests that these are due for the most part to alterations in the amount of water in the circulating blood. There is thus no reason to suppose that the curves indicate variation in the total amount of circulating plasma protein.

The considerable fluctuations in the blood total solids are therefore tentatively ascribed to changes in the water content of the blood. If this be justified it becomes of interest to determine whether these are connected with alterations in the water content of the organism as a whole. As was mentioned in Part I, it is not practicable to construct a body water curve, but the weight changes afford a fair measure of the water changes. So for comparison with the total solids curve we have plotted in Fig. 6 for Patients 1, 2 and 3 the daily differences between the actual value of the body weight at 7 a.m. and the corresponding value given by the straight line fitted through the weight curve (v. section headed " The Diagrams " in Part I). These differences are positive if the body weight is the greater of the two values, and we have called them the " body weight deviations." It will be seen that there is a tendency for

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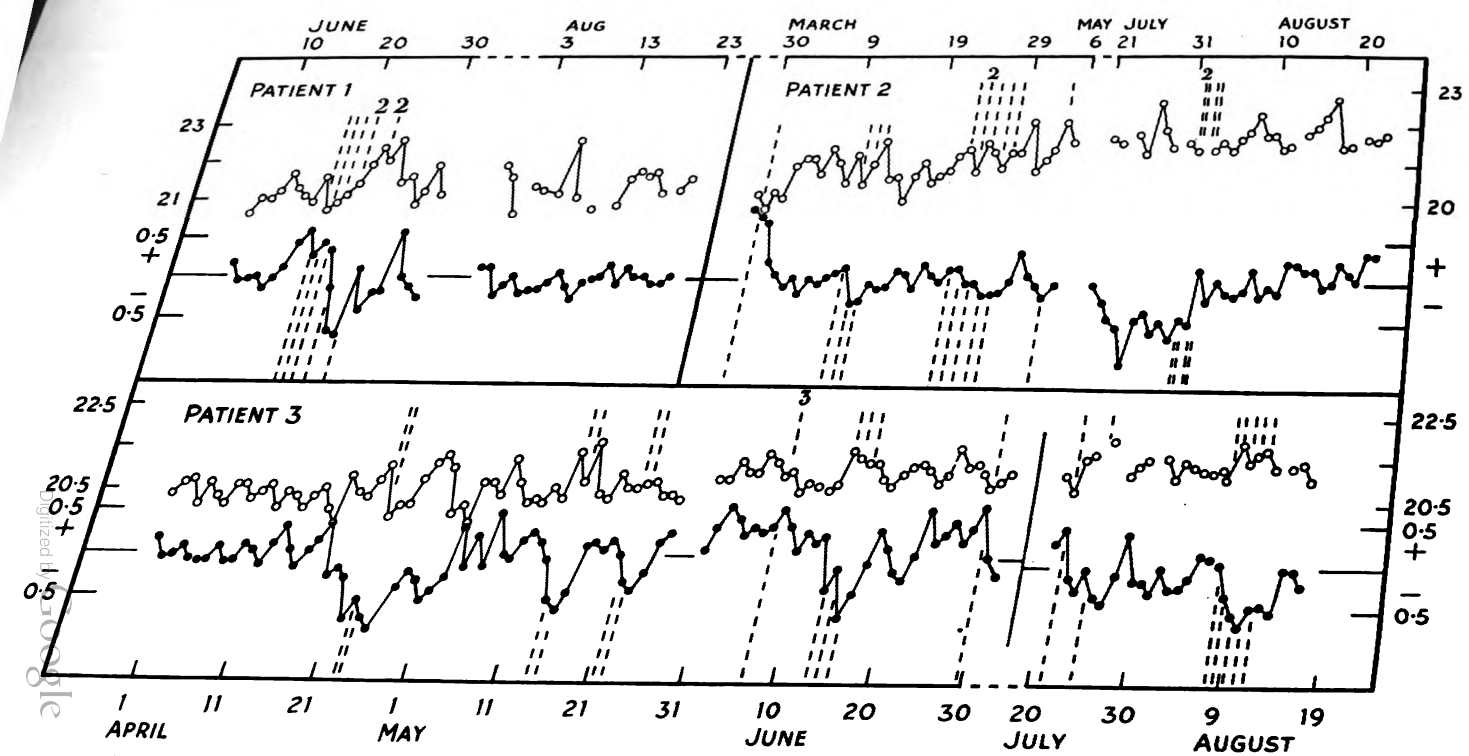

6. 0.— -o- Blood total solids. -●- Body-weight deviation. Each point on the body-weight deviation curve represents the algebraic difference between the actual value of the body weight and the corresponding value given by the straight line fitted through the weight curve (see Figs. 1–3).

simultaneous changes in blood total solids and body weight to be in opposite directions, particularly just before and after fits. The data have been further analysed by plotting the body weight deviation against the blood total solids in correlation diagrams (middle row of Fig. 7). The dots represent data

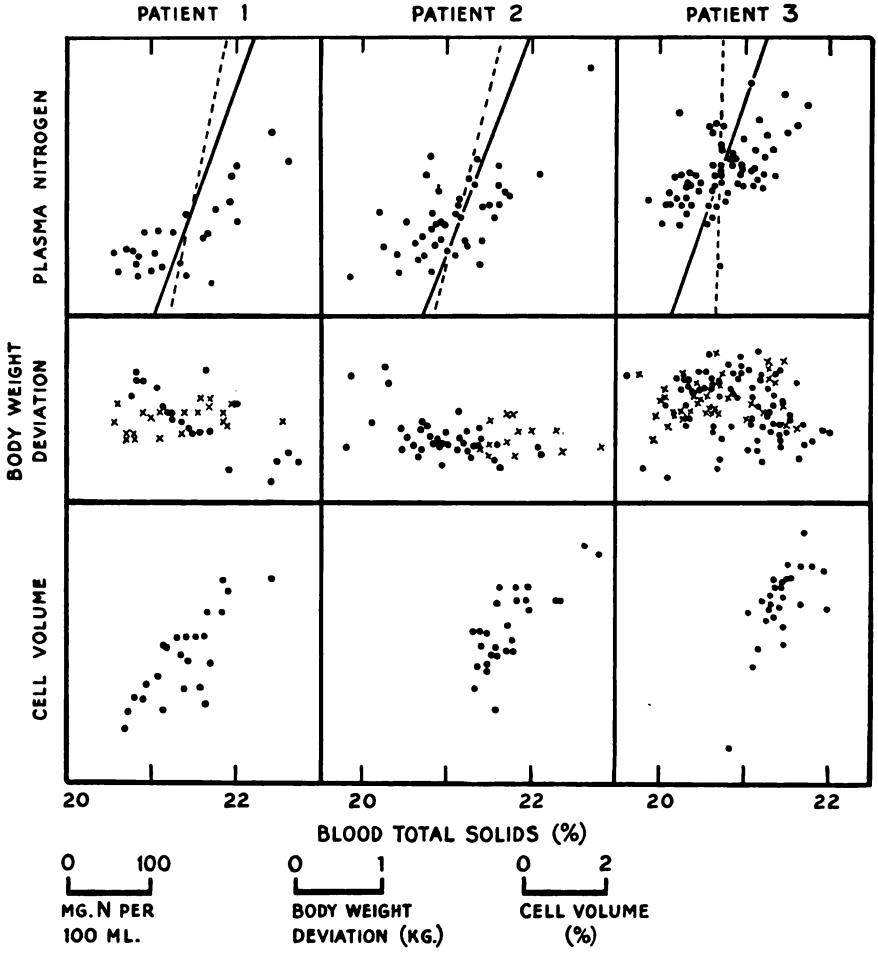

FIG. 7.—Correlation diagrams. Top row: plasma total nitrogen and blood total solids. Middle row: body-weight deviation (as in Fig. 6) and blood total solids. Bottom row: cell volume and blood total solids.

obtained within five days of a seizure; the crosses correspond to days outside these limits. It will be seen that with Patient 1 there is a good negative correlation for the data represented by dots, but no correlation in the fit-free periods. With the other two patients the correlation diagrams give little

information ; nevertheless we would suggest that they do not invalidate the impression gained from Fig. 6.

There thus appears to be a tendency for retention and release of body water to be accompanied by decrease and increase respectively of the total solid content of the blood. This, like the previous finding that the blood total solids and plasma protein tend to undergo parallel changes, is indirect support for the view that these changes are due to water entering and leaving the circulating blood. It therefore seems probable that, especially just before and after fits, the retention of body water is frequently reflected in the blood by dilution, and the release of body water by concentration, of its solid constituents.

We began with the question whether changes in the water content of the body in epilepsy will result in alterations of the concentrations of constituents of the blood. It would seem that this may occur. It was originally visualized as a result of inadequate compensation, but it is recognized that it may arise from other causes.

Summary.

Part I.

(1) The object of the experiments was to determine whether there is any connection between the incidence of *grand mal* seizures and the exchange of water between the epileptic organism and its environment. Certain authors have claimed a retention of water before fits and a release afterwards, with parallel changes in the volume of the urine.

(2) The diurnal water exchange has been studied in two epileptics for five months, and in a third for nearly three months. Control observations have been made on a non-epileptic patient. The subjects were kept under controlled conditions with a fixed diet and water intake.

(3) Values of the water balance (the nett gain in water by the body) have been calculated for two-day periods during the whole of the experiment. Water balance values in which allowance has been made for estimated daily variations in the energy metabolism have also been calculated wherever possible. The methods are fully described.

(4) Changes in the fasting body weight under the controlled conditions afford a fair measure of the changes in body water. At most 10 seizures out of 22 were preceded by a rise in the weight curve, and at most 10 out of 22 were followed by a fall.

(5) The calculated water balances indicate with a high degree of probability that when there was a large rise in weight during the two days before a fit, or a large fall during the two-day period consisting of the day of the fit and the following day, these weight changes were for the most part due to changes in the water content of the organism.

(6) Retention of body water does not by any means invariably precede a seizure. A negative water balance was observed after more than a half of the isolated seizures.

(7) Increased output of urine coincides with loss in body weight and water following a fit.

(8) No regularity was observed in the alterations before and after fits of the rate of extra-renal water loss.

Part II.

(1) Daily measurements have been made of the fasting values of the total solids of the blood and the total and non-protein nitrogen of the plasma of the same three epileptic patients. The haemoglobin content and cell volume of the blood have also been determined for short periods.

(2) There is no constant relationship between the incidence of *grand mal* seizures and the variations in plasma total and non-protein nitrogen and blood total solids.

(3) Changes in the concentration of proteins in the plasma tend to be accompanied by simultaneous changes in the same direction of other solid constituents of the blood.

(4) There appears to be a tendency for retention and release of body water, especially just before and after fits, to be accompanied by decrease and increase respectively of the total solid content of the blood. Reasons are given for supposing that these latter changes are a result of water entering and leaving the circulating blood.

It gives us great pleasure to acknowledge the help received from the Physician Superintendent, Dr. R. Ström-Olsen, who attended to the clinical side of the investigation and provided the case histories. We thank him also for his advice and constant encouragement.

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METHODOLOGY IN PSYCHOLOGICAL MEDICINE.*

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THE development of psychological medicine in Great Britain has been accompanied by a certain feeling of inferiority amongst psychiatrists and psychotherapists. This has shown itself in rivalry, at times brisk and even acrimonious, which may be understood as a striving to obtain the object which another is thought to be pursuing. This state of affairs arises when there is uncertainty of objective; and all will agree that the objectives have been ill-defined and at times nebulous. Here as elsewhere the familiar characteristic has been "muddling along somehow". When we come to consider possible reasons for this, one feature stands out, namely, the lack of originality in our insular school of thought. We have produced no Copernicus to revolutionize our methods and systems, and so sweep away intellectual vested interests. To meet the needs at home we have built up a national debt by borrowing. Our source of inspiration has been largely Continental. Freud, a little bitterly perhaps, alludes to "the numerous psychiatrists and psychotherapists who warm their pot of soup at our fire—without indeed being very grateful for our hospitality" (1). The genius of Freud and of Jung lay in speaking from the heart and setting at naught traditional views. Their very different contributions have been so refreshing that many accepted, without questioning, the teaching of one or other of these pioneers. Others rejected *in toto* (and often unread) what was described as "the new psychology". But a more hopeful note has recently been sounded in this country; for the question of method, or way by which we proceed to the attainment of some aim, has been the subject of numerous contributions; and less attention is being paid to the technique embodied in the method. In this paper certain suggestions upon methodology will be made; and the subject will be examined critically, especially from the clinical aspect.

I.

We are one and all influenced by education, experience and inborn tendencies, consequently we do not fix our attention upon the same objects. One will note the behaviour of a patient, another his physique, and a third the working of his

* A paper read before the Section of Psychology at the Annual Meeting of the British Association, Dundee, 1939.

mind. These three interests, and many others, could have been co-ordinated. But no union was attempted. On the contrary opposing factions claimed a monopoly of wisdom. The expansion of psychological medicine has, therefore, been haphazard and unmethodical. Further, developments in this branch of medicine arose out of the necessities and upheavals of our own time and so bear the signs of unrest. The absence of an accepted plan of campaign resulted in considerable waste of energy. The realization of this has led to a praiseworthy attempt to bring the results of clinical observation in psychological medicine into line with advance in scientific knowledge elsewhere. The scientific method has been familiar to scientists for generations, and its use has resulted in a vast increase of knowledge. Experimental psychology advanced in the sixties and seventies of last century by the use of scientific procedures. It was reasonable to believe, as Charcot and others did, that a like success would follow in psychological medicine if scientific principles were applied to it. Indeed such an attitude seemed almost a matter of common sense in clinical psychiatry which was then so ill-charted. Freud, loyal to his early scientific training, accepted nothing which he did not verify by repeated observation. His findings were often a surprise to him. But he turned aside from nothing which he believed to bear the mark of truth. His originality, both in the handling of clinical material and in the terminology he introduced, led some to suppose that he stood in complete detachment from his age. Some support for this view was forthcoming from Freud himself. In 1928 he wrote: "I ask you to bear in mind that our specific science is still very young—hardly as old as our century, as a matter of fact" (2). Yet in its method the new science, which had been built up through continuous contact with observations (*ibid.*, p. 46), was as old as rationalistic humanism; and it was particularly indebted to the form which this took in the nineteenth century. The method employed from beginning to end was the scientific method. The patient and relentless use of this method in the study of endopsychic processes was never abandoned by Freud, even in his speculative works (*ibid.*, p. 294).

Before his time psychiatrists had not brought the modern scientific outlook to bear upon their clinical material. They had, it is true, utilized the results obtained in the physical sciences in the investigation and treatment of mental sickness. But Freud, believing that the human mind was a part of nature rather than an entity outside nature, accepted the hypothesis that nature was a rational whole; and he proceeded, in consequence, to study the mind itself in a scientific fashion. This would seem to have been claimed as a new method by some psychoanalysts. Thus Rickman writes: "The tendency of psychiatry up to the present time has been to turn for help to the methods of the physical sciences which resolve themselves to number, measure and scales. . . . Psychoanalysis now had to offer another method, which does not enumerate, measure or weigh; it deals with presentations in the mind and tries to find by its technique how they are *arranged*; how they *interact*, and how they take *effect* in

human behaviour" (3). The method thus described by Rickman as " another method " is not in fact a new method at all. What is new is the application of the method in a fresh field. Freud himself was quite content with the method of science. " The contribution of psycho-analysis to science consists precisely in having extended research to the region of the mind. Certainly without such a psychology science would be very incomplete. But if we add to science the investigation of the intellectual and emotional functions of man (and animals), we find that nothing has been altered as regards the general position of science, that there are no new sources of knowledge or methods of research " (4).

The emphasis upon method as such has stimulated interest and even enthusiasm in almost every branch of psychological medicine. The scientific method, so it is believed, is intelligible and free from any suspicion of mysticism or animism. However this may be, this method has come to be accepted almost as an article of faith by some noted psychiatrists of our own day. Mapother, for example, writes : " It may well be questioned whether there is any alternative method if we distinguish belief from knowledge and unless we grant the power of revelation or intuition to provide knowledge as opposed to belief "(5). A further instance is given by Hart : " The main psychological attack upon psychiatry has adhered wholeheartedly to the method of science, and has claimed therein its entire justification " (6). Hart wisely adds that " the method of science is not an unique, absolute and unimpeachable key to knowledge . . . but only a convenient and most efficient weapon ". Nevertheless, his view is that so far as we have gone the scientific method stands supreme.

This canonization of the scientific method would seem to have been inspired by Pearson. He permitted no hesitancy in applying the method wholesale. " It (science) claims that the whole range of phenonema, mental as well as physical—the entire universe—is its field. It asserts that the scientific method is the sole gateway to the whole region of knowledge " (7).

The scientific method for which such far-reaching claims have been made is extremely simple. It does nothing more than define a plan which is to be followed in the pursuit of knowledge. " The unity of all science consists alone in its method, not in its material " (*ibid.*, p. 12). The essentials of this method may be briefly stated. Its primary tool is the objective observation of phenomena. Then comes the classification of the phenomena and lastly the deriving of mutual relations and sequences between the observed data, thereby making it possible to predict future occurrences which, in turn, must be tested by observation and experiment.

Formulations mixed with subjective factors have no right to be labelled "scientific" ; and any system of thought and action which embodies subjective features departs from the principle of the scientific method and employs a method other than the scientific method. Likewise medieval science, which rested upon accepted belief based upon the authority of the Scriptures or of Aristotle, used a method different from the scientific method. Medieval science employed a

dialectical rather than an investigatory method. The consequences of truth already known were its interest rather than new truths (8).

We have then, on the one hand, subjectivity, the mark of those who prefer opinion before knowledge, as it is thought, and on the other the authoritative or dictatorial procedure characteristic of medieval science and, perhaps, of some more recent statements. The adherents to the scientific method set out to steer a new course avoiding these two extremes.

A third group has also arisen, namely, those who claim to be " scientific " in the modern sense but are nothing of the sort. Examples are familiar and all too numerous, but one may be given from a recent work by Gutheil, *The Language of the Dream :* " The scientific material we make use of in our dream research is derived from observation and experiment. . . . We cannot observe dreams in a direct way, but we have a valid substitute for that, namely, recollection " (9). The amassing and systematic arrangement of facts, it should be remembered, is no guarantee that the material is being treated scientifically even though the label " science " be affixed.

In the same category we may place those psychiatrists who correlate states of mind with the supposed functioning of the central nervous system. Of them Golla remarks : " Basing their contentions on superficial resemblances between certain aspects of psychological phenomena and neural processes, we find them attempting to express psychology in terms of neuronic function. It is difficult for anyone with any intimate knowledge of neurophysiology to regard with tolerance attempts to find analogies between the activity of the isolated neurons and mental processes " (10).

Possibly it is owing to the use Bishop Butler made of the word " analogy " that the argument by analogy has been so popular. The value of analogy by way of illustration and comparison is great ; and often a striking analogy has led to fruitful investigation. But it is a mistake, and one often made by psychiatrists and psychotherapists, to think that analogy, in itself, can *prove* anything. We would not be justified, for example, in concluding because of certain vocal similarities that the motivation, if any, in the mental life of the parrot is the same as that of its owner.

The scientific method marks a clear path and so avoids the wanderings of the pre-scientific era. But it is a method with limitations. A great deal of life is outside its terms of reference. The contention put forward here is that we must be prepared to drop this method where it is inappropriate ; and we must be prepared to drop it even if we have not got an entirely satisfactory alternative method.

II.

The scientific method has drawbacks which render it an inadequate method in certain departments of psychological medicine. Observation, its primary tool, is not always free from the taint of subjectivity. The

ideal may be "strictly objective observation" (Mapother, *loc. cit.*). Yet "to observe is not so simple as it seems. Often the observation, on closer inspection, proves to be a series of observations connected by inferences of a subjective nature. This fallacy may be overcome where mechanical recording of observations is practicable. But these cannot always be used. They would be impossible, for instance, in psychotherapeutic practice, for here the observer would require to observe himself in the act of observing. His introspection would, in fact, be retrospection. Also when we observe a patient, he is continuously affected by it; and in consequence the repetition of the observation for purposes of verification becomes impossible" (11).

Moreover, observation has links in memory with the past—what we see or feel is automatically associated with what we have seen and felt. In practice, also, it is almost impossible to prevent the blending of observation and interpretation. The mind works as a whole; and observation cannot be carried out in detachment from other mental activities.

MacCurdy, writing upon psychopathology and social psychology, remarks that "if experiments are opportunities for observation where the majority of the factors are under control, we can say that there is in studying the production of abnormal mental reaction only one truly experimental method, namely, that of hypnotism and suggestion" (12). This reference is made to emphasize still more the limitations of observation.

The only observations of value in science are those which are free from the individual bias of the observer and which could in consequence be made by any other observer. Observations of this order could never be made in psychotherapeutic practice unless we had impersonal and, so-called, objective therapists, the prototype of which would be the skilled mechanic.

The circumstances under which observations are made—and under which alone they can be made so far as the bulk of clinical work goes—limit the value of such observations in the eyes of scientists. Psychotherapy cannot be conducted in public or in a laboratory. Mapother (*loc. cit.*), and others, hold that the observational methods of psycho-analysis have "warped its findings . . . and seem unfitted to provide evidence that is valid for science. "Psycho-analysis", he declares, "is fatally handicapped by its privacy which renders verification by the sceptical impossible". The same argument might well be advanced against other psychotherapeutic procedures. It would, however, be a mistake to conclude that psychotherapy must therefore be abandoned. The obvious answer to such criticism is that the scientific method is not and never has been suited to material of this kind. But apart from observation there is a still greater difficulty in using the scientific method. Unfortunately the critical discrimination of various workers in this field has not led to agreement upon the question of the facts alleged to be observed. Plato, it may be recalled, drew a distinction between lovers of opinion and lovers of knowledge. Protagonists of one school of thought insist that to them alone belongs knowledge

(i.e., the facts) while their benighted critics are mere lovers of opinion. Since no agreement has been reached upon a criterion of the facts, of the data, an indispensable feature of the scientific method is absent.

Gillespie in a paper entitled " Is there a Science of Psychology ? " refers to this : " We find a lack of agreement as to what the subject matter is to be. It is not a question primarily of heterogeneousness or vagueness of data ; but a question first of all as to what the data are, and before even that how the data are to be looked for. . . . When neither the data nor the methods for proving them are agreed upon, you cannot expect to find that comprehensive results will be observed in the form of laws obtained by deduction from the data" (13).

Despite criticisms of this kind a very important group of psychotherapists —the psycho-analysts—believe that psycho-analysis (using the word to denote a certain body of knowledge and the method used in amassing it as well as a psychotherapeutic technique) does possess the standing of a science. Reference has already been made to Hart's advocacy of this claim. Since the publication of Hart's presidential address to the Psychiatric Section of the Royal Society of Medicine, Otto Fenichel, in a book which has behind it the authority of the editors of *The Psycho-analytic Quarterly*, claims that "the theory of the neuroses put forward in psycho-analysis furnishes the scientific foundation for further practical work" (14). Psycho-analysis in this work (translator's preface) is described as a living scientific discipline that has not yet become dogmatized.

The word "dogma" has several meanings : it may be that which is held as an opinion, or else a body of opinion formulated and authoritatively stated. It is difficult to understand what can be meant by " a living scientific discipline that has not yet become dogmatized " when the claim is also made that " psycho-analysis furnishes the scientific foundation for further practical work ". Fenichel, despite these statements, appears (very wisely it would seem) to take up a somewhat non-committal attitude. This is not stated in so many words but is implied in what he says. He admits that " the striving for ' regularity ' permits a formulation only of that which is of general significance, and so does violence in a sense to the uniqueness of the individual case ". And again : " In spite of the progress made by the theory of the neuroses, the genetic method of procedure in each individual psycho-analysis and the difficulties it entails underwent no changes." He continues : " One has the general feeling that actual cases and theoretical description of disease entities becomes less and less congruous as we proceed from somatic to mental diseases. That in neuroses the 'typical' clinical picture is highly coloured by atypical features is proven by the fact that there is no unanimity among clinicians with regard to the systematization and nomenclature of the specific forms of neuroses."

Here indeed is a perfectly straightforward recognition of the difficulties : actual cases and theoretical description become less and less congruous, i.e., less and less coherent, less consistent and less harmonious ; and if, in addition,

there is a lack of unanimity amongst psycho-analysts themselves with regard to the systematization and nomenclature, then it is indeed hard to understand why Fenichel and other psycho-analysts still claim that their body of knowledge is a scientific discipline.

Another criticism of the position adopted by Fenichel and, no doubt, by other psycho-analysts, is that a generalization arrived at inductively by " the genetic method of procedure in each individual psycho-analysis " which " does violence in a sense to the uniqueness of the individual case " would seem to be an unsatisfactory method. Unless justice be done to the individual cases it would seem unlikely that they could ever be unified into a connected system. The striving for " regularity " may be personally satisfying, and most people would agree that it would be an advantage if the regularity could be established. But so far as our knowledge goes we have not yet reached this stage.

C. S. Lewis, writing with facetious irony on the inductive method, wrongly applied, by the mouth of Mr. Enlightenment, says: " Hypothesis, my dear young friend, establishes itself by a cumulative process; or, to use popular language, if you make the same guess often enough it ceases to be a guess and becomes Scientific Fact " (15).

A distinction must be drawn between method and methods. *Method* is the general plan and *methods* are the technical or other procedures used in dealing with certain phenomena. Methods must vary according to the material to be investigated, and every worker uses the methods which have proved useful in reaching the end he has in view. The methods, or to be more exact, the technical methods are, as Wolf points out, " aids either to observation or to inference. Sometimes they render possible the observation and measurement of certain phenomena which either could not be observed and measured at all otherwise, or could not be observed so well and measured so accurately . . . the technical methods are, for the most part, different from one science to another, whereas the logical methods are more or less common to all sciences "(16). The genetic or evolutionary method is well known as one of the logical methods used in science, and it is usefully employed in the effort to trace relationships between groups of phenomena, similar customs, similar trends of mind and so on. It might be used in psychological medicine in order to establish the general significance of certain facts thought to possess a lowest common factor. This is the sense in which it has been used by Jung. The factor common to all, in his psychological system, is the collective unconscious. Jung, as is well known, makes no claim to be " scientific "—the reverse indeed is the case. If we may take Fenichel as representative of the school of psycho-analysis, which does claim to be scientific, then we cannot but regret that their use of scientific method —and, in particular, the genetic method (for this is specified by Fenichel)—has not as yet succeeded in establishing data which are acceptable even to clinicians practising psycho-analysis.

These criticisms of the employment of the scientific method do not, of course,

apply to its use in certain branches of psychological medicine such as pathological and biological investigation and research. There it is the method of choice. In these and allied departments it has borne and will continue to bear an abundant harvest. But we pass the limits of its suitability and must seek another method when as individuals we deal with individuals who, like ourselves, inhabit a world in which purpose and personal values are of extreme importance.

The exclusive use of the scientific method in psychological medicine is surely a remnant of the atomist psychology of bygone days. " Those psychologists," says Aveling, " who are not so ' departmentalized ' as to exclude consideration of the deeper problems of their science, are coming to realize that analysis, though a useful and even necessary method, breaks up in thought what is in fact indivisible. The conception of consciousness as a mosaic of sensations, or products of mental chemistry, has been abandoned. . . . Polemic has been waged fiercely against the theory of faculties (intellect, memory, imagination, etc.) as unitary functions, until definite experimental evidence has been adduced that no such functions exist " (17).

III.

What has been said would seem to yield the conclusion that the form of the scientific method known as the genetic or evolutionary method, which held out expectation of being useful in defining data on which general agreement might be reached, has not justified the expectations formed of it. For the present, then, it would seem wise to resign ouselves to the conclusion that the scientific method, as such, is not suited to the greater part of the material with which we work. The human is not necessarily opposed to the scientific interest. But opposition becomes marked if the latter be regarded as more worthy of attention than the former. A map of the supposed, but as yet conceptual, stages in the evolution of a human being is of little importance if it fails to guide us in our dealings with human beings; and psychological medicine is first and foremost concerned with human beings.

We need not be too much concerned about consistency in our method. A consistency in method which obscures the material is foolish, and as such is " the hobgoblin of little minds " (Emerson). Remembering this, my positive suggestion to the problem of method (previously reported, loc. cit., and now repeated) is that we should, for the present at all events, utilize what I have described as the individualistic method. This, of course, refers only to that part of the field where we must as individuals deal with individuals. This method, by stressing the individuality of the therapist and of the patient, utilizes the subjective characteristics of both, for these are of importance. Inevitably it lacks the codification of the text-book. It differs radically from the method employed in science and in certain branches of medicine where the subjective characteristics of the therapist and of the patient have not (in theory

at all events) been considered as important. The patient exhibits general characteristics, common to the human family, and they cannot be cited as an example of his difference from other men or as individual peculiarities. When these are found in the course of clinical work or noted in dreams reported to us they should be closely studied. Characteristics of this impersonal or general type may lead to the formulation of "laws". Unless we begin with a due regard for individual features we have small chance of discovering general features. Until we know what we are, we cannot pass to that which is beyond our individual differences. It is necessary for the patient to become aware of and to accept his individual differences so that he ceases to be limited by them. When, for example, the patient has come to regard his own problem as part of the problem of the age in which he lives, he has gained an appreciation of a more general attitude. The adoption of the general attitude does not mean the loss of individuality, but rather its enrichment, for individuality has now been correctly focused. The psychoneurotic, having resolved his conflicts and tensions, has at his disposal the energy hitherto manifested in his symptoms; and further his understanding of himself and of the forces operating through him engenders an objectivity in outlook previously unknown. Such persons do not continue in a state of insulation. Thus, while individualism (that is, the use of the individualisitic method) is an end, it is preliminary to other ends; just as education by fulfilling its function leads to that which was not part of the immediate educational aim.

A further advantage to patient and to doctor in this method is that it involves a proper appreciation of the spoken word. The psychotherapist must speak; and he should, it is maintained, thereby reveal himself as an individual (as he expects his patient to do) rather than laboriously conceal his personality. The words which pass between doctor and patient in the consulting-room inevitably possess a subjective coloration. The dictaphone has been used to secure a record of each word spoken by the patient and by the therapist during the course of an analysis. Perhaps its use was governed by the desire to be "scientific" But can we believe that the repetition of such a record would communicate the essential vigour and living accompaniment of the spoken word?

The individualistic method presents difficulties in practice, particularly in the reciprocal relationship inherent in it. But this is not a good reason for abandoning it in favour of another method which is unsuitable in such practice. The individualistic method is not commended merely on account of its results, but because of its suitability. Before we can judge a method by its results alone we must show that the results are true for all time.

Clinical experience in psychological medicine reveals many situations which lie beyond the limitations imposed by the rigorous use of the scientific method. A psychotherapist using the individualistic approach must, therefore, be prepared to recognize that he is using a method which makes no pretence to be scientific.

No method is final—be it the scientific or the individualistic. Wisdom lies in the recognition that one is, or should be, supplementary to the other. Variation in outlook amongst clinical workers in psychological medicine is conditioned by the difference in material. Likewise it is conditioned much by the recognized and more by the unrecognized (that is the unconscious) qualities of the mind of each worker. However great the appeal of a monistic methodology may be, it must be resisted in the interest of clinical reality. The appreciation of individual features in method implies a new humanism in medicine; and with it a revaluation of medical education in which psychiatry and psychotherapy will receive due honour.

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THE USE OF THE CREATINE-CREATININE RATIO.

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A SURVEY of the creatine and creatinine excretion of large numbers of mentally defective patients in circumstances which precluded both keeping them on creatine-free diet and the obtaining of 24-hour specimens, led Penrose and Pugh (1939) to the use of the creatine/creatinine ratio in early morning specimens of urine as an index of the metabolism of these substances in each patient, as compared with controls. The use of the ratio was found to yield results of qualitative significance. Patients suffering from conditions known to affect creatine-creatinine metabolism, such as muscular dystrophies, diplegias, and hyperthyroidism, were readily picked out, and the creatinuria of children was marked; conclusions could be drawn as to the creatine-creatinine metabolism in certain other conditions. In the above survey the numbers allowed of statistical treatment to a considerable extent, and this confirmed the validity of the conclusions drawn from the ratio.

The purpose of the present paper is to apply the creatine/creatinine ratio to two particular problems.

First, however, a few examples are here given of the normal range of variability of the ratio on different days, in one and the same patient, on ordinary institution diet.

Creatine was estimated in terms of creatinine. Ratio = mgms. creatine excreted per cent. multiplied by 100; divided by mgms. creatinine excreted per cent.

	Day.					
	1.	2.	3.	4.	5.	6.
Adult 1	7	8	8	7	6	6
,, 2	7	8	10	6	8	9
Child 1 (aged 13)	52	43	33	59	30	32
,, 2 (,, 12)	60	44	46	56	49	32

PROBLEM A.

Do Phenylketonuric Patients Show Creatinuria?

The estimation of creatine depends on the coloration of creatinine with picric acid, and this estimation is affected by ketonic substances such as acetone bodies and also phenylpyruvic acid. Direct estimation in presence of phenylpyruvic acid shows an unreal creatinuria. It was therefore impossible

to determine directly whether patients suffering from mental defect in association with the excretion of phenylpyruvic acid show creatinuria or not. The following method was devised to find out what correction must be applied in order to reduce apparent creatinuria to real creatinuria.

Creatinine and creatine were estimated in an early morning specimen of urine in the ordinary way, and the phenylpyruvic acid content of the urine was determined (mgms. per cent.) by the method of Penrose and Quastel (1937) using a Lovibond comparator. A normal urine was then taken, its creatinine estimated, and this urine diluted to approximately the same creatinine content as the phenylketonuric urine. To the diluted normal urine was then added an amount of sodium phenylpyruvate corresponding to the amount of phenylpyruvic acid in the phenylketonuric urine. Creatinine and creatine were then estimated in the diluted normal urine with and without added phenylpyruvate. The correction to be applied to the creatine figure of the phenylketonuric urine was thus ascertained. The amount of phenylpyruvate added was checked by estimation.

If the phenylketonuric urine was very concentrated, this was diluted instead of the normal.

Using this method, the following results (except Patient 4) were obtained :

	Creatinine.	Creatine (uncorrected).	Phenylpyruvic acid.	Creatine (corrected).	Creatine/creatinine ratio.	Sp. gr.	Creatinine/sp. gr.
Patient 1 (female)	75	18	160	12	16	1015	50
Patient 1 (repeated)	77	15	160	12	16	1011	70
Patient 2 (male)	29	4	70	2	7	1008	36
Patient 3 (male)	78	23	180	19·5	25	1016	49
Patient 4 (female)	227	58·5	550	36	16	1034	67

Patient 4 was calculated on a basis of a correction of 1 creatine for every 25 phenylpyruvic acid, the maximum correction obtained in the other cases.

The average ratio (Penrose and Pugh, 1939) determined on 158 specimens from adult male mental defectives with no apparent abnormality affecting creatine-creatinine metabolism was 4·9 (standard deviation ± 4·7) and on 36 similarly from females was 5·6 (±5·3). The ratios in the table are therefore high. This is not due to low creatinine figures, taking into account the specific gravity. The average ratios of creatinine to the last two figures of the specific gravity, and multiplied by ten, as determined by Penrose and Pugh, were 60·3 (±16·5) for males and 51·1 (±11·9) for females.

It is evident therefore that the four phenylketonuric patients investigated do show creatinuria. One of them (Patient 1) showed some very slight clinical signs of hyperthyroidism. The cause of the creatinuria is more probably some form of hyperthyroidism than any muscular defect. It seems not

impossible that blocking of the oxidation of the phenylalanine nucleus at phenylpyruvic acid might result in increased concentration of some intermediary in the synthesis of thyroxine.

Owing to the outbreak of war, the intended examination of larger numbers of phenylketonurics, in order to determine whether creatinuria among them is general, had to be abandoned.

Problem B.

Is the Creatine/Cretinine Ratio Useful in Regulating Thyroid Therapy?

It is now well established that thyroid extract and thyreotropic pituitary hormone govern the excretion of creatine without affecting that of creatinine. Hess (1934) and Poncher, Visscher and Woodward (1934) used the excretion of creatine as an aid to diagnosis and treatment of hypothyroidism in children. Urinary creatine showed a response to ingested thyroid before any definite change in any other respect, clinical or biochemical, was noted.

Penrose and Pugh (1939) found that patients under thyroid therapy showed a distinctly higher creatine/creatinine ratio than similar patients not receiving such therapy. In some cases the ratio was excessively high (e.g. dermatitis under thyroid therapy, 10, 28, 28, 17).

It was therefore thought that the use of this simple ratio in early morning specimens of urine might extend the practical usefulness of creatine excretion as an index to thyroid therapy. Previous workers needed 24-hour specimens.

Determinations were therefore made of the ratio in a number of female patients under thyroid therapy. Two specimens were examined.

Patient.	Ratio.	Patient.	Ratio.	Patient.	Ratio.
1	22 ; 13	9	12 ; 3	18	54 ; 14
2	10 ; 14	10	18 ; 10	19	44 ; 28
3	8 ; 5	11	8 ; 10	20	8 ; 8
4	11 ; 24	12	37	21	10 ; 9
(aged 11)		13	22 ; 12	22	68 ; 62
5	7 ; 11	14	4 ; 7	(aged 9)	
6	7 ; 8	15	6 ; 12	23	4 ; 6
7	17 ; 13	16	28 ; 8	24	11 ; 10
8	11 ; 8	17	18 ; 7	25	10 ; 10

For comparison, the following cases of hyperthyroidism were estimated :

Patient.	Ratio.	Patient.	Ratio.	Patient.	Ratio.
A	17	B	35 ; 17	C	12 ; 5

Parallel estimations on 23 female patients on a similar diet to the above gave an average ratio of 7.

It was decided, on these results, in conjunction with a consideration of the clinical state of each patient, to reduce the thyroid dosage of Patients 1, 7, 12, 13, 18, 19; and to raise it of Patients 3, 4, 8, 14, 15.

Emergency circumstances rendered further follow-up only partial. The following patients, however, showed definite alteration before the work had to be abandoned :

Patient.	Ratio.	Patient.	Ratio.	Patient.	Ratio.
13	9 ; 6	19	8 ; 4	3	10 ; 22
8	10 ; 31				

The use of creatine/creatinine ratio evidently shows clearly the high creatine excretion caused by excessive thyroid hormone. It appears to be worthy of trial as a clinical aid in supervising thyroid therapy.

The co-operation and interest of Dr. Jane Bonnell is gratefully acknowledged, in addition to that of Dr. Penrose, and also a grant from the Rockefeller Funds of the Medical Research Council.

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MILLON'S REACTION IN THE URINE OF MENTALLY DEFECTIVE PATIENTS.

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INTRODUCTORY.

UNHYDROLYSED urine does not usually give a strong Millon's reaction in healthy people, but various workers have reported a strongly positive Millon's reaction in the unhydrolysed urine of mentally defective patients. Scheiner (1927, 1928) worked up such urines for tyrosine with negative result, and also showed that the reaction was not due to free phenol or oxy-acid. He claimed (1929) to have isolated the substance responsible, but did not identify it. Lieb and Schadendorff (1929) showed that the substance isolated was impure sodium acetate formed in the method of isolation. The mystery of the substance giving the Millon's reaction was thus left unsolved.

On account of the essential nature of proteins as body constituents, it is probable that certain types of defect in protein metabolism may have serious consequences. The excretion of phenylpyruvic acid, for instance, has always been found to be associated with mental defect. Any defect in protein metabolism in mental defectives is thus of special interest.

It was therefore decided to examine the above problem anew, and the present work is preliminary to that investigation. As a result of the war this has now had to be abandoned, but it is thought that the publication of the line of approach worked out may be of use in future investigations.

While not absolutely reliable by itself, since its intensity is affected by the chloride content of the urine, Millon's reaction would appear to be a very useful preliminary test in seeking the presence of phenolic substances derived from tyrosine, and opening up investigation of protein metabolism in mentally defective patients.

EXPERIMENTAL.

1. *Temporary Reaction due to Diet.*

In the course of a survey of nearly 400 patients suffering from mental defect, a definitely positive Millon's reaction was found in the urine of about 50 patients. Repeat specimens were tested of about half of these, and about

a dozen were positive, the others negative. It is evident that a positive Millon's reaction may occur as a temporary phenomenon. Whether this is more common among mentally defectives than among normals has not been determined. One presumably normal member of the research staff who regularly gave a negative Millon's, once gave a very strongly positive test after an unusual article of diet, which was probably the cause. A drug such as aspirin also causes a temporary positive reaction owing to the phenolic group it contains, and quite probably accounts for some of the positive tests subsequently not confirmed.

2. Strong Reaction due to Hepatic Disturbance.

Gullotta (1929) examined patients suffering from a large variety of diseases, and found complex cyclic compounds in the blood only in those cases in which there was clinical evidence of hepatic disturbance, the presence of cyclic compounds being always pathological.

In the present work, three patients (two male and one female) who repeatedly—each of four times of testing—gave a very strongly positive Millon's reaction, quickly became gravely ill and died. Clinically, the positive Millon's reaction was in these cases quite probably due to hepatic disturbance, as indicated by Gullotta, septic conditions being in each case present, which affected the liver.

Of five recovered cases of acute yellow atrophy, however, only one showed a positive test; the remainder were negative.

3. Intestinal Stasis.

As a result of increased bacterial activity when the passage of the intestinal contents is slow, p-hydroxyphenylacetic acid is liable to be formed. This substance is not detoxicated, and therefore on excretion gives a positive Millon's test in unhydrolysed urine. In such circumstances, however, bacterial action is also likely to give rise to the excretion of phenol and indole conjugated as ethereal sulphate, and the indican test and the urorosein test (for indole-acetic acid) are likely to be positive. Even under institutional care, such cases are apparently to be found, as shown by the following figures:

Patient.	Millon's.	Urorosein.	Indican.	Free phenol.	Conjugated phenol.	Ethereal sulphate.	Sp. gr.
A	sl. +	neg.	sl. +	1·75	1·2	2·8	1020
B	sl. +	sl. +	neg.	1·85	1·55	3·6	1025
C	sl. +	sl. +	sl. +	2·2	2·6	3·2	1028
D	+	str. +	sl. +	3·05	3·15	5·8	1024
E	+	+	+	2·9	2·95	6·4	1019

(The phenol and sulphate (SO_3) figures are in mgms./10 ml.)

4. *Inefficient Mechanism of Detoxication.*

Small amounts of phenol and p-cresol are normally produced by bacterial action in the intestines, and are detoxicated by combination as sulphates in the liver. There is the possibility, therefore, that along with some forms of mental defect, an inefficiency of function of such detoxication may exist, resulting in the excretion of these normal amounts of phenol uncombined, or in a more readily hydrolysed form. A positive Millon's test would result. This is similar to heading 2, but an inherent error of metabolism rather than acquired in disease.

One patient who constantly gave a positive Millon's reaction was compared colorimetrically with a control giving a negative reaction. In the unhydrolysed urines the relative strengths of the coloration were Patient : control = 25 : 4. In the urines hydrolysed under reflux, 2 : 1.

Whether one is dealing with hydrolysed or unhydrolysed urine in the Millon's test depends, it should be noted, on how the test is carried out. The following technique was devised as a rough indication of the relative amounts of free and total phenol respectively :

Millon's test without hydrolysis.—2 ml. urine is brought to the boil. Millon's reagent (B.D.H.) is then added rapidly until there is no further development of red colour. (Drops about half in number to the last two figures of the specific gravity.)

Millon-Cole test.—To 2 ml. urine is added equal volume of mercuric sulphate in 10 per cent. sulphuric acid. Boil half a minute. Add 2 drops 1 per cent. sodium nitrite.

	Millon's.	Millon-Cole.	Urorosein.	Free phenol.	Conjugated phenol.	Ethereal sulphate.	Sp. gr.
Patient	+	+	v. v. sl. +	3·8	2·5	0·4	1029
Control	—	+	+	2·95	3·2	2·25	1028

The missing phenol is in this case probably excreted partly as glycuronate. Blazso (1937) has shown that when phenol is injected, it is mainly excreted as sulphate in adults and in artificially fed infants, but that in breast-fed infants it is excreted mainly as glycuronate. An adult in whom the sulphate mechanism was defective would probably excrete more than usual as glycuronate.

5. *Abnormal Metabolites.*

The actual presence of an abnormal metabolite, or normal metabolite in inordinate amount, in association with the mental defect, as sought by Scheiner (1929), is of course possible in some cases. Stewart (1929) pointed out that tyramine had not been excluded by Scheiner. Some estimations have therefore been carried out of amino nitrogen on the urines of several mentally defective patients giving the positive Millon's reaction. No abnormal results were obtained.

Patient.	Millon's.	Sp. gr.	Ammonia N. (mgms. %.)	Amino N. (mgms. %.)
1	+	1017	47·6	5·95
2	−	1010	16·8	1·75
3	−	1012	60·2	5·25
4	sl. +	1021	48·3	9·45
5	+	1032	109·2	3·5
6	−	1029	135·8	5·25
7	+	1006	11·2	0·70
8	sl. +	1033	35·7	5·6
9	+	1012	30·8	1·75
10	+	1026	140·7	8·75
11	+	1018	77·7	0
12	+	1016	75·6	5·9
13	sl. +	1012	53·2	0
14	+	1016	32·2	4·2
15	−	1015	44·8	11·55
16	sl. +	1025	56·0	1·75
17	−	1026	74·9	6·3
18	+	1032	126·0	4·2
19	sl. +	1026	89·6	7·0

(Bracketed specimens are parallel estimations from patients under similar conditions of diet, etc.)

Conclusion.

The indications of this preliminary work are that a single explanation of the positive Millon's reaction found in the unhydrolysed urine of many mentally defective patients does not suffice to cover all cases. It does not appear permissible, as has sometimes been attempted, to mix all such urines and try to isolate some abnormal substance. Each case is a separate problem, and demands separate investigation to discover whether in that special case some abnormal substance is present, or whether it falls into one of the several other classes of possibility. In addition, a fictitiously strong Millon's reaction due to absence of the usual amount of chloride would have to be guarded against. Used with care, however, Millon's reaction is probably the most useful preliminary test in detecting abnormalities of various sorts in the capacity of patients to deal with protein metabolites.

Grateful acknowledgment is made to Dr. Penrose, and also to the Rockefeller Funds of the Medical Research Council for a grant.

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CONVULSION THERAPY OF THE PSYCHOSES.

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A. COMPLICATIONS AND TECHNIQUE OF CONVULSION THERAPY.

Treatment by convulsion therapy implies the administration of analeptic drugs in massive doses to induce major epileptiform convulsions. Usually a single convulsion is induced on each occasion and this is done two or three times weekly. The number of convulsions varies greatly in different cases, but is commonly from five to twenty.

The introverted schizophrenic or melancholic may be likened to a walled city which has closed its gates and refuses to trade with the rest of the world. Methods of persuasion having failed to get the citizens to open the gates of "Mansoul", the artillery of convulsion therapy is brought to bear on the walls of autism. A breach is blown in the wall, and relations with the world are re-established. Unfortunately we cannot control the amount of damage done in the bombardment. Evidence of damage is seen in the amnesia so common after even a single convulsion. Happily the process is usually reversible.

The two analeptics in common use are cardiazol, and triazol or azoman. While the former has been used widely since it was introduced by Meduna in 1934, the latter has had a less extensive trial, having been introduced by Mayer-Gross and Walk in 1938. The technique of cardiazol therapy is well known, and need not be reiterated here, but there exist certain important differences in the use of triazol. The volume of the average cardiazol injection is from 5–10 c.c., and 1 c.c. more or less makes little difference. The ordinary triazol injection is only 1·0–2·0 c.c., and the dose must be measured accurately to 0·1 c.c. Triazol being more slowly eliminated, the effect is produced more slowly, and when a repeat dose is necessary only a fraction of the original dose must be given. Excessive dosage of triazol is apt to produce multiple fits and *status epilepticus*.

I have adopted the scheme of dosage recommended by von Braunmühl, which is a useful guide. It is as follows:

	C.c. triazol (5% solution) per pound of body-weight.			
	Intramuscularly.		Intravenously.	
	Male.	Female.	Male.	Female.
A. Without hypoglycæmia .	0·018	0·017	0·01	0·01
B. In hypoglycæmia . .	0·011	0·01	—	—

If on any occasion the calculated dose of triazol fails to produce a typical convulsion, a supplementary dose equal to one-third of the original dose should be given after the waiting period, which is five minutes for an intravenous injection and fifteen minutes for an intramuscular injection. In using cardiazol, one is accustomed to administer a supplementary dose equal to or slightly greater than the original ineffective dose, after a waiting period of only one minute. It is important to stress this difference in the method of administration of supplementary doses of the two drugs, since, if cardiazol technique is used with triazol, fatal results may easily follow. When a supplementary dose has been required, on the occasion of the next injection of triazol, the dose given is the previous ineffective dose increased by one-sixth. While cardiazol is given almost exclusively intravenously, triazol is suitable for intramuscular use. The intravenous route, however, is safer and more satisfactory, and should be used whenever possible. When intramuscular injections are given the solution enters at varying proximity to the veins and may arrive among the muscle-fibres or fascial planes. Thus the effects are less constant and less easily controlled than those obtained from intravenous injections. Personally I never give supplementary doses following intramuscular injections, owing to the danger of irregular absorption. The intramuscular route has been recommended for patients with difficult veins. As triazol can be given with an ordinary fine hypodermic needle, and does not cause venous sclerosis, I have found that the small veins of the wrist and those on the dorsum of the hand can almost always be used. The intramuscular route has an obvious advantage for very resistive patients, but I find premedication with hyoscine compound B "tabloid" (hyoscine hydrobromide $\frac{1}{100}$ gr., morphine sulphate $\frac{1}{4}$ gr., atropine sulphate $\frac{1}{150}$ gr.) sufficiently quietens the patient to permit of an intravenous injection being given, and does not materially interfere with the convulsive effect of the drug. The amount of convulsant which can be given intravenously is astonishing. Rickles records the fact that on one occasion he administered 26 c.c. of 10% cardiazol in a single dose without ill-effect. In my own series a male patient was given 3 c.c. triazol intravenously, followed by a supplementary dose of 3 c.c. Multiple fits followed this enormous dose, but there were no permanent ill-effects. By the intramuscular route excessive doses are more dangerous. Thus, in the cases Nos. 2 and 3 below, 3 c.c. and 4 c.c. triazol respectively proved fatal.

Mortality.—The number of deaths attributable to convulsion therapy are few, and although unreported deaths have undoubtedly occurred, their number cannot be great. In my own series of 144 cases there were no deaths. In 2,875 reported cases twelve deaths have occurred from cardiazol convulsion therapy, and in 85 cases treated with triazol four deaths have occurred. Of these fatal cases, the following three, communicated to me by colleagues and hitherto unpublished, are of interest :

1. *Death from cerebral hæmorrhage, following cardiazol therapy.*—A male patient, aged 44, had blood-pressure of 130/85 mm. of Hg., fundi normal, arteries not thickened. A first dose of 5 c.c. cardiazol injected intravenously was ineffective, and was immediately followed by 7 c.c., when a convulsion resulted. Further injections were given on three occasions and were followed by convulsions. On the fifth occasion at 10.30 a.m. the patient failed to respond to 9 c.c., and a supplementary dose of 12 c.c. was given. An ordinary convulsion followed, and consciousness was quickly recovered. At 6 p.m. he complained of headache, and the temperature rose to 100° F. Five minutes later he became comatose, and there were signs of interruption of both pyramidal tracts. He died from respiratory failure at 8.30 p.m. on the same day. At autopsy a massive pontine hæmorrhage was found. The cerebral vessels were not noticeably diseased. Cases of this kind are extremely rare, and it is not easy to understand why the hæmorrhage did not occur at the height of the convulsion. It would appear that the drug produced necrosis of the wall of the pontine vessel, which later collapsed. Probably most workers would consider the supplementary dose of 12 c.c. to be excessive, but as only one convulsion followed, it was evidently not overwhelming.

2. *Deaths from status epilepticus following triazol therapy.*—A female patient, aged 55, received a first injection of 2 c.c. triazol intramuscularly at 11.57 a.m. No convulsion followed, and at 12.12 p.m. a supplementary dose of 1 c.c. was given. Major epileptiform seizures followed at 12.15, 12.20, 12.25, 12.30, 12.40, 12.52, 1.7, 1.25, 1.45, 2.0, 2.10, 2.24. Morphine sulphate gr. $\frac{1}{4}$ was given at 12.40 p.m. The fits continued, however, and she became extremely collapsed, the pulse disappeared, the extremities became cold and clammy, and the lungs œdematous. She died at 2.25 p.m.

3. A male patient, aged about 40, who was strong and healthy, received 7 effective intravenous injections of 5 c.c. cardiazol. Triazol was used for the 8th injection, when 4 c.c. were given intramuscularly. Seven minutes after the injection jerking began in the right arm, rapidly spreading to the rest of the body, and lasting for 3 minutes. A general convulsion and loss of consciousness followed, with tonic and clonic phases. After 3 minutes he had repeated jerking movements of all limbs, and then another fit. He did not regain consciousness after this. After 10 minutes the third and last convulsion occurred, and the respiration ceased, despite attempts at restoration.

At autopsy the viscera were found to be in a state of intense venous engorgement, particularly the lungs. The right side of the heart was dilated. There was no evidence of organic disease of the viscera. The brain was intensely congested. The cerebrum was dark and of firm consistence. On the inferior surface of both lobes of the cerebellum was an area of œdema and softening; the tissue was very friable, contrasting strongly with the firm consistence of the cerebrum. Possibly the cerebellum had exerted pressure on the vital centres lying in the floor of the fourth ventricle, and so brought about paralysis of respiration.

These two deaths from *status epilepticus* demonstrate the danger already mentioned of excessive dosage by the intramuscular route. In Case 2 the

supplementary dose was too large and was given rather soon. The age and sex of the patient did not allow of any latitude in technique and dosage. Case 3 received too large a dose by the intramuscular route, leading rapidly to *status epilepticus* and death, possibly due to pressure on the medulla.

Accidents during the Convulsion.

It is during the tonic phase of the convulsion that fractures and dislocations are liable to happen. Much can be done by good technique to minimize such accidents, while excessive doses causing very powerful convulsions and injudicious handling of the patient during the convulsion tend to produce them. In my series of 144 cases there were 1 case of fracture dislocation of the humerus, 2 cases of unilateral fracture of the neck of the femur, 2 dislocations of the jaw, and 3 simple dislocations of the shoulder-joint.

In a survey of the literature I find that in 2,184 cases treated with cardiazol 25 fractures (1·14%) have occurred, and in 100 cases treated with triazol 3 fractures have occurred. Very serious fractures have occurred during triazol therapy, viz., double vertebral compression fracture of the spine (Stalker), and bilateral fracture of the neck of the femur (Walk and Mayer-Gross). It has been suggested that triazol produces a more severe convulsion than cardiazol, but I have not observed this.

Vertebral Fractures.

Polatin and others in America have reported that vertebral compression fractures occurred in 22 out of 51 cases examined by them. They state that the most frequently affected segments were in the mid-thoracic region. Fragmentation and compression of the anterior portion of the upper surface of the vertebral body was most common. The occurrence and degree of pain in the back complained of by the patients did not bear any relation to the severity of fracture, i.e., severe pain in the back occurred in some cases without fracture, and conversely compression fractures occurred in cases where pain was not complained of. Palmer, in England, did not find such a high proportion of cases with fractures. Of 20 cases, 5 were found to have the typical compression fractures.

I have examined radiologically all my cases at present undergoing treatment, and new cases have been examined before commencing treatment. Of 18 cases, 3 (all female) had vertebral compression fractures. Two of these complained of persistent severe pain in the back, especially on coughing or sneezing, which, however, completely disappeared after a few weeks, while the third did not admit any pain even in response to direct questions. None of the three had any noticeable kyphosis or other deformity or symptoms of pressure on the

cord. One patient who was radiographed prior to treatment was found to have a typical wedge-shaped vertebra, which might readily have been taken for a convulsion fracture if she had been radiographed only after the treatment. It is my opinion that the importance of these fractures has been exaggerated, and that the danger of their occurrence should not be regarded as a contra-indication.

Winkelman recommends a specially devised apparatus for mechanical restraint to prevent dislocation of the shoulder. This is unnecessary and of doubtful value, as the unyielding nature of the support might readily cause injury. It is sufficient to have an assistant controlling each arm of the patient, who is made to lie on his back, avoiding a twisted position. The arms should be gently supported, keeping the elbows close to the sides to prevent abduction at the shoulder and minimize the risk of dislocation. A hand should be placed on the anterior aspect of the shoulder with the same object. Dislocation of the jaw is common and reported by many workers. Some workers have used a gag composed of a covered wooden wedge or tongue depressor, which was responsible for injury to teeth and jaw. The gag ought to be of soft absorbent material, and is conveniently made of several short pieces of rubber tubing wrapped in gauze.

Cardiac Complications.

Minor cardiac disturbances such as temporary tachycardia, auricular fibrillation and extrasystoles have been reported by several workers. Severe cardiac collapse following the injection has been observed by Gillman and Parfitt, Molony and Conlon, and myself. Immediately on receipt of the injection several of my patients, instead of reacting by a seizure, became ashen, with pale cheeks and blue lips; the pulse disappeared, and the respirations became shallow, while a cold perspiration broke out on the palms and soles. The duration of the attack was short, and it was sufficient to wrap the patient in warm blankets till recovery took place.

Molony and Conlon consider that triazol imposes a greater and more prolonged strain on the heart muscle than does cardiazol, but I have not observed this difference.

Activation of latent pulmonary tuberculosis as a result of convulsion therapy has been reported by various authors. Pameijer, in a series of 1,200 cases, reports 7 cases of this complication, 2 of which were fatal. In the present series at Crichton Royal no pulmonary complications occurred. Estimation of the sedimentation-rate of the red corpuscles and X-ray of the chest were used in selecting patients free from latent tuberculosis of the lungs.

Putting aside the immediate dangers, the problem of *later ill-effects* to the mental and physical well-being of the patient has to be considered.

Mental Complications.

With regard to the problem of mental damage done by convulsion therapy which is being much discussed at present, it is noteworthy that very few of my cases treated for involutional melancholia showed prolonged memory defect. Twenty-four cases of involutional melancholia treated in my series, whose average age was fifty years, showed remarkably little memory disturbance. The following case of melancholia, however, which showed marked memory defect after treatment, is worthy of mention :

> The patient was a schoolmaster, aged 59, who made an excellent recovery from a state of severe melancholia after 9 triazol convulsions. He was found thereafter to have a retrograde patchy amnesia, which persisted for several months. Thus he could not recall distinctly a former fellow patient with whom he had been familiar, and who was discharged just before the convulsion therapy commenced.

It is only to be expected that convulsions too frequently repeated might affect the neurones in the same way as the alternate ischæmia and hyperæmia of genuine epilepsy. The damage to cerebral structure is of slight degree, and in persons of humble intellectual development is scarcely discernible. In highly educated persons, on the other hand, it is more apparent and might be serious. It should be remembered that although convulsion therapy may produce intellectual impairment, so also may a long psychotic illness.

In my own series I found a large proportion of cases had an *elevation of blood-pressure* following the treatment. In some cases the rise was of moderate degree (20–30 mm. of mercury), but in a few cases of great degree (60–90 mm. of mercury). This elevation of blood-pressure was persistent, and in one case, a male patient aged 49, the blood-pressure, which before treatment was 122/94 mm., after 12 months remains 182/134 mm. of mercury. Such an elevation of blood-pressure must be injurious to the patient. Similar findings have been recorded by others, but so far no explanation has been offered. In experiments on rabbits subjected to massive daily doses of cardiazol and triazol, I have found degenerative changes in the kidney tubules. These experiments may possibly afford an explanation of the prolonged rise in blood-pressure following convulsion therapy, and are being continued.

B. Results of Convulsion Therapy.

The following account presents the results of convulsion therapy in 144 cases treated at Crichton Royal. Of these, 111 were treated with cardiazol, 9 with cardiazol followed by triazol, and 24 with triazol alone. In all, 2,204 convulsions were induced. The subjoined table sets out the results of treatment in the various psychoses in my series :

Diagnosis.	Number of cases.	Recovered.	Improved.	Unimproved.
Schizophrenics:				
Duration :				
Under one year	14	7 (50%)	6 (43%)	1 (7%)
Over one year	68	3 (4·4%)	33 (48·5%)	32 (47%)
Paraphrenics	9	0	4	5
Manic-depressives:				
1. Melancholics	19	11 (58%)	8 (42%)	0
2. Manics	8	6	1	1
Involutional melancholics	24	8 (33%)	8 (33%)	8 (33%)
Psycho-neurotics	2	1	1	0
All cases	144	36 (25%)	61 (42%)	47 (33%)

I use the term " recovered " as meaning that all symptoms have disappeared, e.g., hallucinations and delusions, at least some degree of insight has been restored, and the patient is fit to be discharged to home conditions and take up his former activities. The term " improved " means that a great change for the better has occurred in the patient's behaviour and habits, but symptoms may remain and insight is not restored. Some such patients are fit to be discharged from hospital care.

Schizophrenia.—Of 14 cases in which the psychosis had been established for less than one year, 7 recovered and 6 were improved, while of 68 cases of over a year's duration only 3 recovered. Although the number of early cases in my series is small, I feel convinced that convulsion therapy is of definite value in the early treatment of schizophrenia. This is in harmony with the findings of most other authors, who report that early cases respond well.

In the treatment of chronic cases also, I found convulsion therapy to be of definite value in bringing the patients to a higher level of social behaviour. Thus 33 (or 48%) were greatly improved. Several of these had been grossly deteriorated, in bed continuously, wetting and soiling without shame for a number of years, and have now become decent patients, able to do some useful work and lead a satisfactory life in the hospital community. As a result, the nurses are encouraged and the despair of therapeutic nihilism is dispelled from their minds, and in addition, their work is lessened by the patients' improved social behaviour. In some cases this improvement was astonishing. Patients who had long ago been given up as hopeless became accessible, rational and employable.

Paraphrenia.—Of 9 cases of paraphrenia, all over $1\frac{1}{2}$ years' duration, none recovered, but 4 improved. The results are similar to those in the chronic schizophrenic group.

The manic-depressive psychosis.—Patients in both the melancholic and the manic phases responded immediately to the treatment. Of the 27 patients treated, 17 recovered and only 1 was unimproved.

A happy feature was the rapid disappearance of suicidal tendencies. One female patient described the sensation following the injection as a feeling of impending death. She said that all her conceptions of Dante's Inferno crowded her mind while the figures of those around faded out. "If death is like this," she said, "I prefer to remain alive." She was convinced that one injection of cardiazol would put the desire for death out of any suicidal person's mind.

Involutional melancholia.—Of 11 cases in this group, in which the duration of illness prior to treatment was under two years, 7 recovered. The prognosis of involutional depressions is on the whole poor. It is the common experience that roughly a third of the cases recover completely in time without special treatment, and a third improve sufficently to live at home under supervision. My number of early cases treated so far is small, but indicates that the prognosis is rendered much more favourable by the introduction of convulsion therapy. It is probably correct to state that a considerable number of cases of involutional melancholia which would otherwise drift into chronicity can be saved by convulsion therapy. Although 1 case of five years' duration recovered, the outlook is much better if the treatment is employed earlier in the illness. Thus the average duration of illness in the recovered cases (including the case of five years' duration) was $1\frac{6}{12}$ years, while the average duration of illness prior to treatment in the unrecovered cases was $5\frac{6}{12}$ years. Twenty-four cases in all were treated and of these 8 recovered, 8 were improved, and 8 were unimproved. It should be emphasized that the recovery-rate in manic-depressives and involutional melancholics is not comparable with the spontaneous recovery-rate in these psychoses. Only patients who did not show signs of recovery after a reasonable period were submitted to convulsive treatment. In the cases which improved or recovered, it was remarkable that after the first or second injection suicidal tendencies disappeared, appetite returned and normal sleep rhythm was restored. The quality of the recovery in favourable cases was excellent. Although most of these patients disliked the injections they were co-operative, and realized and appreciated the beneficial effects. For example, one patient who had made repeated determined suicidal attempts and suffered from ideas of poverty and hopelessness, after five convulsions became cheerful and hopeful and was herself astonished at her recovery, which she described as magical.

Psychoneurosis.—Only 2 patients of this group are included in the series. The first, a case of obsessional neurosis, was greatly improved and is discharged, and the second, a case of hysteria, recovered.

Number of convulsions required.—In cases of involutional melancholia and of the manic-depressive psychosis usually only a few convulsions, 2 to 7, were required to cut short the illness, while schizophrenic patients required a longer

course. The problem of how long to continue inducing convulsions in a particular case is a difficult one for which no rules can yet be given, and upon the physician's clinical intuition in this matter largely depends the success of the treatment. If too few convulsions are induced, relapse is likely to follow, while continuance of the treatment after the maximum improvement has been attained subjects the patient to unnecessary risk and may be harmful.

Relapses.—A disappointing feature of convulsion therapy is the tendency to relapse. Meduna states that relapse is always due to premature cessation of treatment. Several of my patients, however, had a tendency to relapse, which could not be overcome by prolonged treatment. Thus 1 patient had three courses of 20, 20 and 23 injections respectively, another had three courses of 16, 10 and 19 respectively, and another 18, 12 and 14 respectively, in the effort to reach permanent improvement, but all relapsed after cessation of each course of injections. In relapsing cases, it was found that the greatest improvement was brought about by the first series of injections, while ever shorter remissions were secured by the later injections. Govindaswamy, however, found that some of his patients could be maintained indefinitely in mental health by convulsions induced at intervals, and although none of my patients reacted in this way, similar effects are claimed by Nightingale and Harris.

One of my cases, a female, aged 49, suffering from catatonic stupor of two years' duration, was given 3 courses of injections of cardiazol in 1938. After the first convulsion she became responsive, and after five fits was remarkably well. After the 16th convulsion she was recovered and awaiting discharge. She remained well for about a fortnight, and then symptoms of elation and excitement appeared. She quickly relapsed into her former state and the second course of injections was commenced. After ten further convulsions she again improved, although she did not appear to be as stable as after the first course. After 6 days she again relapsed and was given a third course of 19 injections. During this course she was well for about 2 days after each injection, but relapsed before the next injection was due. As the course proceeded the injections were followed by ever shorter remissions. The remission secured by the first course was the best and longest. After the third course it was decided to give her a rest from injections for a year. During the year she relapsed, although not to such a low level as prior to treatment. At the end of the year she was given a course of 5 injections of triazol, with the result that she became again accessible and was able to go home, but relapsed after a week. An attempt is now being made to stabilize her improvement by combining triazol therapy with hypoglycæmic shock therapy.

A possible explanation of these events is that the production of some essential biochemical substance, lacking in the maladjusted organism, or the removal of an abnormal noxious substance, is effected by the stimulus of the

convulsions. In many cases the normal functioning thus restored continues independently of the stimulus, but in relapsing cases the organism fails to maintain the restored function when the stimulus is removed. On this hypothesis the relative ineffectiveness of a second course of injections following a relapse would be explained by the failure of the organism to respond to repeated stimulation.

In my whole series of 144 cases only 18 failed altogether to show some favourable response to the treatment. Forty-one cases (28% of the total) showed a tendency to relapse after improvement was manifest. Of these, 12 relapsed only partially, retaining some benefit from the treatment, while 27 relapsed completely and 2 became worse. Analysis of the cases which relapsed shows :

Of 82 schizophrenic patients, 23, or 28%, improved markedly or recovered, and subsequently relapsed more or less completely within a month. The average age of this group of relapsing cases was 30·5 years, while the average age of the recovered schizophrenic patients was 27 years. Four of these relapses were apparently due to too short a course of treatment, this being interrupted by fracture, parental interference, or the patients' own unwillingness to continue. On the other hand 4 others showed a tendency to relapse, which could not be overcome by a long course of treatment (over 40 convulsions). The remaining 15 had an adequate length of treatment, i.e., an average of 16 convulsions.

Of 27 manic-depressive patients, 5 were much improved following the convulsions, but subsequently relapsed more or less completely.

These 5 had all suffered from previous attacks, while the cases which recovered and did not relapse had had no previous attack, with the exception of one patient who had had one attack 20 years before. The suggestion is that fresh cases react well, while those in which the previous history shows a tendency to relapse seem to manifest this tendency soon after improvement by convulsion therapy has been obtained.

Of 24 involutional melancholic patients, 10 recovered and subsequently relapsed more or less completely. The average age of the relapsing cases in this group was 54·8 years, while the average age of the recovered cases in this group was 48·5 years. A few injections were commonly sufficient to effect recovery in cases of this group. Indeed, some depressed preoccupied patients of this class became hypomanic after 2 or 3 injections.

Comparison of Cardiazol and Triazol.

My series of 24 triazol-treated cases is small, but is comparable with the cardiazol series, the same hospital treatment having been applied to both, and the same criteria of improvement and recovery used. Moreover, the case-material is similar in the two series, the average duration of illness in the

cardiazol group being 4·7 years, and the average duration in the triazol group 5 years. Of the cardiazol-treated cases 34% were of duration less than two years, while of the triazol cases 39% were of less than two years' duration. This difference is, however, not sufficient to account for the difference in the remission-rate. Of the 111 cases treated with cardiazol alone, 25, or 22·5%, recovered, while of 24 cases treated with triazol alone, 10 recovered (41·7%). The following table shows comparison of the results of cardiazol and triazol treatment :

	Cardiazol.	Triazol.
Recoveries	25 (or 22·5%)	10 (or 41·7%)
Improved	47 (or 42·5%)	11 (or 45·8%)
Unimproved	39 (or 35%)	3 (or 12·5%)
Total	111	24

I was led to inquire further whether relapses were more common after cardiazol or triazol.

My figures show that of 111 cases treated with cardiazol 95 were immediately improved or recovered, but 32 (29%) of these relapsed, while of 24 triazol-treated cases 22 were immediately improved or recovered, but 4 (17%) of these relapsed.

These results are strikingly in favour of triazol, and although the numbers are too small to be dogmatic, I am of the opinion that triazol is the more effective in producing stable remissions.

Summary.

This paper is based on the treatment of 144 cases by convulsion therapy at Crichton Royal. The dosage of triazol is reviewed and the danger of excessive supplementary doses is shown. The intravenous route is to be preferred to the intramuscular route.

Three deaths directly following convulsion therapy, hitherto unpublished and personally communicated to me, are described. In general the treatment is safe, involving no great danger to life, and mortality being only 0·54%. Various fractures and dislocations may occur during the actual convulsion, a common and serious fracture being of the neck of the femur. Vertebral compression fractures occur occasionally but are not accompanied by grave consequences. The risk of activation of latent pulmonary tuberculosis can be minimized by careful selection of patients, based on physical examination, determination of sedimentation rate of blood-corpuscles and, if indicated, radiography of chest. Prolonged amnesia occurred in some cases, but it was observed that even in persons of middle age this was not common or of serious degree. Prolonged rise in blood-pressure was observed in many cases, and a possible

explanation is afforded by my experiments on rabbits, which showed damage to the kidney tubules following cardiazol and triazol administration.

Therapeutic results of convulsion therapy surpass the results of ordinary hospital treatment in schizophrenia, involutional melancholia and the manic-depressive psychosis.

Immediate improvement is shown in nearly all cases, but relapses are common.

The number of convulsions required in involutional melancholia and manic-depressive psychosis is small, usually 2 to 7.

Triazol in my experience is more effective than cardiazol in producing stable remissions.

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ANOMALOUS CARDIAC OCCURRENCES DURING CARDIAZOL TREATMENT OF THE PSYCHOSES AND PSYCHONEUROSES.

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IT is proposed, firstly, to summarize some anomalous cardiac occurrences observed and recorded by the writer in a series of seventy-five cases which underwent treatment with cardiazol for various types of mental illness in the mental observation wards of the Southern General Hospital during the period November 11, 1938, to April 30, 1939 ; secondly, to suggest an explanation for the occurrence of these anomalous cardiac occurrences, hereinafter referred to for the sake of brevity as abnormalities.

The writer's attention was first drawn to the occurrence of these abnormalities by a case which presented the clinical features of heart-block, with marked bradycardia, immediately after the occurrence of the convulsion. Routine auscultation was thereafter practised in all cases during and after the convulsion. It was then noticed that the occurrence of these bradycardias and other abnormalities was much more numerous than the literature on the subject might lead one to suppose.

The literature is that of Lubner (1), who describes a solitary case of auricular fibrillation, Dick and McAdam (2), who describe four cases of cardiac abnormality, and Kennedy (3). McAdam (4), in a separate paper, elaborates on three of these cases, and suggests as an explanation for the occurrence of the abnormalities a simple exhaustion of the heart muscle following upon the convulsion. Von Meduna (5) states categorically that he has found no evidence of cardiac abnormality clinically, electrocardiographically or by X-ray following cardiazol convulsion.

Following upon the very frequent discovery of these abnormalities during routine auscultation, the writer decided to investigate the series of cases treated with cardiazol between the above-mentioned dates.

The ages of the patients ranged from 17 to 65 years and their physical states from health to gross organic disease.

In connection with the latter, the writer found that von Meduna's dictum discountenancing the use of cardiazol in convulsive doses for patients suffering

from gross organic disease is, in general, untenable. In a recent paper (6), Meduna gives as absolute contra-indications to the employment of convulsive doses: (*a*) organic cardio-vascular disease, whether arterio-sclerotic, hypertensive or inflammatory; (*b*) acute febrile illness; (*c*) pregnancy; (*d*) active tuberculosis; and (*e*) abnormality of the blood or urinary constituents determined by complete laboratory examinations. Relative contra-indications are given as (*a*) exophthalmic goitre; (*b*) history of severe intracranial injury; (*c*) sero-positive syphilis; (*d*) latent tuberculosis; (*e*) confinement to bed for one year before treatment is undertaken.

The list of absolute and relative contra-indications seems to have been compiled on theoretical grounds alone, since von Meduna has had no fatalities and an absence of major catastrophes in connection with cardiazol treatment. The absence of theoretical justification for these contra-indications caused the writer to convulse, among others, patients who at the time of treatment were displaying such symptoms as albuminuria, severe glycosuria and acetonuria, and in addition an acute asthmatic attack, coryza and bronchitis with a temperature of 101° F., severe chronic myocarditis, in which group was one case whose transverse cardiac dullness was 4½ in. from the mid-sternal line and who showed evidence of mitral regurgitation, one case who showed signs, clinically and serologically, of advanced syphilis with marked arterio-sclerosis. In none of these cases did any adverse results occur. The mental states of the patients of the series were varied, and included hysteria, anxiety states, dementia præcox, paraphrenia, paranoia, frank manic-depressive insanity, manias (including puerperal), melancholias, a case of post-encephalitis, dementia paralytica and senile dementia.

In the investigation, attention was directed chiefly to electrocardiographic records, of which over four hundred were taken. In a few cases the somatic tremor during the post-convulsion confusion made the electrocardiograms unreadable. At all times, however, it was found possible to detect abnormalities in the cardiac rhythm (such as irregularities, tachy-and bradycardias) by simple auscultation; with but little practice it was found possible to determine the rhythm by simple auscultation, the sounds being easily determined from the coarse muscular susurrous of the muscles in the clonic phase and from the rhonchi and râles which make their sudden appearance in the chest after the convulsion.

Scope of the Investigations.

There being no doubt as to the existence of the abnormalities, the question which immediately presented itself was: Were the abnormalities met with due to the administration of cardiazol? The cases were accordingly divided into two groups: (1) those who were treated with sub-convulsive doses, and (2) those who were treated with convulsive doses of cardiazol, and

the E.-Cs. of the two groups compared.* This constituted the main line of investigation, from which several minor ones devolved; e.g., investigations to determine whether or not cardiazol had any action, direct or indirect, upon the heart; whether or not the convulsion consequent upon the administration of cardiazol could be ascribed to the cardiazol itself or to the sudden intravenous administration† of the volume of the 10% cardiazol solution into the circulation, etc. The scope of and the reason for these subsidiary investigations will become apparent from what follows below.

Description.

All the abnormalities met with, with one exception, occurred within five minutes of the termination of the convulsion, particularly in the brief "limp phase" (which immediately follows the termination of the convulsion) and, less so, in the period of stertorous breathing with return to consciousness which follows the limp phase, or, in the case of sub-convulsive doses, within five minutes of the administration.

For convenience of description, the abnormalities are divided into four groups:

(1) Fixed disturbances of rate—
  (*a*) Tachycardias.
  (*b*) Bradycardias.
(2) Irregularities.
(3) Mixed types.
(4) Others, a heterogeneous group.

No one of these types of abnormality was peculiar to any type of patient or to any one patient after any one convulsion, e.g., frequently the same E.-C. would show tachycardia, bradycardia and irregularity, i.e., an example of a mixed type, and it is in this sense that the term "mixed type" is used above.

The occurrence of examples of groups (2) and (3) preponderated over those of groups (1) and (4). The following figures are, for the most part, representative examples of the various groups.

(1) Fixed Disturbances of Rate.

(a) *Tachycardia.*

Tachycardia (used herein to denote a rate of 150 per minute or over) may appear immediately after the convulsion, it may follow gradually from a

* In obtaining these E.-Cs. a record was taken immediately before and, the plates of the leads having been left in position, records taken immediately after the convulsion (Group 2) or after the cardiazol administration (Group 1).

† Unless otherwise stated, "administered" in this article should be taken as applying to the intravenous administration of *x* c.c. of 10% solution of cardiazol in the shortest possible time, the solution being adjusted with di-sodium hydrogen phosphate to a H_2-ion concentration of pH = 7·5–8·0.

normal rate or its onset may be sudden from a normal rate. The reversion to normal is usually abrupt. When, apart from any other abnormality, the tachycardia was invariably found to be at the rate of 150 per minute save on two occasions (both in the same patient) where the rate was over 150 per minute, one of the two examples being given.

FIG. 1.—Case VI, female, aged 17, unmarried: hysteria. 6th injection: dose 4·0 c.c., productive of a convulsion. Lead IV (Groedel)*: note the

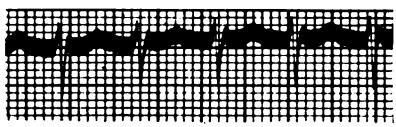


FIG. 1.

tachycardia of approximately 170 per min. Lead I showed tachycardia of exactly 150 per min. Rate before convulsion 105 per min.

(b) *Bradycardia.*

The rate of the bradycardias was found to vary within wide limits, e.g., 25–50 per min. The onset of the bradycardia was usually gradual and its return to normal equally so. It was usually of the sinus type, i.e., the stimulus to contraction arose at the sino-auricular node.

FIG. 2.—Case VIII, female, aged 42, married: manic-depressive psychosis, depressed phase. 7th injection: dose 5·6 c.c., productive of a convulsion. Lead II: bradycardia at the rate of 26 per min., of the sinus type, the Q.R.S.

FIG. 2.

complex being preceded by a P wave; note the varying amplitude of the R deflections and the very high T waves. This bradycardia was of gradual onset. Rate before the convulsion 75 per min.

FIG. 3.—Case IX, female, aged 28, married: manic-depressive psychosis, hypo-maniacal phase. 1st injection: dose 3 c.c., not productive of a

* Lead IV in this article should be taken as applying to Groedel's right ventricular partial electro-cardiogram. Lead V should be taken as applying to Groedel's left ventricular partial electrocardiogram (see Franz M. Groedel, *Das Electrokardiogramm*, Dresden and Leipzig, 1934 edition).

convulsion. Lead IV (Groedel): intense bradycardia, falling at one period to 25 per min. A diphasic P wave was present in one record, with the inversion

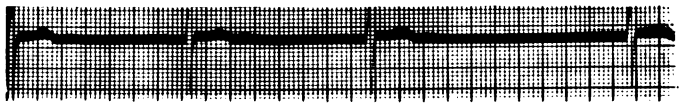


FIG. 3.

of the P wave in the middle and bottom records, not showing well on the print. This bradycardia was of gradual onset and the deflections shown on the E.-C. before administration were normal. Rate before administration 75 per min.

(2) IRREGULARITIES.

FIG. 4.—Case V, male, aged 27, unmarried: dementia præcox. 11th injection: dose 8·2 c.c., productive of a convulsion. Lead I: typical sinus

FIG. 4.

irregularity of a slow rate, also shown in Leads II and III. Rate before the convulsion 95 per min.

FIG. 5.—Case XI, female, aged 30, married: mental defective with a superimposed dementia præcox. 9th injection: dose 5·6 c.c. Lead III: fast irregularity of a sinus type: note the variations in amplitude of the R deflections and the occurrence of waves toward the end of the record similar to

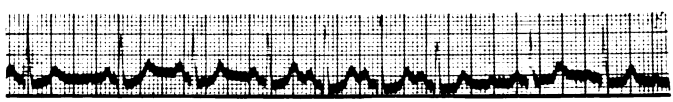


FIG. 5.

those obtained in cases of auricular fibrillation, but also possibly due to somatic tremor. Records of cases of this type are very numerous; clinically, the fast irregularly irregular rate and the deficit between the pulse and cardiac rates that is found make them indistinguishable from cases of auricular fibrillation. Lead I showed a slow sinus irregularity of about 50 per min., and Lead II a slightly faster irregularity intermediate between the rates of Leads I and III. Rate before the convulsion 95 per min.

FIG. 6.—Case I, female, aged 32, married: dementia præcox. 26th injection: dose 9·0 c.c., productive of a convulsion. Lead II: coupling of beats, the second of each of the coupled beats being a ventricular extra-systole. Lead I showed a slow sinus irregularity, and Lead III an irregularity

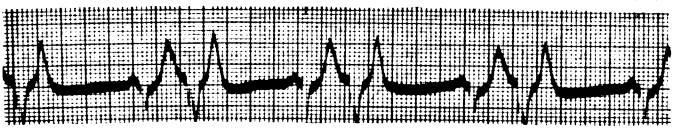


FIG. 6.

which passes clinically for auricular fibrillation. Rate before injection 85 per min. (This patient had shown cardiac abnormality after each of her preceding twenty-five convulsions and, after three of these previous convulsions, there had been coupling of beats.)

FIG. 7.—Case V, male, aged 27, unmarried: dementia præcox. 11 previous injections with abnormality after every convulsion. 50·0 c.c. (5·0 grm.) orally (vide infra), followed in forty minutes by the intravenous administration

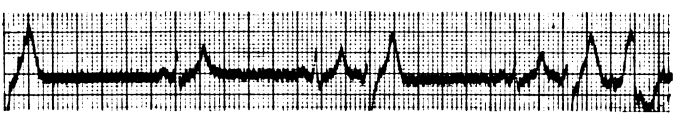


FIG. 7.

of 9·2 c.c. with the production of a convulsion. Lead II: note the occurrence of three left ventricular extra-systoles, the last of which is immediately followed by a left ventricular extra-systole. Lead I showed bradycardia of 40 per min. Rate before injection 83 per min.

FIG. 8.—Case I. See legend to Fig. 6 above. 27th injection: dose 10·0 c.c., productive of a convulsion. Lead I: suggestive of nodal rhythm with absent

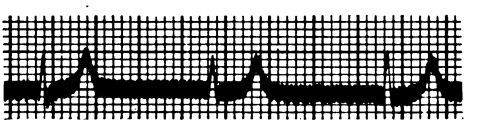


FIG. 8.

P wave contrasting with the nodal rhythm of Fig. 3, where the P wave was present but inverted. (In all cases treated, nodal rhythm was very commonly met with.) Rate before injection 85 per min.

(3) MIXED TYPES.

FIG. 9.—Case IX. See legend to Fig. 3. 3rd injection: dose 4·0 c.c. of unneutralized 10% cardiazol solution, productive of a convulsion. Lead II:

FIG. 9.

note the sudden conversion of a moderate degree of bradycardia of approximately 50 per min. (also present in Lead I) into a moderate tachycardia, which in Lead III attained a rate of 115 per min. Rate before injection 77 per min.

(4) OTHERS.

This heterogeneous group comprised such phenomena as changes in the shapes and dispositions of the deflections, delay in the conduction of the T wave, splintering of the R wave (both upstroke and downstroke), change of preponderance, e.g., from a left ventricular to a right ventricular and *vice versa*, etc.

FIG. 10.—Case XLI, control, male, aged 37, married: advanced disseminated sclerosis. 1st injection: dose 5·0 c.c., repeated once (10·0 c.c. in all),

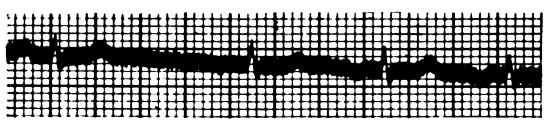


FIG. 10.

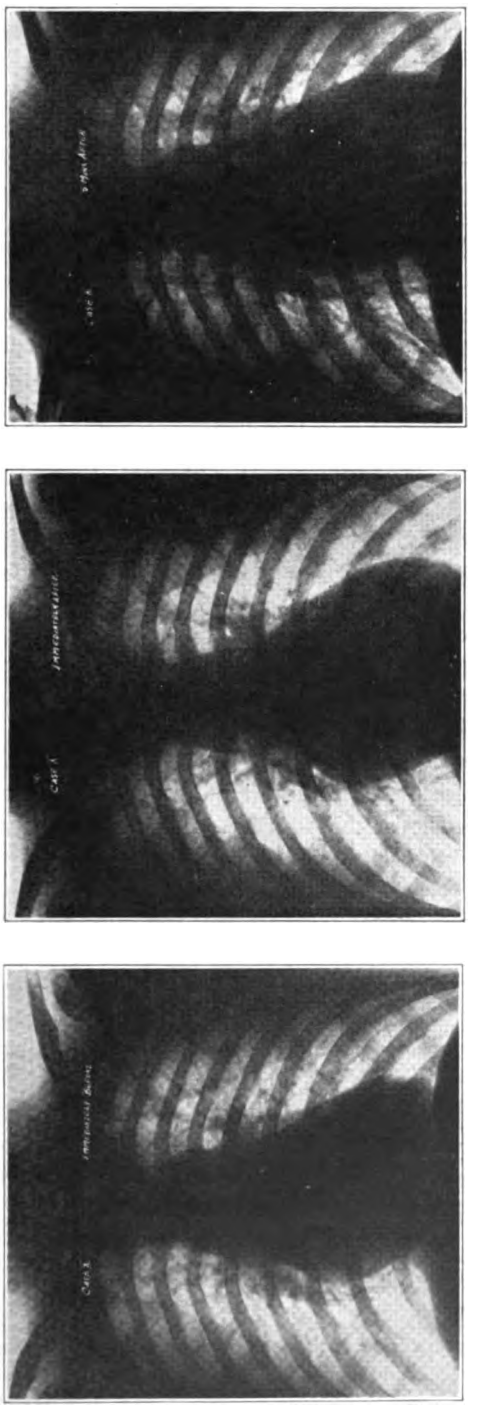
productive of a convulsion. Lead III: note irregularity of rate (also present in Leads I and II) and also the inverted P wave, not present in E.-C. before. Rate before injection 60 per min.

FIG. 11.—Case X. See legend to Fig. 7. 13th injection: dose 8·0 c.c., productive of a convulsion (*a*) immediately before convulsion, (*b*) immediately after, (*c*) five minutes after. Note the acute cardiac dilatation shown in (*b*) and recovered from five minutes later in (*c*).

DISCUSSION.

It may be stated generally that, both in cases with normal and abnormal hearts,* ordinary "analeptic" doses of cardiazol (e.g., 2 c.c. administered

* Two of the cases had severe chronic myocarditis.



a *b* *c*

FIG. 11.

intravenously and slowly through a fine-bored needle) produce no effect on the E.-C.

With regard to 2 c.c. doses given quickly (e.g., in a half to one second or less) and to still larger subconvulsive doses, such as 3 or 4 c.c., it was found from the study of the E.-Cs. of twelve cases that these doses were productive of no change or a slight acceleration or slowing of the cardiac rate, but that (with one exception) there was no irregularity or other abnormality to be noted in the shape or disposition of the P, Q, R, S or T deflections unless the dose (intended to be a sub-convulsive one) convulses (which is common: indeed, as little as 1·5 c.c. may convulse), when the convulsion thus produced may or may not be followed by a cardiac abnormality in the sense previously defined.

The exception referred to is that of Fig. 3, where not only is there an intense bradycardia, but also an irregularity of rate and an alteration in the shape and disposition of the deflections.

It is necessary at this point to discuss the method of action of cardiazol in so far as it bears a relation to mental disorders. From a study of (now) over 100 cases and the administration of over 1,500 doses, the writer is of the opinion that any effect resulting from the administration of cardiazol is due not to any primary action on the heart or lungs or to any direct action on their respective centres on the medulla oblongata, but to direct excitation of the higher centres of the brain. Preceding a convulsion there is invariably an aura, thus indicating that the cardiazol has reached the central nervous system. It is not until some time after the occurrence of the aura (never less than three seconds) that the convulsion occurs or, with sub-convulsive doses, any increase or decrease in the cardiac rate or a diminution or deepening of the respiratory excursion. The writer believes this to indicate that the convulsion is not the effect of the cardiazol on the lower motor neurones, but that it follows the stimulation of the upper centres with a secondary effect on the lower neurones.

It is now proposed to take the three phenomena, the aura, the cardiac rate and the respiratory excursion, for separate discussion and then, secondly, to demonstrate how they are or may be correlated.

To take the aura: the administration of cardiazol is invariably accompanied, even in small doses given quickly, by an aura. This aura for any given patient is practically constant provided the same dose is given in the same time, and the disturbing nature (*vide infra*) of the aura is directly proportional to the dose administered. Thus a patient with a skin condition used as a control* could be depended upon to experience the smell and taste (stimulation of the olfactory and gustatory centres) of toffeed almonds after the administration of 1 c.c. and, after the administration of 2 c.c., he invariably felt that he was being "mildly electrocuted".

* It was found as an incidental fact that in patients who had skin diseases and who were treated with convulsive doses of cardiazol the skin diseases could be depended upon either to improve or cure.

When the dose of cardiazol administered reaches higher amounts, such as 3–4–5 c.c. or more, such as is ordinarily given to mental patients, the aura becomes terrifying in the extreme. Depending upon the intelligence and gift of verbal expression possessed by the patients, the auras are variously described, of which the following are a few examples: "Like murder", the mind standing still, but the head hurtling away from the mind at a speed of 30 m.p.h., "hovering like a disembodied spirit on the brink of eternity", hurtling downwards through an illimitable inky nothingness, being roasted alive in a white-hot furnace, going suddenly blind, "like being in a 'bus smash and wakening up in hospital", and occasionally when asked about the aura the patient is quite inarticulate and can only shudder.

It will be observed that common to all these cardiazol auras is the experiencing of fear, and the writer has never dealt with one case or even one injection where the absence of fear could be conclusively demonstrated. Even in the case where the patient experienced the smell and taste of toffeed almonds, the aura was accompanied by a vague foreboding—a variety of fear.*

From a psychosomatic viewpoint, it is a commonplace that fear may be reacted to chiefly in two ways, even by the same patient at different times and under differing circumstances. In the first place, there is the well-known "flight" reaction, in which the sympathetic nervous system has predominant control. In the second place, there is the fear which "paralyses", in which the parasympathetic nervous system has predominant control, with the production of such phenomena as bradycardia (the heart temporarily "standing still"), diminished depth of respiratory excursion, a desire to defæcate or an involuntary motion of the bowels. That there is or may be a slowing of the pulse and cardiac rate† in people who have been frightened and that people do actually die of fright (7) is well known.

As the rapid administration of cardiazol causes fear, it would be not unreasonable to expect in these cases the phenomena associated with the two types of reaction (flight and paralysis) just mentioned. Such signs are found and, as in normal life, the flight reaction numerically preponderates over the paralysis reaction.

* For a rough pharmacological measure of this fear, Case X may be cited. Ordinarily, ʒij paraldehyde was an excellent night sedative for this patient, but ʒviij paraldehyde per rectum was quite ineffective in producing sleep or even a dulling of the faculties—he was kept awake by the fear of the injection which he knew was coming. The same occurs using other sedatives, e.g., morph. sulph. gr. ½ and hyoscine hydrobrom., gr. $\frac{1}{100}$.

It is, in the writer's opinion, due to the fear that the efficacy of cardiazol in the treatment of mental disorder results, and not to the convulsion or to any postulated and hitherto undemonstrated metabolic happening as is suggested by von Meduna. A separate paper on the psycho-dynamics of cardiazol treatment is in preparation.

† This subject is mentioned very briefly in Sir T. Lewis's *Diseases of the Heart*, 2nd edition, 1939, p. 98. The writer has noticed the same phenomena occur in himself when he has been both the agent and witness of unexpected seeming catastrophes in connection with the administration of cardiazol. He has questioned several medical colleagues upon the same subject, and is quite satisfied that a bradycardia of varying severity is among the signs of the paralytic type of reacting to a fright.

It is difficult, however, to obtain E.-C. records, for, to produce intense fear, large doses of cardiazol are required and such usually convulse within a period too brief (generally under ten seconds) to obtain a record, or, when it is obtainable, the somatic tremor arising from the patient's agitation makes the record unreadable; besides, handling of the patients to prevent them from injuring themselves also produces blurred records.

In such cases, therefore, one is forced to rely on clinical observation, e.g., in the flight reaction there is apparent an increase in the respiratory rate and depth of respiratory excursion, explicable, in the writer's opinion, by the fear rather than by a direct action on the medulla—the hyperpnœa of emotional states is well known. In the other and much less common paralytic type of reaction the respiratory rate and excursion are markedly diminished. In one such case an E.-C. *was* obtained; the patient had the feeling of being coffined prior to being killed with the injection; this feeling passed into one wherein she believed herself to be dead. Her resemblance to a corpse was a very close one; she was extremely pale, lay motionless, stared fixedly and signs of respiration were not detected—an extreme case of the paralytic reaction, and the E.-C. showed an intense bradycardia of gradual onset—Fig. 3. In another case the heart-rate fell from 75 to 60 per minute after the administration of 2 c.c.

The patient whose E.-C. is shown in Fig. 3 was given a further 3 c.c. two minutes after the bradycardia was at its greatest and another 4 c.c. was administered half a minute later (10 c.c. in all), after which latter dose the patient convulsed.* The E.-C. after the convulsion showed no abnormality beyond a slight fluctuation in the cardiac rate ranging from between 50 and 100 per minute. The complexes showed no alteration. These fluctuations in rate are very common and comprise the majority of abnormalities. The intravenous dose was again administered in the same time two days later. The cardiac rate before injection was 65 per minute, and the rate after injection did not drop below 50 per minute and showed no alteration in the shape of the complexes. The aura of this second day was different (the exception to the general rule that the aura is constant for the same dose) as the patient said that she "was ready for it"; in other words, the element of the unexpected had gone and she was thus able to brace herself against a coming ordeal.†

In respect to other causes of bradycardia, in the case of Fig. 3 heart-block can be excluded. The existence of a high vagal tone in the patient (a gradual

* Paradoxically, when a patient fails to convulse after a large dose of cardiazol has been administered, it is often desirable for humanitarian as well as for nursing reasons to terminate the patient's mental distress resulting from the aura by giving a convulsive dose forthwith, and it was for this reason alone that, although the author is convinced of the efficacy of subconvulsive doses in cases of mental disorder, convulsive doses were given in the majority of cases.

† There is evidence in all cases that all patients endeavour (after the first injection) to brace themselves against the ordeal of the aura. The slight degree of tolerance to cardiazol in practically all cases may be an indication of this.

slowing of the cardiac rate from 75 to 60 per minute on pressure of the eyeball) does not vitiate the hypothesis, as the stimulus acting on the autonomic nervous system causes the predominant part (the parasympathetic) to manifest itself.

It should be noticed that in two cases, one of which had severe chronic myocarditis, the rapid intravenous injection of 20·0 c.c. of distilled water produced a slowing of the heart-rate from 93 to 70 and from 65 to 60 per minute; in a third case, with severe chronic myocarditis, the rate was unaltered. The slowing of the cardiac rate in these two cases was so infrequent as to be negligible in considering the E.-Cs. of the whole series. These findings dispose of sensitization due to "speed shock" (8). The administration of 20·0 c.c. distilled water intravenously was followed in all three cases within two minutes by 2 c.c. cardiazol intravenously given in under one second. No convulsion followed in any of the three cases or any signs of a "nitritoid crisis"—or indeed signs of any description other than the above-noted.

These abnormalities still occur if cardiazol be administered alone in solution (see Fig. 9) without the addition of di-sodium hydrogen phosphate.

The absence of abnormality save in Case IX, Fig. 3, resulting from sub-convulsive doses of cardiazol points to the occurrence of the convulsion as the necessary factor in their production,* and it is difficult to escape the hypothesis advocated by McAdam that these abnormalities are due to a simple exhaustion of the heart muscle, to which the writer would add the proviso of an anoxæmic heart muscle unaccustomed to the strain of an epileptic attack.

No E.-Cs. immediately before and after a single attack of idiopathic epilepsy were able to be taken, but such E.-Cs. were obtained during *status epilepticus* in a case of idiopathic epilepsy before and after the 42nd (major) convulsion following his admission to hospital, and no difference between the two E.-C.s is to be noted save a very slight difference in rate; possibly this patient's numerous previous attacks extending over a period of twenty years had "accommodated" his heart to any adverse effects of the convulsions.† An E.-C. of this patient was taken two months after his dismissal from hospital and it showed no difference from those taken during his period of *status epilepticus*.

There is abundant evidence of exhaustion after the convulsion therapeutically induced with cardiazol; the cessation of respiration with increasing anoxæmia and cyanosis, the increased cardiac rate during the convulsion (also present in cases of idiopathic epilepsy), the extreme violence of the

* The writer has an E.-C. record of such abnormality occurring after a convulsion produced by triazol. Other cases are recorded—see Molony and Conlon, *Journ. Ment. Sci.*, September, 1939.

† Support for this accommodation theory (for want of a better term) of the writer's is to be found in his inability to find references on the subject of cardiac abnormalities occurring after attacks of idiopathic epilepsy, despite the great antiquity of the disease, although the writer obtained an irregularity in one such other case (a *status epilepticus* of idiopathic epilepsy) and McAdam (personal communication) has had two, one after a convulsion of a *status* and the other after a single attack of idiopathic epilepsy. Unfortunately, E.-Cs. of these cases were not obtainable.

muscular movements, which may cause fractures (9), are sufficient reasons for exhaustion in themselves. Of this exhaustion there is abundant clinical evidence—tricuspid bruits were heard in three cases after the convulsion, mitral bruits in three, reduplicated first sounds at the tricuspid area in five cases; sometimes the first sound would disappear altogether at the mitral and tricuspid areas (although a pulse was felt at the wrist): the sudden appearance in the chest of rhonchi and râles after a convulsion is an indication of an exhausted heart as it is, say, in decompensated heart disease; the enlargement of the area of cardiac dullness to the left, which is comparatively often found to percussion (sometimes in the writer's experience to the extent of half to three-quarters of an inch); the delayed T waves often found (delay in conduction); the high T waves such as are found in other relative anoxæmic states, such as after normal exercise—all these facts point unmistakably to an (acute) exhaustion and anoxæmia of the heart muscle.

The cardiac enlargements met with clinically were verified by X-ray examination. The eight cases were unselected, with one exception in which a frank cardiac dilatation was found clinically. A straight X-ray was taken immediately before the convulsion, after which the patient was convulsed lying on top of the unexposed second X-ray plate, which was exposed immediately after the last of the clonic movements of the convulsion, the necessary adjustments to the unconscious patient having been made; the third plate was exposed 4–5 minutes after the termination of the convulsion as there were clinical (e.g., disappearance of cardiac abnormalities and the rhonchi and rales) and E.-C. evidence that the hearts of those convulsed with cardiazol had recovered from their acute dilatation in that period, which point was confirmed by X-ray (Fig. 11, *a*, *b*, *c*). Five of the cases showed enlargement which taken individually might not have been regarded as significant, but taken together with the frank enlargement found in the remaining three of the cases, may be regarded as evidence of acute dilatation in every case.

Case XXI died during a convulsion "*in statu epileptico*". The post-mortem examination demonstrated that the right side of the heart was much dilated and the organs of the trunk, especially the lungs, were acutely congested. A sub-arachnoid hæmorrhage of considerable size had occurred into the posterior cranial fossa; a porencephalic cyst, 1 cm. in diameter, was situated in the lateral portion of the left cerebellar hemisphere. Although the sub-dural hæmorrhage was undoubtedly a contributory factor in causing death, from a general consideration of the case the opinion was formed that the main factor was a gradual myocardial insufficiency associated with acute dilatation of the right side of the heart.

The duration of the cardiac abnormalities above described was not found to exceed five minutes (the time taken for the acutely dilated heart to return to normal) save in one case very similar to the one who died. This second case is illustrative of many points.

CASE V.—Cardiazol treatment had been discontinued by a previous house-physician owing to the onset of auricular fibrillation during a convulsion, and the patient's mental and physical condition had progressively deteriorated over the intervening six months' interval. Cardiazol treatment was re-instituted by the writer and produced both mental and physical amelioration. The patient showed cardiac abnormality after each of his convulsions, particularly of the "auricular fibrillation" type referred to on p. 264. On April 28, 1939, the day he would normally have received his 12th convulsive dose, as part of a subsidiary investigation into the effects of cardiazol when administered orally, he was given 50 c.c. (5·0 grm.) of cardiazol by mouth at 3 p.m.

The B.P. (150/90 mm. Hg.) and E.-C. did not alter, and clinically no change was noted in the depth or rate of the respiratory excursions.

As he did not seem likely to convulse, he was given 9·2 c.c. intravenously at 3 40 p.m. (see Fig 7).

At 4.45 p.m. he took the first of a series of six major convulsions without intervening lucid periods which lasted until 10.40 p.m.

He was next seen by the writer at 1 a.m. of the following morning, being comatose, incontinent and of a peculiar bluish-grey pallor. He was in a state of profound collapse with a B.P. of 90/70 mm. Hg. He had had two hæmatemeses (each of 5 oz., coming presumably from the congested stomach, such as was found in Case XXI, who had died in *status epilepticus*), and later, when the writer was still present, a third of one ounce.

The heart-rate was then regular, though the cardiac sounds themselves were soft in tone.* The cardiac rate was 122 per min., and the area of cardiac dullness enlarged from 3½ to 4½ in. to the left of the mid-sternal line in the fifth interspace. The temperature was 102° F. Owing to the ceaseless fibrillary and myoclonic movements which the patient exhibited, together with spasmodic twitchings of the whole limbs and trunk, it was found impossible to take an E.-C.

The persistence of these movements and the time taken for active treatment prevented an E.-C. being taken until 5.30 a.m., when no abnormality was revealed save a solitary extrasystole occurring very late (at the end of the R wave) in Lead III.

During the course to complete recovery from the "*status*" (a broncho-pneumonia and a slight hæmoptysis intervening) no further abnormality was noted.

The persistence of cardiac abnormality for seven hours ten minutes after the last convulsion of the "*status*" is easily understood—the extreme exhaustion of the patient and the dilatation of the heart, which was still present at 5.30 a.m., but returned to normal at the end of thirteen hours ten minutes

* This contrasts markedly with the cardiac sounds that are to be heard after a solitary cardiazol convulsion when they are of a clear and more determined tone such as is found in a patient excited from any cause, e.g., lying on an operation table awaiting an operation for which no sedative premedication has been given.

at 11.30 a.m., when normal E.-Cs. were obtained. The physical condition of the patient did not permit of an X-ray being taken.

With regard to the ultimate effect of cardiazol upon the heart, the writer is unable to say anything beyond the fact that those patients who were able to be followed up demonstrated no abnormality at any time, either clinically or electrocardiographically, even after several months' dismissal from hospital, and during which time they had been leading normal, active and healthy lives.

Summary.

The total number of cases (excluding controls) herein reviewed was 75. Of this number, 65 were given convulsive doses, 42 of these cases showing abnormalities, i.e., 65%. Ten cases were treated with subconvulsive doses, and of these ten only one showed abnormality.

In view of the fact that circumstances precluded the taking of an E.-C. of every patient after every convulsion (at one period seventeen males and twelve females were treated in one afternoon), and that frequently an E.-C. showed abnormality where simple clinical methods showed none, it is very probable that the figure given above for the occurrence of cardiac abnormality following cardiazol convulsions would have been much higher (probably in the region of 100%) had a more rigorous investigation been possible.

No relation was determined between the occurrence of these abnormalities and, say, age, sex, stature, state of nutrition, physical health, duration of the convulsion, the dose of cardiazol administered or its rate of administration, the depth of cyanosis, etc.

Conclusions.

A series of cases which underwent treatment with cardiazol is reviewed and the following conclusions drawn :

(1) Cardiazol administered intravenously in ordinary "analeptic" doses (e.g., 2 c.c. given slowly) has no effect either directly or indirectly upon the heart ; it is equally without effect when given by mouth.

(2) Administered quickly (e.g., within half a second) ordinary "analeptic" doses (e.g., 2 c.c.) and larger sub-convulsive doses may produce no change, an increase or decrease of the cardiac rate, the increase or decrease being a consequence of a primary stimulation of the higher centres of the brain and the production of an aura.

(3) Administered in still larger doses, cardiazol produces convulsions (not due to the sudden entrance of fluid into the circulation) which are epileptiform in nature, but differ from the convulsions of idiopathic epilepsy in the occurrence of such phenomena as cardiac abnormalities (anomalous cardiac occurrences) which result from an exhaustion and anoxæmia of the heart muscle as a consequence of the convulsion—a heart muscle unaccustomed to the strain of a

convulsion and which undergoes a varying degree of acute dilatation. This exhaustion and anoxæmia are soon recovered from and leave no permanent damage to the heart.

(4) Paradoxically, the occurrence of these abnormalities should be regarded as normal after a convulsion and is thus no indication for cessation of treatment.

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BRAIN RESPIRATION AND GLYCOLYSIS IN CARDIAZOL CONVULSIONS.*

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SINCE Hildebrandt (1926) described the convulsant effect of cardiazol injection, several studies have been carried out on the mechanism of such convulsions. Zung and Tremonti (1931) suggested a direct action on the respiratory centre when cardiazol is used as a stimulant; Kerr and Antaki (1937) found no effect on brain glycogen or phosphocreatine in cardiazol-induced convulsions; Hashimoto (1937) found differences in distribution of calcium and potassium ions in the central nervous system after cardiazol. Goodwin and Lloyd (1938) recorded a direct effect on brain potential changes as shown on oscillographic records. Leibel and Hall (1938) found a large (75 per cent.) diminution of cerebral blood-flow at the onset of cardiazol convulsions. Weigand (1938) found no effect on liver glycogen or vitamin A content, reducing power of suprarenal cortex or blood picture. Denyssen and Watterson (1938) and Watterson and Macdonald (1939) attribute the convulsions to action on the vasomotor centre and note the action of vasodilator drugs in inhibiting convulsions. Wortis (1938) quoted by Quastel (1939) found no effect on brain respiration.

Labes, Wedell and Soehring (1937) found that sublethal doses of cyanide sensitized animals to cardiazol (50 per cent. decrease in the minimal convulsive dose), and suggested that there might be some similarity of action between cyanide and cardiazol. As cyanide is known to produce a very large inhibition of tissue respiration generally, it was considered worth while, in the present work, to examine the effect of cardiazol on the respiration and glycolysis of isolated cerebral cortex. The methods of Warburg (for description see Dixon, 1934) were employed.

Slices of dry weight about 4 mgm. were cut from cerebral cortex of rat brains and suspended in glucose-Ringer (2 ml.) in 10 ml. Warburg conical flasks. Oxygen uptake was determined by the direct method in an atmosphere of oxygen, carbon dioxide being absorbed in 0·2 ml. 5 per cent. potassium hydroxide in the centre cups. Measurement of anaerobic glycolysis was carried out in 5 ml. flasks containing 1 ml. glucose-bicarbonate Ringer solution,

* A paper read at a meeting of the South-Western Division of the R.M.P.A. held at the Burden Neurological Institute, Bristol, on October 26, 1939.

the flasks being filled with 95 per cent. nitrogen–5 per cent. carbon dioxide mixture. The lactic acid produced in glycolysis liberates carbon dioxide from the bicarbonate, and this is measured manometrically.

The results are expressed in the usual manner :

Respiration :

$$Q_{O_2} = -\frac{\mu l.\ \text{oxygen used per hour}}{\text{Mgm. dry weight tissue}}.$$

Anaerobic glycolysis :

$$Q_{CO_2}^{N_2} = \frac{\mu l.\ CO_2 \text{ evolved per hour}}{\text{mgm. dry weight of tissue}}.$$

All measurements were carried out at 37° C.

In one set of experiments, the effect of cardiazol in vitro was determined by addition of the drug to the tissue in the flasks. In carrying out experiments of this kind a difficulty is met with in the fact that different slices from the same brain may show some variation in activity. Accordingly, it was considered advisable to measure the respiration and glycolysis of the slices over a suitable initial period, add cardiazol from the side-bulb, and redetermine the activity. The respiration and glycolysis of control slices without cardiazol were determined over the same time intervals to allow for any possible falling off of activity with time. The results of such experiments are shown in Tables I and II. It will be seen that there is no apparent difference of behaviour between control and experimental slices.

In view of the possibility that direct addition of cardiazol might not simulate the conditions of cardiazol injection, some further experiments were carried out on cerebral cortex of animals which had been injected with cardiazol. Rats (60–80 gm.) were used and injected subcutaneously with cardiazol solution (6–9 mgm./100 gm. body-weight). This was sufficient to induce prolonged convulsions.

The animals were killed at different times from the onset of the convulsions, and measurements of respiration and glycolysis carried out on the cerebral cortex. The results are shown in Table III. No appreciable difference emerges between normal and treated animals.

Experiments carried out on the total respiration and glycolysis of slices cut at random from the cerebral cortex cannot of course exclude the possibility of a highly localized effect on respiratory processes in some particular area, an assumption which is, however, not very probable on general biochemical grounds ; or that there might be an effect on one of the many processes involved in the total respiration, which though quantitatively small, might be highly important for functional activity.

TABLE I.—*Respiration. Cardiazol in vitro. Cerebral Cortex Slices (3–4 mgm. dry weight) in 2 ml. Ringer. Cardiazol added to the Flasks.*

Q_{O_2}.			
Without cardiazol.		With cardiazol.	Added cardiazol.
A.	B.		
−6·6	−8·3	..	..
−7·4	−8·0	..	..
−7·0	..	−8·0	1 mgm.
−7·8	..	−9·3	1 ,,
−7·6	..	−8·8	2 ,,
−7·5	−7·5	..	..
−7·3	..	−7·1	2 mgm.
−8·4	−6·1	..	..
−9·0	..	−7·9	2 mgm.
−8·2	−6·7	..	..
−7·9	−9·8	..	..
−6·8	..	−6·9	2 mgm.
−7·6	−7·5	..	..
−7·6	..	−7·6	2 mgm.
−7·3	−6·9	..	..
−7·1	−6·3	..	..
−7·6	..	−6·4	2 mgm.
−8·7	−7·0	..	..
−8·2	..	−6·2	2 mgm.
−7·5	−6·0	..	..
−8·5	..	−6·9	2 mgm.

Column A: Respiration in initial period (40 min.) before addition of cardiazol to experimental slices.
Column B: Respiration of control slices during experimental period.

TABLE II.—*Anaerobic Glycolysis. Cardiazol in vitro. Cerebral Cortex Slices (3–4 mgm. dry weight) in 1 ml. Bicarbonate-Ringer. Cardiazol added to the Flasks.*

$Q^{N_2}_{CO_2}$.		
Without cardiazol.		2 mgm. cardiazol added.
A.	B.	
+17·4	..	14·7
+16·5	13·8	..
+24·2	..	20·7
+23·3	17·3	..
+19·2	..	16·3
+18·1	15·5	..
+17·6	..	14·5
+18·8	17·3	..
+17·3	..	14·5
+22·0	..	19·6

Column A: Glycolysis in initial period (15–20 min.).
Column B: Glycolysis of control slices in experimental period.

TABLE III.—*Cardiazol in vivo.*

	Normal. N_2 Q_{CO_2}.		Cardiazol-injected. N_2 Q_{CO_2}.	Min.
	16·4	.	14·7	
	16·9	.	25·2	
	18·2	.	19·6	11
Mean	17·2	.	18·5	
	20·6	.	24·4	
	19·9	.	23·8	30
Mean	20·2	.	24·1	
	23·2	.	18·8	
	25·7	.	20·6	
	17·2	.	16·3	15
Mean	22·0	.	18·6	
			17·6	
			19·7	
			20·6	12
		Mean	19·3	
			20·0	
			21·1	0
		Mean	20·5	
	Q_{O_2}.		Q_{O_2}.	
	−8·8	.	−9·1	10
	−7·4	.	−9·1	
	−9·9	.	−9·6	4
	−9·2	.	−9·5	

The column headed "Min." indicates the time of killing after the onset of convulsions.

Further, it must be admitted that some uncertainty exists as to how far biochemical processes occurring in isolated cerebral cortex resemble those involved in functional activity in situ. At present the former class of processes is much more accessible than the latter, and so much remains to be found out about them that efforts in this direction cannot be considered as valueless; and further knowledge of this type of process must in fact precede advances in knowledge of the relationship of function to biochemistry, in which the neurophysiologist is primarily interested.

To sum up, the results quoted seem sufficient to show that cardiazol does not produce any general, well-marked disturbance of the main processes of respiration and anaerobic glycolysis in the isolated cerebral cortex of rats.

Summary.

1. Cardiazol added in vitro to surviving rat cerebral cortex slices does not influence oxygen uptake or anaerobic glycolysis.

2. No significant differences could be found in the oxygen uptake and anaerobic glycolysis of cerebral cortex slices as between normal and cardiazol-injected animals.

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THE INFLUENCE OF THE ENDOCRINES ON CEREBRAL CIRCULATION.*

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THIS paper represents a preliminary attempt to investigate some aspects of the influence exercised by the endocrine glands on the cerebral blood supply at various stages of development.

Our method consisted of a direct chemical determination of the blood content in the brain. For the quantitative estimations we used a method for small portions of tissue suggested by Golla and Tingey (1), which is based on the extraction of blood pigments by means of acetone acidified with HCl. The hæmatin content in the brain extract was determined with the Pulfrich photometer, and the hæmatin content of the blood of each animal was measured in the same way. After determination of the extinction coefficient of the extract of a measured amount of brain tissue and of a known quantity of blood extract, the total blood content of the brain could be calculated.

The rat was chosen as the experimental animal, because rats are especially suitable for work on the physiopathology of the brain when long serial experiments are necessary. The operations that can be carried out on this animal take very much less time and present fewer sources of error than those with larger animals.

The rat was killed by fixing the head in a clamp, so that the circulation was immediately interrupted between the brain and the rest of the body. It was then decapitated below the clamp and laid aside for at least 20 minutes, in order that the blood which was in the head at the time of clamping might coagulate. The brain was then dissected out, and the surface freed from dura and pia, ground up with sand, and extracted.

Up to the present we have only estimated the blood content of the brain as a whole, but it is hoped subsequently to investigate the content of the different parts of the brain.

Before mentioning any special influence of the endocrine system on the cerebral blood content it is necessary to point out that during the different periods of life the relation between the brain circulatory system and the amount of brain tissue varies. The immediate post-natal development of brain tissue and brain vessels does not show any parallelism. Table I shows how the blood content changes throughout the different ages. In the four-day-old rat it is about 1·7 per cent., but within a few days it decreases to the

* A paper read at a meeting of the South-Western Division of the Royal Medico-Psychological Association held at the Burden Neurological Institute, Bristol, October 26, 1939.

lowest amount of 1·2 per cent., increasing again up to the age of three months, when it is 2·2 per cent. Some significance may be attached to the fact that the dry substance of the whole brain of the new-born animal (as shown in Table II) is about half that of the adult animal. From this table it may be seen that the amount of the dry substance of the brain is continuously increasing during the first few months of life.

Table III shows that as early as ten days after the removal of the pituitary the amount of blood in the brain is markedly decreased.

The blood content in the brain of castrated animals is also considerably lowered. Table IV shows that it is possible by means of treatment with sex hormones for eight days to increase the brain blood content in these animals.

Normal rats were also influenced by administration of sex hormones. This was particularly significant in young animals which had been treated with sex hormone over a long period of time. Increases of up to 100 per cent. were by no means uncommon. There appears to be no specificity in the action of the male and female sex hormones. It is quite immaterial whether female rats were treated with male or female hormones and vice versa. The length of treatment necessary before the effect was apparent was roughly about a week. Twelve to 24 hours after the injection we were rarely able to see any change, and then only after the administration of very high doses. In normal adult animals similarly treated the effect was not so marked, but was nearly always noticeable (Table V). Finally the cerebral blood content of female rats was observed during oestrus and dioestrus. An increase was found in nearly all animals during oestrus (Table VI).

After treatment of young animals with gonadotrophic hormone of the anterior pituitary lobe, an increase in the cerebral blood content was also found (Table VII).

The foregoing experiments convinced us that certain ductless glands exert a very considerable influence on the cerebral circulation. We have not yet been able to investigate the action of all the endocrine organs, but the influence of the sex hormones in young animals seems to be very important. We do not know whether the increase of the cerebral blood content after hypophysectomy is not entirely due to the atrophy of the gonads following the operation. In any case we intend shortly to investigate the influence of all the other glandulotrophic hormones on the brain circulation. The suggestion of the influence of the sex hormones on the brain circulation is not new ; Steinach (2), for instance, showed that the blood content in the brain of a castrated rat can be increased by the administration of follicular hormone, using an unquantitative vital staining method.

It is obvious that a useful check on these results will be furnished by histological methods such as those of Pickworth (3), Sloninski and Cunge (4) and Scholz (5), and the thermo-electric investigations of Gibbs (6). We are at present engaged in checking some of our results by histological methods.

TABLE I.—*Blood Content Age Curve.*

Age (days).	Body weight (gm.).	Blood content of brain. (per cent.).
4	11	1·77
8	16	1·35
24	23	1·29
	40	1·40–1·60
	60	1·50–1·80
	100	1·70–2·2
	150	1·90–2·4
	200	2·0–2·6
	300	2·3–2·9

TABLE II.—*Dry Substance Age Curve.*

Age (days).	Body weight (gm.).	Dry substances (averages per cent.).
2	7·3	11·7
8	13·2	12·4
13	..	13·6
18	15	16·8
24	28	19·1
	80	21·3

TABLE III.—*Blood Content after Hypophysectomy.*

Body weight (gm.).	Time after hypophysectomy (days).	Blood content of brain (per cent.)
182	12	2·18
175	12	1·89
170	12	1·95
195	30	1·72
160	62	2·06
320	Control	2·74
260	,,	2·86

TABLE IV.—*Adult Male Rats Spayed Three Weeks ago Treated with Progynon.*

No.	Sex.	Weight. (gm.).	Treatment.	Blood content (per cent.).
1	♂	380	9 days 250 u. progynon daily	4·27
2	♂	350	,, ,, ,,	2·54
3	♂	350	,, ,, ,,	2·79
4	♂	370	Control	1·78
5	♂	340	,,	1·67

TABLE V.

Littermates, Four Weeks old, Treated with Progynon.

No.	Sex.	Weight (gm.).	Treatment.	Blood content (per cent.).
1	♂	37	7 days 2 × 1 u. progynon daily	2·75
3	♀	30	7 ,, 2 × 1 u. ,, ,,	2·71
7	♀	31	7 ,, 2 × 5 u. ,, ,,	2·40
5	♂	35	Control	1·70
6	♀	35	,,	1·49

Young Animals Treated with Progynon.

Sex.	Weight (gm.).	Treatment.	Blood content (per cent.).
♂	34	9 days 2 × 1 u. progynon daily	2·41
♂	35	9 ,, 2 × 10 u. ,, ,,	2·47
♂	35	9 ,, 2 × 20 u. ,, ,,	2·64
♀	34	9 ,, 2 × 1 u. ,, ,,	2·19
♀	36	9 ,, 2 × 10 u. ,, ,,	2·70
♀	40	9 ,, 2 × 20 u. ,, ,,	3·16
♂	42	Control	1·63
♂	33	,,	1·53
♀	32	,,	1·81
♀	32	,,	1·70
♀	27	,,	1·40

Young Animals Treated with Testoviron.

No.	Sex.	Weight (gm.).	Treatment.	Blood content (per cent.).
1	♀	51	7 days 1 mgm. testoviron daily	2·01
2	♀	57	7 ,, 1 ,, ,, ,,	2·12
3	♀	54	7 ,, 2 ,, ,, ,,	2·82
4	♀	59	7 ,, 2 ,, ,, ,,	3·18
5	♀	49	Untreated control	1·53
6	♀	48	,, ,,	1·57
7	♂	58	,, ,,	1·70
8	♂	60	,, ,,	1·48
9	♂	56	7 days 1 mgm. testoviron daily	2·26
10	♂	51	7 ,, 1 ,, ,, ,,	2·78
11	♂	58	7 ,, 2 ,, ,, ,,	2·85
12	♂	54	7 ,, 2 ,, ,, ,,	2·89

TABLE V—*continued.*

Adult Normal Animals Treated with Progynon.

No.	Sex.	Weight (gm.).	Treatment.	Blood content (per cent.).
9	♀	230	Untreated control	2·52
10	♀	270	,, ,,	2·38
13	♀	230	,, ,,	2·34
15	♂	310	,, ,,	2·48
6	♀	250	8 days 250 u. Progynon daily	3·16
7	♀	250	8 ,, ,, ,,	3·63
8	♀	260	8 ,, ,, ,,	2·78
11	♀	210	8 ,, ,, ,,	2·84
12	♀	260	8 ,, ,, ,,	3·59
14	♂	250	8 ,, ,, ,,	3·16

TABLE VI.—*Adult Female Rats, Normal Genital Cycles.*

Body weight (gm.).	Weight of uterus (mgm.).	Oestrus stage.	Blood content (per cent.).
155	122	—	2·06
130	102	—	2·08
110	31	—	2·38
104	..	—	2·02
100	..	—	2·18
100	..	—	2·33
150	420	++	3·20
135	164	++	2·98
95	110	++	3·14
155	330	++	2·74
110	280	++	2·84
89	620	++	3·14

TABLE VII.—*Blood Content after Treatment with Gonadotrophic Hormone of the Anterior Pituitary Lobe.*

Sex.	Weight (gm.).	Treatment.	Blood content (per cent.).
♀	100–150	Control animals	1·9–2·5
♀	149	Daily 5 units	3·58
♀	165	Gonadotrophic hormone	3·01
♀	110	Subcutaneous 14 days	2·77
♀	23–40	Control animals	1·29–1·60
♀	45	0·2	1·39
♀	43	0·4 Units	2·36
♀	45	0·4 gonadotrophic	1·90
♀	40	0·6 hormone, daily	2·58
♀	33	1·0 for 4 days	2·56
♀	30	1·0	3·20

TABLE VIII.—*Doryl Action.*

No.	Weight of body (gm.).	Treatment.	Blood content of brain 1 hour after injection (per cent.).
1	56·2	0·1 c.c. doryl subcutaneously	2·58
2	57	0·2 ,, ,, ,,	2·26
3	51	0·2 ,, ,, ,,	2·28
4	51·5	0·2 ,, ,, ,,	2·41
5	52	Control	1·98
6	52	,,	1·87

The extent to which these observations afford an explanation of several pathophysiological phenomena is, of course, a matter for further investigation ; it has, however, long been recognized that circulatory disturbances of the central nervous system occur during puberty, menstruation and menopause.

A useful comment on the validity of our methods is furnished by our experiments with the parasympathetico-mimetic drug doryl (carbaminoylcholine chloride). Stimulation of the parasympathetic is well known to cause cerebral vasodilation (Cobb and Talbott (7)). In treated animals we found that one hour after injection the blood content was increased by as much as 20 per cent. as compared with the untreated control animals (Table VIII).

CONCLUSIONS.

The blood content of the brain was investigated in a series of rats. In the four-day-old rat it is about 1·7 per cent., but within a few days it decreases to the lowest amount of 1·2 per cent., increasing afterwards again up to the age of three months, when it is 2·2 per cent.

The blood content in the brain of castrated rats is diminished.

After administration of sex hormones the blood content was always increased in castrated and normal young and adult animals. Gonadotrophic hormone was also found to cause a marked increase in the cerebral blood content of young animals.

An increase of the blood content of the brain of female rats during oestrus was observed.

After hypophysectomy the cerebral blood content was diminished. A possible explanation may be that this is due to the subsequent atrophy of the gonads.

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AN ATTEMPT TO INDUCE PATIENTS SUFFERING FROM CATATONIA TO ACTIVE AND VOLUNTARY MOVEMENTS.

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THE management and treatment of patients suffering from catatonia are constantly presenting a problem for mental hospital staffs, particularly in modern times, when more emphasis is laid on treatment than on custodial care.

The problem of making people suffering from catatonia into useful members of the hospital community seemed, from the very beginning, to be bound to fail, as long as the difficulty of inducing them to active and voluntary movements was not overcome.

That task seemed to be incapable of solution, in so far as voluntary movements are only affected through interests or motives, which necessitate a contact with the environment of the person in question, and we are only too ready to deny that catatonics possess these qualities.

We proceeded from the following hypothesis: we assumed that every psychotic has retained a " remaining link " with life, i.e. with his environment, with the ego-present and with the ego-past. The problem to be solved is this: how is this " remaining link " to be found, how is it to be approached, and how is it to be got into action ?

We found that the three catatonics whom we investigated were great eaters. We assumed that their desire to eat was their " remaining link " with life, and that it might be made the means of inducing these people to more active movements.

INVESTIGATION.

An apparatus was designed to help us to put this hypothesis to a practical test.

The apparatus (I called it " Move-Skill," because it was found that it not only induces mobility in the person using it, but also because it enables us to examine a certain form of skill of catatonics) consists of a quadrangular wooden box (height 8 ft. 3 in.) (see Fig. 1). This box is completely closed on three sides. At the front at a height of 7 ft. 2 in. we find two grooves, 11 in. distant from each other. Various wooden planks with holes (A) of different sizes (radius 9, 8, 7, 6, 5 in.) can be inserted between the grooves. A wooden door (B) 3 ft. 6 in. is fixed at a height of 3 ft.; through this door one can easily reach the interior of the box. A small opening (C) radius 1 in. is to be found below the door, and just under the latter a protruding wooden bowl (D) (length 8 in., breadth 9 in., depth 4 in.).

Beneath this bowl in the front wall is an opening (E) which has a radius of 5 in. and has for its lower part the form of a circle. Below this opening is a protruding wooden bowl (F) (length 1 ft., breadth 1 ft. 2 in., depth 5 in.).

In the wooden box at the height of 6 ft. 8 in. to 5 ft. 10 in. is a funnel (G). It is made of cardboard, length 1 ft. to 1 ft., breadth 8 in. to 5 in. A second funnel (H) is fixed at a height of 5 ft. 10 in. and 4 ft. 9 in. respectively, the radii being 7 in. and 4 in., and a cylinder (I) at the height of 4 ft. 9 in. to 3 ft. 8 in. with a radius of 3 in.

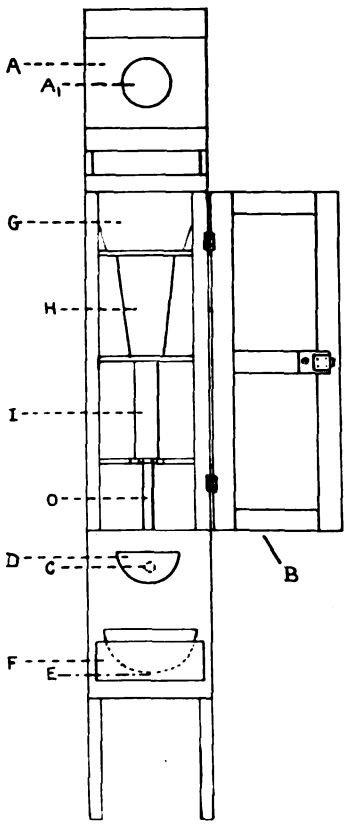

FIG. 1.

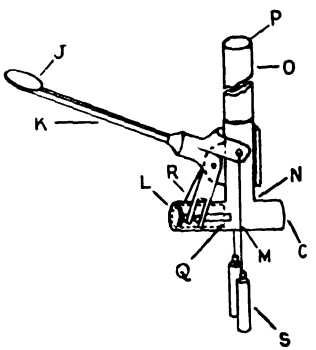

FIG. 2.

Directly below the lower opening of the cylinder at a distance of 8 in. (i.e. 3 ft. above the floor) is a small round iron plate (K) (see Sketch II) (radius 3 in.), at the lower part of which a piece of iron (K) 8 in. long is fixed. This points horizontally towards the front and is connected with a mechanism counterbalancing it.

This mechanism (fixed at a height of 2 ft. 9 in. and 3 ft. 1 in. from the floor) consists of 2½ in. long iron tube (L). This tube has a slit on both sides (M), and is connected by a right-angular joint (N) with a 3-in. long iron tube (O). To tube (O) another iron tube (P) 20 in. long can be affixed. All the iron tubes have the same radius (1 in.).

In the iron tube is a steel piston (Q) which fills the hole, but which can be moved freely. The length of the piston is 1½ in. This piston is connected by two iron pegs (R) and by the slits (M) with the piece of iron (K).

The pegs (R) are on one rectangular prolongation of the piece of iron (K), the counterbalances (S) are on the other.

The whole mechanism is arranged in such a manner that the plate (J) is in the centre of the box, and the piece of iron (K) as well as the iron tube (L) run horizontally towards the front in such a way that the upper end of (L) enters the opening (C).

(O) and (P) run vertically upward along the front part of the box.

Technique.

If a ball with a radius of 2½ in. is thrown through (A1), it falls on account of its weight downward, and having passed through the two funnels and the cylinder, impinges on the iron plate (J). The latter being pushed downward, the steel piston (Q) is pushed forward, and by means of it any object is pushed out of the iron tube (L) into the wooden bowl (D) after passing through the hole (C).

The ball bounces off the disc and falls through (E) into (F) and is then again ready for use. At the same time the piston (Q), which is counterbalanced by the weights (S), returns into its original position at the lower end of (L).

(O) and (P) are filled with sweets. The door of the apparatus is closed. The patients who were being investigated were taken to the apparatus during their lesson in gymnastics, and at the same time all their actions were photographed.

Cases.

Case 1.—No. 28/106. Man, aged 23, five-and-a-half years in more or less the same catatonic state.

"He is suffering from catatonia. He is in a stuporose condition and totally inaccessible to examination. He adopts bizarre postures and attitudes and is much given to grimacing. He walks about with his head bent and his arm in a position of flexion. He is extremely slovenly and untidy, and appears to have no appreciation of his surroundings."

Case 2.—No. 678/914. Male, aged 26, has remained eleven years in his catatonic state.

"He is suffering from catatonic stupor. He is extremely negativistic and almost inaccessible to examination. He gives an occasional monosyllabic reply to questions. He appears to resent examination. He shows marked emotional flattening and is completely apathetic about his future. Mannerisms and meaningless smiling are much in evidence. P.H. weak, poor state of nutrition, but with no definite evidence of organic disease."

Case 3.—No. 118/960. Male, aged 30, has remained ten years in his catatonic state.

"He is suffering from catatonia. This patient is completely inaccessible to examination and cannot make any intelligible reply to questions. He displays marked stereotypy of behaviour with antics and facial grimaces. Meaningless smiling is also much in evidence. Emotional flattening is extreme. At times he becomes impulsive and noisy. His habits are faulty, and he requires constant attention."

Results.

Patient 1 took a great interest in the apparatus, abandoned, of his own accord, his catatonic posture, and having watched the exercise once, took the ball and began to aim at the hole. Whenever the ball did not hit the hole, he asked to have it given to him again. Frequently, however, quite forgetting his

catatonic posture, he ran after the ball which was rolling along in the large hall till he caught it, then he picked it up, returned to the apparatus and continued to throw.

Whenever he succeeded in hitting the hole he took the sweet out of the wooden bowl, which is fixed in the front of the automaton, took the ball again and went on with the exercise.

When he had aquired a large number of sweets, he did not eat them all at once, but hoarded them in his waistcoat pocket. If he succeeded in hitting the hole at a first attempt, one could see a smile on his face; frequently, however, he had to throw the ball 10, 20 or more times, but only very seldom did he lose patience; he got over these disappointments surprisingly well and showed an extraordinary amount of perseverance.

The reaction of Patient 2 was similar to that of Patient 1, but he was less persevering than the former.

The reaction of Patient 3 was different. He refused to take the ball and to throw it. We put the patient beside the apparatus and made the others throw the ball. He watched them with great interest, then he attempted to get hold from behind of one of the patients who was throwing the ball at the very moment when that patient was on the point of taking his sweet out of the bowl. Eventually Patient 3 took the sweets, which the others had earned, till without anyone saying anything he recognized that he was acting unjustly. Having thought the matter over carefully, he gave the sweet, which he was on the point of putting into his own mouth, to the patient who had earned it.

It was, however, interesting to observe that this action was preceded by a "sensible" smile, which seemed to imply, "Well it will not do after all that you should go on drudging and toiling whilst I am continually enjoying the fruits of your labours."

The patient now took the ball of his own accord and participated in the exercises in the same way as the others.

The following parallel experiments were now made: A medicine ball was thrown at each of the three patients in turn. If they were called by their names beforehand they nearly always caught the ball, or at any rate attempted to do so. If they were not called by their names they reacted in the same manner, with the difference, however, that not noticing the ball, they jumped aside or tried to ward the ball off at the last moment. It scarcely ever happened that the patients allowed the ball to be thrown at them without making a move.

The reaction of the patients was the same, except that Patient 1 showed much greater skill than the two others.

The patients were then made to do various physical jerks together. This was tried in two ways, by means of "sharp, military commands" and by means of a "friendly persuasive tone." The results differed greatly; in the first case the patients reacted without exception, in the second case only rarely.

A further experiment was made, the patients being placed with their hands

on rings, which were hanging down from the ceiling. They remained in their catatonic posture and even intensified it.

The reaction of the three patients to these experiments was identical.

In the case of Patient 1 there is one other possibility of inducing him to move. When his mother throws a small ball (not a medicine ball) to him, he catches it and throws it back to her.

After I had convinced myself that these catatonics were prepared to abandon their catatonic posture, I decided to submit their skill, i.e. their ability to concentrate, to a systematic analysis. I made the catatonics throw the ball eight times, together with other patients and normal people, but in such a manner that each one had to throw the ball by turns and only once at each turn. In order to avoid the effect of chance I took the average number. Having repeated this experiment for six days, I arrived at the following average number for each patient on each day :

1	C—	Catatonic	23 years	37	37	16	21	21	26 = 26	Catatonic
2	G—	,,	26 ,,	43	41	10	23	34	35 = 31	average 28·5
3	M—	Schizophrenic	28 ,,	47	43	38	33	13	36 = 35	
4	D—	Confusional insanity	23 ,,	33	35	34	30	49	39 = 36	
5	H—	Schizophrenic	47 ,,	23	23	25	31	25	22 = 24	
6	H—	,,	35 ,,	31	43	24	48	31	36 = 35	
7	R—	,,	36 ,,	48	36	52	60	64	52 = 52	Schizophrenic
8	H—	,,	36 ,,	35	49	35	42	23	22 = 34	average 34·7
9	H—	,,	33 ,,	41	64	45	48	51	34 = 47	
10	S—	,,	34 ,,	39	37	39	55	39	25 = 39	
11	B—	,,	25 ,,	15	23	13	19	13	32 = 19	
12	G—	,,	29 ,,	12	20	21	52	26	27 = 26	

This table goes to prove that the skill of the catatonic is about 20 per cent. above that of the other schizophrenics, but as our deductions are taken from so few cases we cannot dogmatically assert that their skill is 20 per cent. greater.

We may however say that the skill of the catatonic is not less than that of the schizophrenics.

Conclusion and Discussion.

In the case of the three catatonics who in the normal way could not be induced to purposeful actions, we have found through experiments that they can be induced to involuntary movements by fear and to voluntary movements by our making use of their well-developed food-seeking instinct, and in addition to it, in the case of one of the catatonics by using his particularly strongly developed attachment to his mother (widow, only child).

These experiments can be represented schematically in the following way :

Means.	Causes.	Results.
1. Swimming-pool . . .	Fear of death	Involuntary, not pleasurable movement ("nicht lustbetont").
2. Medicine ball . . .	Fear of injuries	
3. Sharp command . .	Fear	
4. Move-Skill . . .	Food-seeking instinct	Voluntary movement, pleasurable ("lustbetont").
5. Ball games . . .	Love of mother	
6. "Friendly persuasive tone"	Lack of fear	No movement.
7. Rings	Negative fear	

We have not verified experiment (1) ourselves, but as it has been verified in many mental hospitals, we could use it without hesitation in order to complete our scheme.

All the other experiments we have conducted ourselves, as mentioned in detail above.

The " voluntary " type seem to us to be important from the practical point of view, because they can be repeated and used to induce the patient to move.

From the theoretical point of view the whole scheme seems to us to be important for the following reasons:

These experiments give us the right to assume that the complete isolation of the catatonics is avoidable.

One must further assume that there are other means besides the two above mentioned by which to induce the catatonics to voluntary movements.

The aim of further investigations will be the solution of the problem as to how far the " last remaining link " can be determined beforehand and put into action.

From what has just been said it is clear that it is now difficult to maintain the theory that there is a qualitative difference in the attitude of the catatonics to their surroundings in comparison with that of other schizophrenics, and it is further obvious that the psychological determination of the contents of the psychosis has not only a theoretical value, but can also be made use of in a practical sense.

SUMMARY.

(1) We proceed from the hypothesis that every psychotic has retained a " last remaining link " with life (i.e. with his environment, with the ego-present and the ego-past).

(2) The problem to be solved is, whether this " remaining link with life " can be defined and brought into action.

(3) In the case of three catatonics it was shown how their "last remaining link " was found in their food-seeking instinct, and how this instinct can be brought into action.

(4) It is being shown by means of " Move-Skill," a newly constructed apparatus, that the three catatonics are able to make active, continuous and voluntary movements.

(5) An attempt will be made to design a scheme for the " last remaining link," and it is hoped to show by future investigations how far the patients react and how far they do not.

(6) As a result of the experiments the conclusion is drawn that the complete isolation of the catatonics from their surroundings can be avoided.

It is further being shown that the skill of the catatonics as measured by the " Move-Skill " apparatus, is above or at any rate equal to that of other schizophrenic patients.

I am indebted to Dr. R. Ström-Olsen, Physician Superintendent of the Runwell Hospital, for his helpful advice, and for providing the facilities to carry out this work, and to Mr. Flack for making the apparatus.

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Part II.—Reviews.

An Outline of Medical Psychology. By E. FRETSON SKINNER, M.A., M.D., F.R.C.P. London: H. K. Lewis & Co. Ltd., 1939. Pp. viii – 173. Price 6*s*.

This little book, intended for the non-technical reader and for medical students, is clearly and concisely written. It should prove a useful introduction to some of the facts and hypotheses of modern psychology as applied to the causation of nervous diseases and to their treatment by its means.

Dr. Skinner prefers a physio-psychology. Physiology is, in his opinion, the only sure basis for psychology. In the first section of the book he makes much use of Pavlov's theories, attempting to explain all mental phenomena on materialistic lines. In the second section he passes on to psycho-pathology. Here such matters as the unconscious, dream psychology, the psycho-pathology of everyday life and the evolution of the sexual instinct are dealt with. The author's bias is strongly Freudian and his exposition is on psycho-analytical lines.

The final section describes the psycho-pathology, clinical features and the treatment of the psycho-neuroses. It is stressed that anxiety is the primary neurosis, and that anxiety states account for some 60% of all neurotic illness. Hysteria, obsessional states, perhaps even the psychoses, are secondary conditions. They are maladjustments as their aim is to avoid the anxiety and fear reaction. Hysterical and obsessional symptoms can often be removed only to expose the original underlying anxiety state. Until the basic cause for this is found and readjustment achieved the patient will relapse.

In a chapter on therapy, Dr. Skinner points out that one-third of all certified illness in this country is of the neurotic type. If properly treated it holds out excellent prospects of cure. It is, therefore, a matter of great economic importance. By contrast, cerebral tumour and disseminated sclerosis are of purely academic interest. They are comparatively rare and treatment, up to the present, is of little economic value.

Most of us would agree with the author that it is unfortunate that in the teaching schools a disproportionate amount of time is devoted to conditions of purely academic interest. S. M. COLEMAN.

Superstition and Society. Psycho-analytical Epitomes No. 3. By R. MONEY KYRLE. London: Hogarth Press. Pp. x + 163. Price 4*s*. 6*d*.

Money-Kyrle provides an excellent introduction to psycho-analytical findings in the field of anthropology. His main sources are Freud's *Totem and Taboo*, Abraham's *Dreams and Myths*, Rank's *Myth of the Birth of the Hero* and Roheim's many important contributions.

A parallel is drawn between primitive customs, superstitions and so on and psycho-pathological phenomena. The myth and the dream are found to have much in common. Here Greek mythology is chosen for illustration, and it is

shown that both myth and dream have as their basis the problems of incest, parricide and castration. The totem is shown to have its parallel in the animal phobia, so common in young children, and the taboo in obsessional states. Both are found to be derived from the incest prohibition and to be an essential component of the exogamic structure. In the chapter on animism, animatism and magic, the parallel is found in the wishful thinking of the deluded psychotic.

In his analysis of these phenomena the author makes free use of Klein's theory of good and bad part objects. To some this dualistic conception may seem an over-simplification and of doubtful value. The two final chapters deal with the origin and development of culture and with education and culture respectively. Here again, in the reviewer's opinion, much interesting matter is marred by the constant intrusion of Klein's truism.

The above criticism apart the book can be confidently recommended.

S. M. COLEMAN.

Nouveau Traité de Psychologie. (Tome Sixième : Les fonctions systématisées de la vie affective et de la vie active.) Edited by GEORGE DUMAS. Paris: Librairie Félix Alcan. Pp. 544. Price 125 frs.

Each volume of this large system of psychology consists of a number of monographs by various authors. Groups of two or three monographs may also be obtained in brochure form at prices ranging from 20 to 40 francs. The present volume, as its title indicates, deals with the more complex and highly evolved affective and conative functions. Space precludes individual criticism. The titles and authors of the articles are listed : " La logique des sentiments " and " Les passions " by L. Dugas ; " L'évolution, la spiritualisation et la socialisation des tendences" by F. Challaye; "L'amour et la peine" by D. Lagache (a critical study of the genetic and phenomenological approach to psychology) ; " Les sentiments sociaux et les sentiments moraux " by C. Davy ; " Les sentiments religieux " by C. Belot ; "Les sentiments esthétiques et l'art " by H. Delacroix ; " Les volitions " by Ch. Blondel ; " Psycho-physiologie de l'effort physique" by H. Langier and W. Liberson; and "L'invention et le génie " by H. Delacroix.

The essays are of a very high order and the whole work should form a valuable reference library. Of the four further volumes contemplated, two are to be devoted to studies in psycho-pathology. S. M. COLEMAN.

Psychobiology and Psychiatry : By WENDELL MUNCIE. St. Louis, U.S.A.: The C. V. Mosby Company, 1939.

This book is one of the most important major psychiatric works of recent years. It is a statement of the work and teaching in the Phipps Psychiatric Clinic, Johns Hopkins Hospital. As such, it is an exposition of the principles of psychobiology formulated by Prof. Adolf Meyer. Dr. Muncie, who is Associate Professor at Johns Hopkins University and Assistant Psychiatrist at the Clinic, has been in contact with Meyer for ten years ; and although he makes clear his debt to Meyer, his book is at the same time a formulation of his own and has been built up out of his own daily practical experience. Based as it is on psychiatric practice in the Phipps and the Diagnostic Clinic of the Johns Hopkins Hospital, it is the outcome of a very large number of cases, and is also founded on the necessity for the disciplined thinking required for teaching.

The book is, in consequence, a most valuable one for all psychiatrists, and it should find an important place.

The sections of the book dealing with psychiatric case-work and treatment are admirable. The cases are most lucidly presented, and the principles of treatment are detailed and in the highest degree practical. Particular mention must be made of the very full examination technique, which contains, amongst other useful features, an unusually clear scheme of examination for aphasia, and a broadly orientative outline of the examination of the nervous system. It is very much to be hoped that Dr. Meyer's classification into "ergasias" (from the Greek "ergasia—work or labour," and selected by Meyer because "behaviour" has no plural or adjective, and tacitly excludes implicit activity) will be made better known, and ultimately be adopted in this country. It is a classification based on pluralism and the facts. In these sections Dr. Muncie says a great many things which have needed saying. He speaks of the "bankruptcy of the original Kraepelinian conception"—of dementia præcox, amongst other venerable errors, in a refreshingly brisk manner.

Although the word "psychobiology" has passed into the language, its principles are not as well understood in this country as they should be. The psychobiological conception of the organization of personality, and the scrutiny of it in Prof. Meyer's scheme of personality study as formulated here, should be a great stimulus to those to whom it is new. Those already familiar with it will take pleasure in the clearness with which it is arranged. It is very much to be hoped that this book will attract in this country the attention it deserves, for it is a meaningful system and approach, and a much-wanted alternative to a good deal of confusion.

Considerable value is added by a chronological bibliography compiled by Dr. Marion Booth and Dr. Adelaide Johnson.

The book is well described by Prof. Meyer in a foreword where he says: "It is a voice from a workshop making articulate in its own way the mode of working, inquiring, and sharing, practised for 'the whole of man and his setting and not only the parts of man.'"

W. McC. HARROWES.

Sketches in Psychosomatic Medicine. By SMITH ELY JELLIFFE. New York. Nervous and Mental Disease Monographs No. 65, 1939. Pp. v + 155. Price $3.00.

The volume comprises a selection of Jelliffe's papers originally published between 1930 and 1937. The fact that all the articles are concerned with the psychological component in organic disease processes gives the book a certain continuity. The author's thesis, put very shortly, is that by the mechanisms of repression, regression and conversion, the psychological component may participate in bringing about irreversible tissue changes in an organ, finally resulting in organic disease. The organ neurosis would be an intermediate stage, while the somatic disorder is still reversible. In the various papers here presented, the theory is illustrated by psycho-analytical comments on such varied conditions as skin lesions, arthritis, hyper-thyroidism, cardio-vascular diseases, gastro-intestinal disorders, asthma, pulmonary tubercle and disease of bone.

Jelliffe epitomizes his view-point in the Socratic principle, "One looks to the cure of the soul in order to cure the body."

The only criticism of this interesting selection of papers is the amount of

overlapping. Favoured similes and case-histories are cited more than once, and the matter of one whole paper can be found paraphrased elsewhere in the volume. S. M. COLEMAN.

Medical Psychology. By Dr. ERNST KRETSCHMER. Leipzig: Georg Thieme, 1939. Fifth edition. Price RM. 15.

The translation by E. B. Strauss of the previous edition of this book was reviewed in this journal in January, 1936. The fifth German edition does not show much change. However, a few additions have been made. The most interesting is the more detailed discussion of the temperament of persons of athletic type. Typical of the author's eclecticism is the inclusion of Kleist's theories with their highly speculative localization of mental symptoms. Among the psychotherapeutic procedures he has now described "the autogenous training" of J. H. Schultz, which is a new method of using auto-suggestion, paying special attention to the autonomic system. It may seem that certain theories, are given undue prominence, but this is unavoidable in a short book dealing with numerous aspects of medical psychology. Also this inclusion of so many hypotheses has made the author's writings more stimulating than most psychological text-books. S. L. LAST.

Part III.—Bibliography and Epitome.

AMER. J. PSYCHIAT.
VOL. XCVI. SEPTEMBER, 1939.

Cortical Spread of Epileptic Discharge and the Conditioning Effect of Habitual Seizures.

The cerebral cortex of the epileptic passes through varying phases of stimulability. Simple response, both motor and sensory, may occur as the result of stimulation at a distance. Such distant response is due to focal lowering of threshold and to selective neuronal conduction. In general, cortical stimulation produces movements and sensations which are not like normal movements and sensations, but qualitatively identical with those that may occur in epileptic seizures. The cortex of an epileptic may be found to be refractory to electrical stimulation, and at such times may still be functionally available to the patient for volitional purposes.

An habitual seizure, by virtue of its frequent repetition, may eventually establish a complicated neurone pattern, so functionally organized that it may be stimulated electrically, although no such complicated response could be obtained from stimulation of the normal brain. Induced seizures do not arise from distant stimulation. They begin by discharge in the neighbourhood of the stimulating electrode. This is followed by spread, which is not diffuse, but which is along a definite neurone system, which may be preformed or acquired. By

" preformed " is meant a system of neuronal connections ordinarily recognized as physiologically functional in all normal brains. By " acquired " is meant a pattern of neuronal connections established by the conditioning influence of previous individual experience. In this sense habitual epileptic seizures should be considered true conditioned reflexes in the cortex of any patient.

In complicated seizures the advance of discharge along this neurone pattern may be slow and episodic as to suggest that isolated ganglionic collections are fired in an advancing series, each collection being set off only after neuronal bombardment of sufficient intensity and duration from other cell collections already discharging. (Authors' abstr.)

A Review of the Results of the Pharmacological Shock Therapy and the Metrazol Convulsive Therapy in New York State.

1. One thousand seven hundred and fifty-seven patients suffering from dementia praecox have been treated thus far with insulin hypoglycaemia in the New York State Department of Mental Hygiene, and 1,140 patients have been treated with metrazol.

2. The recovery and improvement rate in the cases of insulin-treated cases is significantly in excess of the rate in the control group. Metrazol, on the other hand, produced even fewer recovered cases than were found in cases not treated by any shock therapy.

3. Recent reports indicate that metrazol, besides being not especially effective, also produces serious complications, notably fractured spines. While it is effective if used in selected cases in combination with insulin it is a dangerous drug, and should not be used indiscriminately.

4. A follow-up study of cases approximately one year after completion of treatment indicates that a significant proportion of the patients tend to retain their improved state.

5. The prognosis in insulin treatment depends largely on—
   (*a*) Duration of the illness before treatment.
   (*b*) Type of dementia praecox.
   (*c*) Personality prior to the onset of the illness.

6. The adoption of the uniform application of treatment and a standardized method of recording will make possible more uniform success.

(Authors' abstr.)

Results and Observations on the Insulin-shock Treatment of Schizophrenia.

1. In every hospital using insulin-shock the patients treated should be followed for five years. Another group of patients, or other groups, as near alike as possible should be followed for the same time as controls. It seems certain that relapses after favourable responses will follow in all groups.

2. Insulin-shock therapy is not a complete answer. But the transformation of the patient's condition is so immediate and favourable in a majority of cases that it will have place in, or provide suggestions for a future therapy, and this without regard to whether good results last for an afternoon or indefinitely. It is only fair to remember that Sakel spoke of insulin-shock as the artillery in a general combined attack on the disease process.

3. Insulin in convulsive doses alters the metabolic processes of nerve.

(Authors' abstr.)

Regarding Sodium Amytal as a Prognostic Aid in Insulin and Metrazol Shock Therapy of Mental Patients (Dementia Praecox).

A total of 55 cases of dementia praecox were tested by the intravenous injection of prenarcotic doses of sodium amytal prior to treatment with insulin hypoglycaemic therapy.

An ameliorating response to the injection of sodium amytal was obtained in

30 patients, and of these 23, or 77 per cent., had a favourable therapeutic response to insulin hypoglycaemic treatment.

No ameliorating response to sodium amytal was obtained in 25 cases, and of these, 16, or 64 per cent., failed to respond to insulin treatment.

The results of metrazol convulsant therapy in cases that failed to respond to insulin treatments are also compared with the sodium amytal test.

The response to sodium amytal test appears to be of prognostic value in insulin hypoglycaemic shock therapy. (Authors' abstr.)

Irreversible or Hyperglycaemic Insulin Coma: Its Cause and its Response to Blood Transfusion.

1. Irreversible or hyperglycaemic insulin coma presents a typical picture consisting of a sustained high blood sugar (following intravenous glucose administration), fever, rapid pulse and respiration, and frequently fits, vomiting or diarrhœa. It is a serious complication occurring not only in shock treatment, but no doubt in the management of diabetes as well. It may result in death or in permanent brain damage, but recovered psychiatric cases often show dramatic improvement in their mental state.

2. Hyperglycaemic coma is probably due to over-prolongation of therapeutic coma beyond an hour or an hour and a half.

3. Over-prolongation of coma is often unintentionally allowed, because the presence of gastric retention makes termination by tube-feeding ineffective.

4. As a practical consequence coma should generally not be allowed to last more than an hour or an hour and a half, especially in cases that tend to rouse slowly, and sugar should be given by vein in all cases that do not begin to rouse 15 or 20 minutes after tube-feeding.

5. Treatment of irreversible coma by intravenous glucose and blood transfusion of 500 c.c. of citrated blood appeared effective in three successive cases.

6. It would appear that the whole blood contains substances, other than oxygen or sugar, essential for brain metabolism, which have been destroyed or depleted by protracted coma.

7. The dramatic psychiatric improvement in certain cases following prolonged coma suggests that if a safe method for prolongation of coma could be devised, it would further extend the value of shock treatment. (Authors' abstr.)

Evaluation of Therapeutic Factors in Pharmacologic Shock.

1. Seven of 20, or 35 per cent., of a group of chronic schizophrenic patients were benefited by insulin to the point of social recovery or marked improvement, as compared with a 20 per cent. spontaneous remission-rate in a control group of 30 patients.

2. Coma was found to be essential for the production of improvement, its effectiveness being increased when combined with intensive resocialization activities.

3. Metrazol was only one-half as effective as insulin in chronic schizophrenia, but justified its use because of its greater ease of administration and lesser cost. In chronically disturbed patients its use frequently resulted in moderate degrees of improvement, resulting in better ward adjustment.

4. Paranoid schizophrenia responded best to insulin; agitated catatonia to metrazol.

5. Neither the age of the patient nor the degree of hereditary taint could be correlated with the therapeutic responses.

6. In involutional melancholia and manic-depressive psychosis, depressed phase, metrazol treatment appeared to constitute a direct attack upon the specific psychopathology of the disease. A theoretic formulation to explain this action was offered.

7. The relatively long duration of schizophrenia in first admissions to the Eloise Hospital was noted and the need for earlier recognition and more prompt admission stressed, so as to enhance our therapeutic effectiveness. (Authors' abstr.)

The Mechanism of the Symptoms of Insulin Hypoglycaemia.

1. Simultaneous observations of clinical symptoms, cerebral oxygen utilization, blood-sugar level and electrical activity of the brain were made on patients with schizophrenia receiving the insulin treatment.

2. Blood sugar decreases during the first hours after the injection of insulin and then remains at a low level until termination with sugar, while the clinical signs continue to develop progressively throughout the entire course of hypoglycaemia.

3. The march of the symptoms is correlated with a gradual decrease of cerebral oxygen uptake and the electrical changes.

4. The regression of the symptoms is accompanied by a gradual increase of the oxygen uptake and a reduction of the delta index. The sequence of the symptoms during regression is in an order which is the reverse of their appearance.

5. During hypoglycaemia the alpha waves disappear approximately at the time when the functions of the cortex are completely suppressed and reappear with the restoration of cortical functions.

6. It is therefore concluded that as a result of the hypoglycaemia caused by the administration of insulin the metabolism of the brain is diminished. This reduction of cerebral metabolism is the cause of the clinical symptoms as well as the alterations of the cerebral electrical activity of the brain.

7. These conclusions concerning the correlations between the clinical and physiological changes are to be regarded only as a working hypothesis because of the small number of the experiments performed. (Authors' abstr.)

Central Nervous System Changes Produced by Insulin.

Findings on a group of animals were restricted to histopathological changes of the ischaemic type. They were in agreeement with the observations of Schmid and of Weil and his associates. They are not as severe as those noted by Tani nor those reported by Steif and Tokay. Variations in technique are sufficient to explain this difference.

The mechanism by which these ischaemic changes are produced is conjectural. A possible explanation which is also subscribed to by Weil and his co-workers is that it results from an inability of the brain to carry on its oxidative processes because of the action of insulin. In support of this are the experiments of Holmes, Dameshek, Myerson and Stephenson and Wortis, showing that insulin reduces the oxygen utilization of the brain. (Author's abstr.)

AMER. J. PSYCHOL.

VOL. LII. OCTOBER, 1939.

Intelligence Level and Occipital Alpha Rhythm in the Mongolian Type of Mental Deficiency.

The present study represents one of a series undertaken to determine whether there are significant correlations between the electro-encephalogram and intelligence

level. The feeble-minded offer important methodological advantages in the investigation of this question, since they provide the possibility of a wide range of variation in intelligence level, and permit independent control of mental age and chronological variables. Properties of the electro-encephalogram examined were the alpha index, alpha wave frequency, and alpha wave amplitude of the occipital electro-encephalogram. The experimental group was limited to subjects of the mongolian type of mental deficiency. Intelligence level was measured by means of the 1916 form of the Stanford-Binet Scale, supplemented by the Kuhlman-Binet Scale for test levels under three years.

Considerable attention was given to subsidiary conditions which might have led to changes in the electro-encephalogram independently of mental age effects, or which might have obscured the characteristics of any record. The conditions of this sort taken into account were instrumental artefacts, muscle potentials, conditions in subject during recording, such as states of sleep, emotional excitement, and visual stimulation variations in electrode position, inter-electrode resistance, chronological age-variations, and the proportions of the two sexes at different mental age-levels. Procedures for control of such factors occurred by way of selection of subjects, control of experimental conditions, techniques of record-analysis, and statistical corrections in the treatment of data.

The final results obtained after steps were taken to exclude possible errors due to such factors are represented by product-moment correlations between mental age-level and alpha index, alpha wave frequency, and alpha wave amplitude. Statistically significant correlations were obtained of mental age-level with alpha index and alpha wave amplitude, but not with alpha wave frequency. The criteria of statistical significance used were those of Fisher.

The finding of these significant correlations points to the existence of common physiological factors underlying certain properties of the electro-encephalogram and mental age-level in the mongolian type of mental deficiency, and opens the way to the use of the electro-encephalogram in the discovery of the nature of these factors.

(Author's abstr.)

New Methods of Obtaining Neurotic Behaviour in Rats.

Acute neurotic behaviour was produced on 40 occasions in 15 rats, by a graded series of stimuli. The least "severe" stimulus produced seizures in 3 of 6 chronically disordered male rats, had no effect on 24 normal males, and produced a seizure in 1 of 26 normal females. The most "severe" stimulus produced seizures in 11 of 23 normal males. The rats were throughout in good physical condition, as far as could be judged. Experiments are now proceeding to effect a standardization of the stimuli and, since the number of the chronically disordered animals is admittedly small, to confirm the results on a larger scale.

(Authors' abstr.)

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NO. 3, OCTOBER.

NO. 4, NOVEMBER.

ARCH. NEUROL. PSYCHIAT.

VOL. XLII. DECEMBER, 1939.

AMERICAN ASSOCIATION OF NEUROPATHOLOGISTS.

DETROIT SOCIETY OF NEUROLOGY AND PSYCHIATRY.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY.

NEW YORK ACADEMY OF MEDICINE: SECTION OF NEUROLOGY AND PSYCHIATRY AND THE NEW YORK NEUROLOGICAL SOCIETY.

Preliminary Analysis of Functions of the Temporal Lobes in Monkeys.

The behavioural effects of the removal of both temporal lobes, including the uncus and the greater part of the hippocampus, were studied in macaques. The monkeys exhibited the following symptoms: (1) Forms of behaviour which seem to be indicative of "psychic blindness"; (2) strong oral tendencies in examining available objects (licking, biting gently, chewing, touching with the lips, "smelling"); (3) a strong tendency to attend and react to every visual stimulus ("hypermetamorphoses"); (4) marked changes in emotional behaviour or absence of emotional reactions in the sense that the motor and vocal reactions generally associated with anger and fear are not exhibited; and (5) an increase in sexual activity. These symptoms also appeared if the olfactory tracts were cut previous to removing both temporal lobes. Even the oral tendencies, except for the "smelling," were present.

The symptoms typical of monkeys with both temporal lobes removed did not appear after (1) bilateral removal of the first temporal convolution; (2) bilateral removal of the second and third temporal convolutions; (3) severing the connections between the temporal and the occipital lobes, i.e. duplicating the posterior margin of the lesion produced by temporal lobectomy. The symptoms also did not appear after unilateral temporal lobectomy, except that there was in some cases a change in the direction of greater "tameness." This "tameness" was also observed when after previous extirpation of both prefrontal areas one temporal lobe was removed.

Differential reactions to visual stimuli established pre-operatively were seriously disturbed after bilateral temporal lobectomy, but it was possible to re-establish the response through training. The ability to "generalize" in responding to visual stimuli did not seem to be impaired. (Authors' abstr.)

Histopathogenesis of Cerebral Abscess.

It is consistent with the histologic and metabolic peculiarities of the tuberosclerotic nests in the cortex and of the spongioblastic tumours in the ventricles that many of them should eventually become opaque to Roentgen rays. The pronounced tendency to deposition of calcium is indeed a characteristic trait of both varieties of tubero-sclerotic lesions. In the ventricular spongioblastic tumours the calcification begins, and is always more dense, in the centre of the tumour, where calcareous granules, forming clusters, are usually heaped around proliferated, calcified, hyalinized and degenerated capillaries.

In tubero-sclerotic nodules in the cortex, the relation of calcareous precipitates in the nerve tissue to the nodule is different. Here the calcification tends to occur not in the centre of the nodule, but in the periphery of the subcortical softening facing the white matter, that is, under the cortex in the depth of the convolutions.

The heterotopic nests of monster nerve-cells and glia, forming nodules, may occur not only in the convolutions but also deep in the white matter of the centrum semiovale.

The precipitation of calcium in the nodules is a secondary process developing as a sign of degenerative changes in the congenital neoplastic lesion. At first slight and invisible, the precipitation in the course of years gradually grows denser, and eventually becomes sufficiently opaque to Roentgen rays to appear clearly evident on the plates. Clinically, this is an important roentgenologic sign in cases of tuberous sclerosis, for it is directly related to and is revelatory of specific cerebral pathologic changes underlying the condition.

It is noteworthy that the tendency to calcification of the brain substance is a feature of tuberous sclerosis which it shares with another characteristic congenital neurocutaneous syndrome, namely, trigeminocerebral angiomatosis. The roentgenographic picture of the calcification in the two conditions is, however, quite different. In tuberous sclerosis the opacities resemble " cotton balls " with fuzzy periphery, whereas in angiomatosis the calcareous depositions in the cortex acquire a garland-like appearance, not unlike that of ribbon candy.

There exists another variety of intracerebral calcification demonstrable roentgenographically, and frequently associated with mental deficiency, epilepsy and a neuropathic family history. The intracerebral calcification as shown on roentgenograms in this condition is characterized by a diffuse, massive and remarkably symmetric deposition of calcium, particularly in the region of the basal ganglia. The roentgenographic image obtained is therefore different from that of multiple, discrete and scattered (nonsymmetric) areas of calcification in tuberous sclerosis.

(Authors' abstr.)

Pallidofugal Fibres in the Monkey.

Large, deeply-staining, myelinated fibres arising from the cells of the media division of the globus pallidus form the ansa and fasciculus lenticularis. The pallidohypothalamic tract consists of fibres which run ventromedially into the hypothalamus, passing either through the fornix or over its dorsomedial surface.

Finer striofugal fibres, which probably arise in the caudate nucleus and putamen and possibly also in the lateral division of the globus pallidus, can be traced to the substantia nigra and the subthalamic nucleus.

The cells of the medial division of the Globus pallidus are larger and more angular than those of the lateral division, and they disappear after interruption of the fibres of the ansa and fasciculus lenticularis.

Monkeys in which the ansa and fasciculus lenticularis have been interrupted bilaterally show no gross disturbance of movement. The movements, however, are slow and lacking in spontaneity. The faces of these monkeys are immobile and masklike. (Authors' abstr.)

Dementia Paralytica. Effect of Continuous Intensive Therapy with Tryparsamide and Bismuth on Cerebro-spinal Serologic Reactions and Frequency of Relapse.

Thirty-eight patients with dementia paralytica were treated intensely and continuously, for periods varying from ten months to seven years, with the maximum doses of tryparsamide and thio-bismol until the Wassermann reactions of the spinal fluid were negative or until death supervened; 84 per cent. of this group also received malarial treatment in the beginning. Of the series, 28·4 per cent. showed complete, and 18·4 per cent. partial remission; 36·7 per cent. were unimproved or slightly improved; 5·2 per cent. died of causes other than dementia

paralytica, and 10·5 per cent. died presumably of dementia paralytica. 2·6 per cent. of the entire group after showing a negative Wassermann reaction of the spinal fluid had a reversal to positive. (Author's abstr.)

Cells of Origin of Fibres of Corpus Callosum. Experimental and Pathologic Observations.

In order to identify the cells of origin of the fibres of the corpus callosum, the retrograde cell changes in fields 4, 6, 8 and 12 of the frontal cortex were studied after destruction of the contralateral frontal lobe in one dog, section of the anterior two-thirds of the corpus callosum in three dogs, and section of the posterior two-thirds of the corpus callosum in another dog. There were also studied the pathologic changes in human brains with lesions in the occipital, parietal, central, frontal and temporal lobes, involving fields 1, 2, 3, 6, 7, 8, 18, 19, 22, 39, 40 and 42.

In the experimental as well as in the human pathologic material there were observed in the corresponding fields of the contralateral hemisphere pronounced pathologic changes in layers III, V and VI, except in field 12, in which no alterations were seen. After section of the corpus callosum analogous alterations were observed in the fields of the two hemispheres. The cells of origin of the fibres of the corpus callosum lie in layers III, V and VI. The last two layers of the cortex must be considered as giving origin not only to efferent but also to efferent commissural fibres.

Only a part of the cells of these layers were affected. The commissural fibres do not all arise from one layer, and their cells of origin in layers III, V and VI are intermingled with cells which have other connections.

The results of this investigation show that the homotopic fields are always injured. Further investigation will be required to elucidate the question of heterotopic connections. (Authors' abstr.)

Diffuse Progressive Leukodystrophy in the Adult, with Production of Metachromatic Degenerative Products (Alzheimer-Baroncini).

The adult form of diffuse sclerosis may have a particularly long evolution (17 years in the case reported), with a clinical picture, at the same time, of pseudoparalysis and athetosis. The clinical diagnosis is always difficult. It is based on the association of mental disturbances with an epileptic spasmodic component and a progressive cerebellar and athetotic evolution with gross disorders of speech, ending in loss of articulation.

In the case reported here the disease was characterized pathologically by a metachromatic disintegrative process. It presents, otherwise, all the histologic characteristics of the heredo-degenerative forms of leukodystrophy, in which the disintegration predominates over the proliferative and exudative vascular process. In the glial and mesenchymal tissue one finds in our case the same functional incapacity to metabolize the derivatives of the myelin that one observes in the familial forms. Formation of these disintegrative products is retarded in the parenchyma in a metachromatic form. Five observations of unequal value, but of the same type, are found in the literature. In the case reported here there is no decisive clinical or histopathologic argument to support a separate nosologic classification. One is dealing with a disturbance, apparently of heredo-degenerative type, in which the disintegration, for some unknown reason, has been observed in a metachromatic stage. (Authors' abstr.)

ARCH. DI PSICOL NEUR. PSICHIAT. PSICOTER.

VOL. I. NOS. 1 and 2, 1939.

ARCH. GES. PSYCHOL.

VOL. CIII. 1939.

ARCH. PSYCHOL. GENÈVE.

VOL. XXVII. 1939.

BRAIN.

VOL. LXII. DECEMBER, 1939.

A Biochemical Study of Cerebral Tissue and of the Changes in Cerebral Oedema.

(1) Eighty-three specimens of cerebral tissue were analysed and their water, Na, Cl, K and P contents determined. Various parts of both normal and pathological brain were examined.

(2) Cortical grey matter contains considerably more water (average 84·3 per cent.) than the white matter of the cerebral (70·7 per cent.) and cerebellar (70·6 per cent.) hemispheres, while intermediate values are found for thalamus (75·1 per cent.) and corpus callosum (75·7 per cent.).

(3) By considering the interstitial fluid as a colloid-free ultrafiltrate of serum containing all the chlorides, the composition of the tissue cells themselves is calculated and contrasted with muscle and red cells, the only other tissues for which reliable figures are available. Grey matter has more extracellular tissue (33 per cent.) than white matter (18·3 per cent.), and its cellular tissue contains more water (76·5 and 64·1 per cent. respectively). White matter closely resembles both muscle, which has 15·5 per cent. extracellular tissue and the cellular tissue of which contains 67·8 per cent. water, and red cells, which contain 66·2 per cent. water.

(4) In the cells of white and grey matter there are 7·8 and 6·9 milliequivs of Na per 100 gm. of cell water respectively, whereas in red cells there is only a small quantity (2·5 milliequivs per cent.), and in muscle cells a negligible quantity (0·29 milliequivs per cent.). The amount of potassium (11·3 and 11·2 milliequivs per cent. in white and grey matter respectively) is approximately equal to the amount in both blood and muscle cells (11·4 and 12·4 milliequivs per cent. respectively). The phosphorus, being nearly all organic, is related rather to the solid than the fluid content; it is present in very large amounts in brain cells, being about equal in grey and white matter when expressed as a percentage of the dry weight (40 and 41·7 milliequivs per cent. respectively). This is over twice the quantity present in muscle cells (17·7 milliequivs per cent.), and eight times the quantity in red cells (5 per cent.).

(5) Seven cases of local cerebral oedema, six of which were associated with tumour of the brain and one with a recent vascular haemorrhage, were examined. The differences between water and electrolytic contents of the oedematous brain tissue is restricted to the white matter of the centrum ovale and does not affect the cortex, the thalamus, corpus callosum or internal capsule.

(6) The increases in water, Na, Cl and K in the oedematous tissue are in the same relative proportions as would be the case if the added fluid were a serum filtrate, suggesting that in cerebral oedema, as in oedema of other tissues, there is an increase in the interstitial fluid, derived from the circulating blood. A considerable quantity of additional oedema fluid was found in all cases examined. On the normal side 100 gm. of cellular tissue were associated with an average of 110 gm. extracellular fluid, and on the oedematous side with 249 gm., representing an addition of 139 gm. of oedema fluid.

(7) The phosphorus content is slightly but consistently lower on the oedematous side. This may be related to the breakdown of the coupled organic compounds in the cellular tissue, associated with the degenerative processes which are seen histologically. This change is probably too small to be of significance.

(8) Identical changes were found in the oedematous tissue related to the recent cerebral haemorrhage as in the cases of tumour, showing that the changes in cerebral oedema from both these conditions are the same.

(9) In this study there was no evidence to support the concept that in association with cerebral tumours there also occurs a condition of swelling of the brain ("Hirnschwellung") which is not due to hyperaemia or excess of free fluid, and which can be differentiated from cerebral oedema. (Author's abstr.)

BRIT. J. EDUC. PSYCHOL.

VOL. IX. NOVEMBER, 1939.

BRIT. J. PSYCHOL.

VOL. XXX. JANUARY, 1940.

IL CERVELLO.

VOL. XVIII. SEPTEMBER, 1939.

NOVEMBER.

CONFINIA NEUROLOGIA.

VOL. II. NO. 6, 1939.

The Regulatory Influence of the Sympathetic on Brain Centres.

Stimulation of the cervical sympathetic enhances the rise of blood pressure produced by clamping of the carotid artery. The rise may be higher or longer maintained, or both.

Abolition of sympathetic impulses to the brain by local anaesthesia either causes a lower rise of blood pressure or a less sustained one during clamping of the carotid artery.

After restoration from local anaesthesia the reaction of the vasomotor centre again becomes normal.

From these experiments the conclusion is drawn that the sympathetic exerts an augmentory influence on the vasomotor centre and probably on other vegetative centres of the brain. (Authors' abstr.)

L'ENCEPHALE.

VOL. XXXIV. APRIL, 1939.

Views on the Value of Psycho-analysis.

A critical appreciation of R. Dalbiez's work, *La méthode psychanalytique et la doctrine freudienne*. For Dalbiez, psychoanalysis is the science of intrapsychic relationships and its objective is the study of unconscious causality. With this aim in view it legitimately makes use of certain rational hypotheses and methods. This paper contains an excellent summary of Dalbiez's arguments in favour of the hypothesis of the unconscious mind. Dalbiez's essential thesis is the acceptance of the method and refusal of the doctrine. Ey's criticism is mainly directed towards the second part of this thesis.

Interpretations can, in Dalbiez's opinion, be subjected to scientific discipline and he propounds five criteria, which would justify the analyst in finding a causal relationship between manifest and latent content. These are: (1) The criteria of evocation, that is to say the simultaneous appearance of sign and signified (for instance, when a subject thinks of a knife, he also immediately thinks of his father). (2) The criteria of similarity, by which is meant an immediately intelligible relationship between two contents of consciousness (penis and sword). (3) The criteria of frequency. (4) The criteria of convergence; this is supplied when a number of symbols can be shown to have the same latent meaning. (5) The criteria of verification; this consists in proving the reality of a psychical relationship between A and B, by showing that this relationship is bound up with C in the past and/or will produce D in the future.

S. M. COLEMAN.

REV. FRANÇ. PSYCHANAL.

VOL. XI. AUGUST, 1939.

The Relationship between the Ego and the Super-Ego.

Besides the important role played in the endopsychic sphere by the relationship between the ego and super-ego, it is shown that this relationship also functions in the rapport between an individual and other persons. The latter are identified with the super-ego and invested with qualities taken from it. These qualities were derived from the original models out of which the super-ego was first formed.

S. M. COLEMAN.

The Unconscious and the Sense of Time.

A review of the principal methods by means of which the individual under the urge of an unconscious will-to-live, attempts to deny time, as soon as it has acquired consciousness of and realization of its destructive qualities. Some of the components of the time factor studied are: the child's, the adolescent's and the adult's conception of time; the intuition of the flight of time in the mind of the dreamer, the day-dreamer, the lover, the alcoholically intoxicated and the mystic in a state of ecstasy.

S. M. COLEMAN.

OCCUP. THER. AND REHABIL.

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VOL. XVIII. OCTOBER, 1939.

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VOL. XXIV. 1939.

INT. J. PSYCHOANAL.

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J. APP. PSYCHOL.

VOL. XXIII. 1939.

J. BELGE NEUR. PSYCHIAT.

VOL. XXXIX. OCTOBER, 1939.

NOVEMBER.

DECEMBER.

J. COMP. NEUR.

VOL. LXXI. DECEMBER 15, 1939.

J. COMP. PSYCHOL.

VOL. XXVIII. DECEMBER, 1939.

The Effect of Benzedrine Sulphate on Learning.

1. There is a marked difference in the learning scores of a control group and an experimental group which was given daily subcutaneous injections of 0·5 mgm. of benzedrine sulphate. That this marked difference is a direct consequence of benzedrine sulphate is evident.

2. That benzedrine retards appetitive functions has been seriously questioned.

3. That there is a definite retardation of general performance levels has been demonstrated. The exact cause of this retardation remains speculative.

4. Increased activity levels in the white rat injected (and perhaps fed, too) with benzedrine manifest themselves apparently more than thirty minutes (the very minimum) after injection. (Author's abstr.)

J. CRIM. PSYCHOPATHOL.

VOL. I. NO. 2, 1939.

J. EDUC. PSYCHOL.

VOL. XXX. 1939.

J. EXP. PSYCHOL.

VOL. XXV. 1939.

J. NERV. MENT. DIS.

VOL. XC. OCTOBER, 1939.

Progressive Interstitial Hypertrophic Neuritis.

A case of interstitial hypertrophic neuritis is reported. The point of interest was the presence of Argyll Robertson pupils in the absence of serological or pathological evidence of syphilis. The clinical picture resembled that of the Charcot-Marie-Tooth type of muscular atrophy, the differentiation depending upon the presence of thickened, palpable peripheral nerves. S. M. COLEMAN.

Hysterical Amnesia Relieved by Induced Convulsions.

A case of hysterical amnesia lasting eight weeks, resistant to the usual therapeutic methods, was relieved by induced metrazol convulsions. Following the fourth convulsion she was confused for 30 minutes and then gradually regained her memory of her past completely. S. M. COLEMAN.

The Significance of Infantile Sucking.

Sucking appears to satisfy three different aims of the developing organism, namely the getting of nutriment, the better reflex stimulation of the respiratory mechanism, and finally the getting of tactile stimulation, which seems to be as necessary for the progressive development of the higher associative faculties as food is for tissue development. The integration of these elemental drives in sucking activity gives it considerable importance. When it is not easily established, or when it is not sufficiently exercised or prematurely interrupted, significant dissociations take place in general maintenance of reflex tone and in the sensory motor integrations of vision, hearing and grasp which result in retardation of central nervous control. Dissociated thumb-sucking or some habitual object comes about when the infant does not get enough sucking exercise in connection with the taking of nourishment.

S. M. COLEMAN.

Genesis of a Case of Paranoid Dementia Praecox.

A case of paranoid dementia praecox is presented, showing clear evidence of a homosexual conflict, with suppression of the overt homosexual tendencies, occurring just before the onset of the psychosis. The delusional beliefs, also, are shown to reflect the fundamental homosexual bias of the patients' personality.

S. M. COLEMAN.

Convulsive Therapy in the Psychoses.

Forty patients were treated with convulsive shocks. Of the 14 recent schizophrenics 5 improved. Of 15 chronic schizophrenics only 1 showed slight improvement. Three involutional cases reacted promptly with remissions. Of 6 melancholias, 5 had remissions. Two cases of anxiety hysteria with conversion symptoms obtained remissions with insight. S. M. COLEMAN.

J. NEUROPHYSIOL.

VOL. III. JANUARY, 1940.

Spinal Cord Regeneration in the Rat.

(1) Spinal rats (cord section between T5 and T13, with tension on the tail causing the cut to gape 2-3 mm. and insuring a complete lesion) will live indefinitely (8 months) with moderate care.

(2) Oedema and gangrene of the hind legs (as well as hydronephrosis and hydroureters) are the main cause of early death and depend directly on urine retention. Manual expression of urine three times a day during the period of returning bladder control, seven to ten days, eliminates this difficulty.

(3) Flexion reflexes are present immediately after section, crossed responses appear after three days, scratch reflexes after eleven days. Complex and fractional responses of hind legs and tail develop, but with no sign of coordination with the front quarters.

(4) By one month, the typical spinal animal has reached a steady level of behaviour and fails various tests of sensation and voluntary motor control. At the time of sacrifice electrical stimulation of the cerebral peduncle does not evoke motor responses below the level of section. Cell stains show normal neurones close to a complete transverse scar, and silver methods reveal new axones entering and becoming tangled in the connective tissue of the lesion.

(5) In some cases (13 in all), after four weeks of typical spinal performance, further sensory and motor recovery occurred, including voluntary climbing, walking and hopping movements, and placing and seeking based on good proprioception. At sacrifice, stimulation of the brain stem produced hind-leg movements. Silver stains showed a complete scar bridged by bundles of new axones passing continuously between cord tracts on either side of the lesion. The fibres entering and crossing the scar ordinarily arise from both the cord tracts and spinal roots, but when the latter are excluded physiological recovery still occurs.

(6) The most marked recovery was in rats with properly oriented nerve or muscle implants in the cord gap. Recovery was poor with embryonic brain implants which degenerated, formed acinar cell stumps, or developed into small pyramids.

(7) Spinal neurones with adequate blood supply start to regenerate cut processes. These fibres grow along structural pathways like peripheral nerves and using bands of glial nuclei when possible, but are mainly blocked by glia and scar tissue running transversely across the cord. When they successfully cross a scar, restoring anatomical continuity, nervous transmission across the lesion and coordinated function also return.

(8) True anatomical and physiological regeneration can occur in the rat spinal cord. This is aided by an implant of degenerating sciatic nerve. Such implants may find clinical application. (Authors' abstr.)

Paleocerebellar Inhibition of Vasomotor and Respiratory Carotid Sinus Reflexes.

The author's previous experiments have shown that weak faradic stimulation of the vermian cortex of the anterior cerebellum causes strong inhibition, not only (as is well known) of decerebrate rigidity, but also of vasopressor and vasodilator reflexes and of the spontaneous vasomotor waves. The present paper concerns the action of the same cerebellar stimulation on vasomotor and respiratory carotid-sinus reflexes. The following effects have been observed :

1. Inhibition of carotid-sinus vasopressor reflexes brought about by the occlusion of the common carotid arteries. The depressor action on normal blood pressure is less evident or absent.

2. Inhibition of carotid-sinus respiratory reflexes produced by a carotid occlusion as above. There is also less evident inhibitory action on normal respiration.

3. Inhibition of the carotid-sinus reflexes, chiefly respiratory in nature, provoked by an intracarotid injection of potassium cyanide.

Experiments of local cocainization, total or partial curarization and occasional observations show that the vegetative effects observed are (like the somatic ones) due to a central inhibition of bulbopontine centres by the paleocerebellar cortex. We must, therefore, admit the existence of a cerebellar control, not only in the somatic, but also in the vegetative sphere. The mechanism and the functional significance of the vegetative action of the paleocerebellum are discussed.

(Author's abstr.)

Brain Potential Changes in Man during Cyclopropane Anaesthesia.

1. There are six discrete changes in the frequency of brain potentials in man during cyclopropane anaesthesia and recovery from it. The frequency changes in the approach to anaesthesia are not mirrored in the recovery from anaesthesia.

2. Potential patterns from corresponding regions of the head during anaesthesia and recovery are almost identical. However, the front, top and back of the head form three relatively independent units of activity. Differences in time of onset of slow activity, rate of recovery, amplitude and regularity of potentials in the three units are described.

3. Just as in normal sleep, a well-defined 12 to 14 per second rhythm is found most predominantly on top, less so in front, and least commonly in the back of the head. This rhythm differs from that in normal sleep in that it appears late in the recovery from the anaesthetic.

4. Although there is not as great individuality of potential patterns during anaesthesia as in the waking state, it is nevertheless possible to differentiate between anaesthetized individuals on the basis of their electro-encephalograms.

5. CO_2 hastens the onset of deep anaesthesia and makes slow rhythms more regular.

6. Factors which may contribute to the frequency changes seen in cyclopropane anaesthesia are discussed. (Authors' abstr.)

Conditioned Vestibular Reactions.

In four dogs, using a galvanic current between the external auditory meatuses as unconditioned stimulus to produce vestibular reflexes (loss of balance, falling to one side, characteristic head and body movements), these reflexes readily appeared as conditioned responses to an auditory stimulus. Differentiation in these animals was also attained (by reversing the current to produce opposite movements which became conditioned to a new auditory stimulus). Prolonged sleep and peculiar motor phenomena developed in one dog. The conditioned vestibular responses persisted without practice for at least eight months. (Authors' abstr.)

Modification of the Cortical Frequency Spectrum by Changes in CO_2, Blood Sugar and O_2.

The responses of the electrical activity of the human cortex to alterations in normal blood constituents have been analysed with the Grass frequency analyser. Decrease in CO_2 content in the internal jugular blood is associated with a shift in energy distribution in the cortical frequency spectrum toward the slow side, an increase with a shift in energy distribution to the fast side; these effects become less marked with extremely high or extremely low CO_2 tensions. Oxygen and glucose, on the other hand, can be varied within wide limits with little change in the cortical frequency spectrum, but when the O_2 saturation or glucose concentration in the internal jugular falls to a critically low level, there is a sudden shift of energy distribution to the slow side. With exceedingly high concentrations of glucose, the energy distribution in the cortical frequency spectrum shifts toward the fast side. Experiments on rabbits indicate that the effects of high O_2 tension are similar to the effects of high concentrations of glucose.

The results suggest that the electrical activity of the cortex is a manifestation of the activity of a great number of chemical oscillators having different natural periods. Though differing in their periods, these oscillators tend to respond similarly to any given factor. A factor which affects one frequency tends to affect all frequencies in the same direction, though not necessarily to the same degree. (Authors' abstr.)

Ocular Rotation in Anaesthesia and under the Influence of Supranuclear Centres.

1. Under the influence of anaesthetics, particularly of the so-called brain-stem anaesthetics, various types of ocular rotation (heteronymous and homonymous rotation) occur.

2. Stimulation of the cortical oculogyric centres may produce, besides conjugate deviation in a horizontal or vertical direction, a slight rotation (most frequent reaction: rotation of the opposite eye towards the side of stimulation). Tonic effects of the cortex upon the position of the eyeballs in regard to rotation could not be found. Elimination of the cortex plus subcortical ganglia in front of the midbrain produces moderate degrees of rotation, but not such high degrees of rotation as are observed under the influence of anaesthetics.

3. After unilateral labyrinthectomy, rotation to the side of the operation is more marked on the opposite side than on the homolateral eye; this rotation may outlast the spontaneous nystagmus. A similar homonymous rotation may be produced by a unilateral lesion of the vestibular nuclei, suggesting that disturbances of the equilibrium between the vestibular nuclei of the two sides may play a part in the genesis of homonymous rotation observed in barbiturate anaesthesia.

4. Ocular rotation is still produced by brain-stem anaesthetics such as dial-urethane in mid-brain animals. It is inferred that the ocular rotation produced by anaesthetics is only partly due to depression of prosencephalic and diencephalic activity and partly to direct action upon the lower centres.

5. Separation of the mesencephalon from the rhombencephalon in normal as well as in mid-brain animals diminishes the rotation produced by barbiturates, but does not abolish this rotatory effect; this indicates a direct action of the anaesthetic upon the midbrain, besides the action upon rhombencephalic supra-nuclear centres. (Authors' abstr.)

Effect of Various Cortical Lesions on Development of Placing and Hopping Reactions in Rats.

Complete removal of that area of the cortex which in rats one to five days old corresponds to the sensorimotor area of the adult results in a permanent deficiency of the placing and hopping responses. This deficiency is indistinguishable from that caused by a similar operation of the other hemisphere of the same rat after it had reached maturity.

Small lesions confined to the fore-leg or hind-leg areas produce permanently detectable deficiencies in these postural reactions. It is possible to determine the position and extent of the lesion by a study of the deficiencies in the placing and hopping reactions. The deficiencies following incomplete ablation of the sensori-motor area are not as great as those resulting from complete removal of this portion of the cortex.

There is no detectable improvement in the placing and hopping reactions after they have been rendered deficient by removal of the sensorimotor cortex. Even when lesions are made in the sensorimotor cortex immediately after birth, the remaining cortical and subcortical tissues are unable to assume, as they mature, the function normally executed by that portion of the sensorimotor cortex which has been ablated. (Authors' abstr.)

Activity of Isocortex and Hippocampus: Electrical Studies with Micro-electrodes.

1. Micro-electrode techniques suitable for examination of electrical changes occurring in the nervous system are described. A satisfactory type of micro-electrode has proved to be a micropipet, filled with Ringer-agar, into which dips a chlorided silver wire. Its limitations are discussed.

2. The following two predictions have been verified by experiments on the iso-cortex and on the hippocampus: (*a*) large potential differences should be recorded from micro-electrodes at certain positions in active tissue (i.e. from positions close to active elements); (*b*) under certain conditions micro-electrodes should record predominantly the activity of only a small volume of tissue immediately adjacent to them.

3. Deep pentobarbital anaesthesia greatly simplifies the electrical patterns recorded from the isocortex (cat). Only isolated voltage changes of considerable

size and duration appear; their characteristics are such that they must be due to organized activity in groups of related neurons.

4. Further experiments have been performed on the hippocampus (cat; rabbit) because of its relatively simple structure. In addition to changes manifestly due to stimulation by injury three types of activity may be described.

5. "Slow waves" appear as spontaneous excursions of 20–70 msec. duration. They are recorded from the surface of the hippocampus as well as from micro-electrodes placed at various positions within it. Their nature is obscure, but there is no evidence that they are composed of overlapping spikelike components.

6. Rapid deflections of about one millisecond in duration and always negative in their predominant phase are recorded only from micro-electrodes placed in or very near the strata containing the cell bodies of the pyramidal cells of the Ammonshorn.

7. The stimulation of the afferent fibres going to the hippocampus from the Area entorhinalis results in responses which may be recorded from the surface of the hippocampus and from points within it. The surface response ordinarily appears after a latency of one or a few milliseconds, and is characterized by an initial surface positive phase (10–20 msec.), followed by a smaller, longer and more variable surface negative phase. The responses recorded from micro-electrodes inserted within the hippocampus appear of opposite sign when the micro-electrode (monopolar lead) is in the deeper parts of the Ammonshorn. In a significant atypical experiment the response was surface negative and reversed at a shallower depth in the hippocampus. The results have been analysed in terms of potential theory and the membrane hypothesis. It is concluded that the responses to stimulation are due largely to potential changes characterizing the activity of the perikarya of the pyramidal cells of the Ammonshorn. (Authors' abstr.)

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PROCEEDINGS OF THE CENTRAL PSYCHONEUROLOGICAL INSTITUTE OF THE UKRAINE.

VOL. IX. 1937.

PROBLEMS OF THE FUNCTIONAL CORRELATION OF THE VEGETATIVE NERVOUS SYSTEM.

VOL. X. 1938.

PROBLEMS OF THE PATHOPHYSIOLOGY AND TREATMENT OF THE SCHIZOPHRENIAS.

Nitrogen Metabolism in Catatonia.

The author investigated girls between 16 and 21 years of age suffering from catatonia of from two to eighteen months' duration. He found an increase in the residual nitrogen in the blood and the ammonia nitrogen reaching pathological proportions. Urea and uric acid nitrogen were normal. With the passage from acute to chronic the residual nitrogen returned to normal. The ammonia nitrogen returned sharply to normal.

The writer thinks that in dementia praecox there is an auto-intoxication with intermediate products of protein metabolism with retention of these abnormal nitrogenous products in the body. G. W. T. H. FLEMING.

The Treatment of Schizophrenia with Hyposulphite.

This treatment is based on the theory that schizophrenia is due to toxic products which are neutralized by the sodium hyposulphite injected. Sulphocyanate and double ethylsulphuric acids are formed. The author treated 377 cases of acute schizophrenia. In 27 there was a rapid cure, the patients leaving the hospital cured. In other cases after a short amelioration the disease flared up again. A course of 10–15 intravenous injections of 10 c.c. of a 20 per cent. solution of sodium hyposulphite was given. G. W. T. H. FLEMING.

The Effect of a Mixture of Bromide and Caffeine in Mental Diseases.

The author based his work on the effect of bromide and caffeine on experimental neuroses in animals in Pavlov's laboratory. He gave 8–15 intravenous injections of sodium bromide and caffeine. The chief effect was on sleep, which was restored, and on motility, which was diminished. Hallucination diminished and the effect lasted from 2–10 days. G. W. T. H. FLEMING.

PSYCHIATRY.

VOL. II. NOVEMBER, 1939.

A Critical Appraisal of the " Shock Therapies " in Major Psychoses. I. Insulin.

Insulin shock therapy has been used in a fair number of cases in which the diagnosis remained uncertain. This is the more evident because many institutions have followed the recommendation that treatment be carried out in acute cases from the very onset of the psychosis, and even before completion of the diagnosis.

Considering that there is no consistent relationship between the therapeutic results, on one hand, and, on the other hand, the number of individual treatments and intervals between them, the number of comas and the kind and severity of other reactions, it stands to reason that aside from the pharmacodynamic effect of insulin there must be other influences at work.

The great care taken of the patient, and its spectacular form, the creation of a situation for the patient in which he needs the help of the physician and personnel and gets plenty of it, result in a betterment of patient-physician rapport, whose effect in making the patient more receptive to other types of treatments cannot be ignored.

The evaluation of various degrees of improvement—social recovery, remission, much improved, improved—obtained with insulin is more influenced by the subjectivity of the examiner than is the evaluation of similar conditions of patients under usual hospital management only.

In estimating the therapeutic successes with insulin one should also bear in mind the high rate of so-called spontaneous remissions and the relapses which occur in the insulin patients just as well as in the non-insulin patients.

While the high figures for success with insulin cannot be accepted without serious reservations, the fact remains that in certain cases one succeeds with insulin where the usual hospital treatments had failed.

It would, therefore, be unwise to drop the insulin therapy altogether—after the era of enthusiasm is over. But it is indeed unwise to use it indiscriminately, as if it were a panacea for all cases of schizophrenia. (Author's abstr.)

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VOL. XXVIII. SEPTEMBER–OCTOBER, 1939.

The Surface Tension of the Cerebro-spinal Fluid in Nervous and Mental Pathology.

The writer examined 150 spinal fluids with the ring tensiometer of Du Nouy. The results were of value only in cerebro-spinal meningitis and in cerebral syphilis.

G. W. T. H. FLEMING.

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VOL. XI. 1939.

1. Biochemistry, Pathology and Physiology.*

A Chemical Study of Brain Swelling. Riebeling, Carl. [*Z. ges. Neurol. Psychiat.*, **166**, 149–60 (1939).]

Increase in brain-size, as observed in neurosyphilis patients, may be due to both oedema and "swelling." The oedema is due to increase in intercellular water content, while the "swelling" is due to increase in tissue protein, generally accompanied by a decrease in the ratio of brain dry substance to water. For the diagnosis of "swelling" the protein-N rather than the dry-weight should be determined. No increase in urea content could be determined microchemically in cases of brain "swelling" in man. MARION HORN (Chem. Abstr.).

Function of Nervous System and Oxidations Occurring in it. Mansfield, G. [*Magyar Orvosi Arch.*, **39**, 626–37 (1938).]

The concentration of narcotic which paralyses the isolated frog spinal cord does not affect its oxidation processes; with concentrations 10–20 times greater, oxidation is depressed. Deep narcosis does not affect the O_2 consumption of a rabbit brain. Acetylcholine formation is unaffected by narcosis.

B. C. P. A. (Chem. Abstr.).

Metabolism of Brain Tissue. Noyons, A. K. M., and Goor, H. van. [*Acta Brevia Neerland. Physiol., Pharmacol., Microbiol.*, **9**, 167–9 (1939); *cf. C.A.*, **33**, 6410⁶.]

The CO_2 output of the brain tissues of guinea-pigs decreased from 8·448 mm.³/g. tissue/minutes 30 minutes after death to 6·184 mm.³/g. 50 minutes after death in an atmosphere of 20·9463 per cent. O_2. As the percentage of O_2 in the air increases the CO_2 production also increases. The brain stalk has a more intensive metabolism per unit of weight than the brain cortex.

E. CURZON (Chem. Abstr.).

Glucolysis and Glucogenolysis in Brain and Blood of Normal and Psychotic Persons. Maruyama, H. [*Fukuoka Acta Med.*, **31**, 145–7 (1938).]

Glucolysis and glucogenolysis in brain tissue from psychotic patients are accelerated. Glucolysis in the blood of such patients is within normal limits. Glucogenolysis in the blood is within normal limits, save in patients with mania, in which it is somewhat accelerated. B. C. P. A. (Chem. Abstr.).

Glycogen of Brain. I. Microdetermination of Glycogen and other Reducing Substances in Brain. Naka, S. [*Japan. J. Med. Sci. II Biochem.*, **4**, 121–31 (1938).]

Fresh tissue is boiled for two hours under reflux with 30 per cent. aq. KOH, the solution is left overnight, 96 per cent. alcohol is added, and the precipitated glycogen, after washing with 66 per cent. alcohol, is dissolved in boiling water

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and hydrolyzed with concentrated HCl. The reducing power of the hydrolysate is determined by the method of Bang (*cf. C.A.*, **12**, 2333), or Hagedorn and Jensen (*cf. C.A.*, **14**, 2352). The glycogen of brain is accompanied by reducing galactosides partly soluble in 66 per cent. alcohol.

II. Distribution of Glycogen in Brain : Comparison of Chemical and Histological Methods of Determining Glycogen. [*Ibid.*, 133–43.]

The results of the chemical and histological methods agree. By the histological method, which can be applied to material stored for several years, 0·02–0·17 per cent. of glycogen is determined in fresh cerebral cortex and 0·04–4·5 per cent. in fresh liver. Fresh, healthy, human cerebral cortex contains 20 mgm. of glycogen per 100 gm., but in disease the value rises to 170 mgm. or more ; glycogen is found rarely and in small proportion only in the medulla.

III. Effect of Disease on Glycogen Content of Brain. [*Ibid.*, 145–65.]

The glycogen content of human cerebral cortex is independent of sex or age, but varies greatly in disease. After death the content decreases only slowly, no appreciable diminution being observed until 26 hours have elapsed.

IV. Constancy of Content of Reducing Substances in Brain. [*Ibid.*, 167–92.]

The glycogen and galactoside contents of the brain of *Uroloncha domestica* are not affected by fasting, fatigue or certain other factors (e.g. administration of insulin), which affect general carbohydrate metabolism ; the galactoside content increases from birth until maturity. B. C. P. A. (Chem. Abstr.).

Pyruvate Oxidation in the Brain. VI. The Active Form of Vitamin B, and the Role of the C_4-Dicarboxylic Acids. Banga, I., Ochoa, S., and Peters, R. A. [*Biochem. J.*, **33**, 1109–21 (1939) ; *cf. C.A.*, **32**, 2596[8] ; **33**, 5459[8], 7370[6].]

The system of Szent-Györgyi for the C_4 dicarboxylic acids is catalytically concerned in the oxidation of pyruvate in the brain. With brain slices and brei from avitaminous pigeons co-carboxylase (I) is less active in the catatorulin test than free vitamin B_1 (II). With two types of finely-ground brain, I is much more active than II, one preparation reacting not at all with II. The monophosphate of II is no more active than II. Brain preparations which respond to II are able to synthesize I in amounts which account for the additional O uptake. The maximum response to I is produced with a $1·5 \times 10^{-7}$ *M* concentration ; each molecule of I catalyzes optimally the uptake of 1,500 molecules of O per minute. The hypothesis of Lohmann and Schuster (*C.A.*, **32**, 1289[6]) that the active form of I in animal tissues is the pyrophosphate is considered to be proved. E. W. Scott (Chem. Abstr.).

Vitamins and the Nervous System. Grünthal, E. [*Z. Vitaminforsch.*, **9**, 255–80 (1939).]

A review devoted to anatomical findings in the nervous system in vitamin deficiency, vitamins A, B_1, C, D and the irradiation products of ergosterol, and E, lactoflavin and nicotinic acid. Bibliography of 3¾ pages.
Joseph S. Hepburn (Chem. Abstr.).

Chemical Pacemakers. I. Catalytic Brain Iron. II. Activation Energies of Chemical Pacemakers. Hadidian, Z., and Hoagland, H. [*J. Gen. Physiol.*, **23**, 81–99 (1939).]

Fe spicules found in the brains of general paretic patients are formed from endogenous brain Fe normally present in haematin derivatives such as cytochrome. Cytochrome-cytochrome oxidase is especially abundant in the brain. The critical

thermal increment, μ, of 16,000 calories for α-brain wave frequency in advanced paretics is a measure of cortical respiration. It results from the slowing of an Fe-catalysed link in cortical respiration, and thus is a chemical pacemaker. To test the theory of chemical pacemakers, the succinate-fumarate enzyme system containing succino-dehydrogenase and cytochrome-cytochrome oxidase acting sequentially was studied. The μ value of the normal system is 11,200 calories. When a critical amount of NaCN (a specific poison of the cytochrome-cytochrome oxidase system but not of the dehydrogenase) is added, becomes 16,000 calories in agreement with theory. The addition of selenite, a specific poison of the dehydrogenase, stops all respiration without shifting also in agreement with theory. When it is shifted from 11,000 to 16,000 calories by NaCN, and a critical amount of selenite is then added, again returns to 11,000 calories. Conclusion: Approximately 11,000 calories is the energy of activation of the succino-dehydrogenase-catalysed step, and 16,000 calories that for the cytochrome—cytochrome oxidase step. These are the most frequently encountered values in physiological systems. The shift of μ for α-brain-wave frequency from 11,000 to 16,000 calories occurs in advancing syphilitic brain infection and is accompanied by a change in the form of brain Fe. C. H. RICHARDSON (Chem. Abstr.).

Brain-tissue Phosphates in Various Animals. Kotkova, K. I. [*Biochem. J.* (*Ukraine*), **13**, 19–31 (*in Russian*, 31–3; *in English*, 33–4) (1939).]

Brain phosphates (I) exhibits two pH optima (at 4·3–5·6 and at 8·9–9·6). Tissue from the following animals was examined (arranged in descending order of I activity): hedgehog, dog, sparrow, pigeon, frog, rat, rabbit and grass snake. The substrate was β-glycerophosphate. Mgrm. ++ activates the alkaline I. F^- inhibits the acid I. R. LEVINE (Chem. Abstr.).

Buffer Properties of Nervous Tissue. Kovalskii, V. V. [*Trans. Conf. Med. Biol.*, **82**, 6, 269–70 (1937).]

The buffering capacity of nerve tissue rises in the series: starfish, skate, haddock, cod, carp, frog, turtle, pigeon, siskin, hedgehog; this order corresponds with that of the position of these animals in the phylogenetic scale. The results for different mammalian species are diversified, but in general buffering capacity falls with higher phylogenetic development; this is ascribed to increasing efficiency of the blood-brain barrier. The buffering capacity of nerve tissue is less that than of blood, and is less variable; that of grey matter exceeds that of white matter. B. C. P. A. (Chem. Abstr.).

Some Metabolic Investigations in Endogenous Psychoses with Special Reference to Liver Function. Lundquist, G. [*Z. ges. Neurol. Psychiat.*, **166**, 546–56 (1939).]

No evidence of liver-function disturbance was obtained in studies of the blood protein and quinine-resistant lipases in 18 patients with schizophrenia or depression. However, variations in the blood total protein and protein fractions during the day were somewhat different in the schizophrenic and non-schizophrenic patients. MARION HORN (Chem. Abstr.).

Protein Swelling of the Liver in Psychoses. Riebeling, C. [*Z. ges. Neurol. Psychiat.*, **166**, 170–7 (1939).]

Riebeling has observed swelling due to high protein content in the liver in three psychotic patients with, and in two psychotic patients without similar swelling in the brain. One psychotic patient with brain protein-swelling showed a low liver protein content. The results are discussed in relation to Riebeling's theory of the importance of liver injury in psychosis. MARION HORN (Chem. Abstr.).

The Determination of Liver Insufficiency by Santonin in Melancholic Patients. Gökay, F. K., and Polvan, N. [*Z. ges. Neurol. Psychiat.*, **165**, 470–3 (1939).]

Santonin excretion tests revealed hepatic insufficiency in all of three patients with melancholia, and in neither of two control human subjects.

MARION HORN (Chem. Abstr.).

Disturbances of the Carbohydrate Metabolism of Cerebral Origin. Lups, S. [*Z. ges. Neurol. Psychiat.*, **164**, 644–56 (1939).]

Lups describes two cases of carbohydrate disturbance attributed to lesions in the diencephalon region of the brain, and gives the results of metabolic studies on 13 patients with acromegaly. One of the patients believed to suffer from diencephalon lesions exhibited migraine, a temporary period of glucosuria and a diabetic blood-sugar curve, and periods of hypoglucaemia during the migraine attacks; the other patient exhibited excessive thirst, rapid loss of weight, psychic disturbances and abnormalities in the urinary and blood sugar, finally developing into diabetes. Among the 13 acromegalic patients diabetic blood-sugar curves were found only in the three exhibiting very large pituitary tumours. No disturbances in carbohydrate metabolism were found in the other acromegalic patients, including four with fairly large pituitary tumours.

MARION HORN (Chem. Abstr.).

The Role of Potassium in Familial Periodic Paralysis. Pudenz, R. H., McIntosh, J. F., and McEachern, D. [*J. Amer. Med. Assoc.*, **111**, 2253–8 (1938).]

Attacks of paralysis were associated with a marked fall of serum K. Administration of KCl, 5–10 gr., produced rapid recovery. During the paralysis K was drained from the serum to meet the needs of the tissues. Experiments indicate that the chemical defect responsible for paralysis lies in the central nervous system and not in the muscles. F. P. GRIFFITHS (Chem. Abstr.).

Respiration in the Central Nervous System. Quastel, J. H. [*Physiol. Rev.*, **19**, 135–83 (1939).]

The respiration and R.Q. of the brain, the effects of various substances and ionic environment on brain respiration, the breakdown of carbohydrate, oxidation of lactic acid, pyruvic acid, succinic acid and many other substances by the brain, the effects of drugs and poisons on respiration in the central nervous system, and the content of vitamins concerned with respiration and of glutathione in the central nervous system are discussed. F. B. SEIBERT (Chem. Abstr.).

The Dry-substance Content of Various Parts of the Brain. Strobel, Th. [*Z. ges. Neurol. Psychiat.*, **166**, 161–9 (1939).]

The proportion of dry substance to water was markedly low in brains from senile patients, and high in brains from catatonic, hyperkinetic or uraemic patients. These phenomena were more marked in the cerebral cortex than in the medulla.

MARION HORN (Chem. Abstr.).

Amount and Distribution of Lipoid Pigments in the Normal Human Cerebral Cortex at Various Ages. Keller, Ludwig. [*Z. ges. Neurol. Psychiat.*, **164**, 259–72 (1939).]

The lipoid pigment contents of the ganglia cells, glia and blood vessels of the human cerebral cortex tended to increase somewhat with age. However, marked individual variations prevented determination of any norm for a given age.

MARION HORN (Chem. Abstr.).

The Rapidity of the Re-establishment of the Normal Chemical Composition of the Cerebro-spinal Fluid after Artificial Derangement. Kassil, G. N. [*Bull. biol. med. Exptl. U.R.S.S.*, **3**, 50–2 (1937); *Chem. Zentr.*, **1**, 2390 (1938).]

From the cerebro-spinal fluid of narcotized dogs suboccipitally administered glucose and $CaCl_2$ were eliminated very slowly; KCl was eliminated very promptly; Na_2HPO_4 was eliminated in part rapidly, in part slowly. During excitation elimination is more rapid than during rest or under narcosis.

M. G. Moore (Chem. Abstr.).

Organic Phosphorus in the Spinal Fluid. Germain, A., and Morand, P. [*Bull. mém. soc. méd. hôp. Paris*, **55**, 793–9 (1939).]

Values of organic P in the spinal fluid higher than 0·5 mgm. per cent. are evidence of the disintegration of phospholipides and nucleoproteins of the nervous tissue regardless of the nature of this disintegration, provided only that it is extensive and rapid. These are also the conditions for the production of a high cholesterol content in the spinal fluid (*cf. C.A.*, **33**, 9390[4]). The P test, however, is apparently a little more sensitive. Ruth Berggren (Chem. Abstr.).

New Notes on the Cholesterol in the Spinal Fluid. Germain, A. [*Bull. mém. soc. méd. hôp. Paris*, **54**, 1592–6 (1938).]

The earlier results (*C.A.*, **33**, 3444[8]) are confirmed and extended. Disintegration of the nervous tissue, regardless of its nature (haemorrhagic, ischaemic, bacterial, parasitic), must be sufficiently extensive and rapid if the cholesterol of the spinal fluid is to exceed 1 mgm. per cent. Ruth Berggren (Chem. Abstr.).

A Study of Enzymes in Normal and Pathologic Cerebro-spinal Fluid. Kaplan, I., Cohn, D. J., Levinson, A., and Stern, B. [*J. Lab. Clin. Med.*, **24**, 1150–71 (1939).]

Normal fluids and that from patients with a diagnosis of tuberculous meningitis (I), purulent meningitis (II), hydrocephalus (III), brain tumour, abscess and cyst (IV), and a miscellaneous group (V), were examined for trypsin, antitrypsin, phosphatase, lipase, tributyrinase, esterase and amylase, as well as for cellular contents, sugar, chlorides, total protein and non-protein N. The fluid of I had increased enzymic activity; trypsin, which was never found in normal fluid, was always present; antitrypsin and tributyrinase were found in 75 per cent.; phosphatase and amylase were above normal; and lipase was found in an appreciable number of these cases. The fluid of II contained trypsin and phosphatase in much greater amounts than in I; values for antitrypsin, tributyrinase and lipase were similar to those found in I; esterase was present in a few fluids; and amylase was practically normal. In III there were two groups, depending on whether there was a lesion of the brain which invaded the meninges or ventricles. Those with lesions showed xanthochromia, high protein content, lipolytic activity, high antitryptic power, elevated phosphatase and tributyrinase activity; those without were normal except for occasional marked lipolytic activity. In IV increased enzymic activity occurred with lesions of meninges or ventricles; if not, the deviations from the normal were much less. In V the fluids were normal except for a patient with suspected polio-encephalitis, and isolated cases of multiple sclerosis, CO poisoning and cerebral arteriosclerosis. The possible sources of the enzymes found in normal and pathological fluids are discussed, and the possible application of enzyme studies in diagnosis is considered.

Howard W. Robinson (Chem. Abstr.).

The Vitamin C Content of the Cerebro-spinal Fluid. VII. The Seasonal Variation of the Vitamin C Content of the Cerebro-spinal Fluid of Nursing Infants. Kasahara, M., and Gammo, I. [*Z. ges. Neurol. Psychiat.*, **164**, 492–3 (1939).]

In 33–40 Japanese nursing infants, the vitamin C contents of the cerebro-spinal fluid were determined by dichlorophenolindophenol titration after meta-phosphoric acid deproteinization. The average values were lowest in March, April, August, September and October (3·7–4·1 mgm. per cent.), and highest in February, May, July, November and December (4·7–5·3 mgm. per cent.). (*Cf. C.A.*, **33**, 5048[8].) MARION HORN (Chem. Abstr.).

Changes in the Composition of Cerebro-spinal Fluid in Circulatory Disturbances. Aviosor, M. L. [*Conf. Insuff. Circ.*, 229–37 (1938); *cf. C.A.*, **33**, 6431[5].]

In circulatory insufficiency P, Ca and uric acid are within upper normal limits, while non-protein-, amino acid- and urea-N, and K are considerably above normal. The results vary according to the nature of the associated complications.

B. C. P. A. (Chem. Abstr.).

The Diagnosis of Schizophrenia by the Lehmann-Facius Test of the Cerebro-spinal Fluid. Roeder, F. [*Z. ges. Neurol. Psychiat.*, **165**, 462–7 (1939).]

Roeder has found the Lehmann-Facius test for schizophrenia (a flocculation reaction between the cerebro-spinal fluid of the patient in question and a phosphatide-containing extract of brain) highly unreliable as a diagnostic agent.

MARION HORN (Chem. Abstr.).

The Phosphatide Metabolism in the Cerebro-spinal Fluid. I. Report of a New Extraction Method for Small Amounts of Fluid. Roeder, F. [*Z. ges. Neurol. Psychiat.*, **166**, 557–67 (1939).]

Phosphatides are determined in 0·5–1 c.c. cerebro-spinal fluid by drying the fluid, extracting the residue with alcohol-$CHCl_3$, evaporating and ashing the extract, and colorimetrically determining the P by the molybdate reaction. The use of $CHCl_3$ in the extraction permits the extraction of alcohol-insoluble phospholipides which were missed by previous methods employing alcohol-ether.

MARION HORN (Chem. Abstr.).

Acetylcholine Synthesis in a Sympathetic Ganglion. Kahlson, G., and MacIntosh, F. C. [*J. Physiol.*, **96**, 277–92 (1939); *cf. C.A.*, **33**, 7188.]

The finding of Brown and Feldberg (*C.A.*, **31**, 1087[3]) that the perfused superior cervical ganglion can synthesize acetylcholine during prolonged stimulation is confirmed. Only a limited synthesis can occur when the perfusion fluid contains only inorganic salts. A ganglion so perfused rapidly fatigues when its preganglionic fibres are stimulated, since its acetylcholine soon becomes exhausted. Fatigue can be removed by the addition to the perfusion fluid of glucose, mannose, galactose, lactate or pyruvate. These substances promote the synthesis of acetylcholine. Fructose, lactose, arabinose, dl-glyceraldehyde, acetate, aceto-acetate, succinate and acetaldehyde are ineffective.

E. D. WALTER (Chem. Abstr.).

Liberation of Potassium by Acetylcholine in the Central Nervous System. Dulière, Walter, and Loewi, Otto. [*Nature*, **144**, 244 (1939).]

Acetylcholine, when applied after eserine, liberates ionic K in the isolated nervous system of the frog. E. D. WALTER (Chem. Abstr.).

Central Action of Anticholinesterases. Schweitzer, Alfred, Stedman, Edgar, and Wright, Samson. [*J. Physiol.*, **96**, 302–36 (1939); *cf. C.A.*, **32**, 3486[6].]

The action on the reflex activity of the spinal cord of various anticholinesterases and the derived phenolic bases, after removal of the urethane grouping, was examined in cats under chloralose anaesthesia. The potency of the action on the spinal cord in vivo and the inhibitory action on cholinesterase in vitro were compared. Eseroline (the phenolic base derived from eserine-HCl) has a negligible anticholinesterase action in vitro and a very feeble stimulating action on spinal reflexes in vivo. Eserine methiodide is a central depressant, in contrast to eserine-HCl or $-H_2SO_4$, which are powerful central excitants. Preparation 3393 (dimethylcarbamic ester of [m-hydroxyphenyl] diethylmethylammonium iodide) and miotine methiodide are central depressants. Stedman's " meta "-HCl is a central convulsant, in contrast to the corresponding " meta " methiodide, which is a central depressant. Miotine-HCl has a mixed depressant and excitatory action on the spinal cord. Eseroline methiodide has a weak anticholinesterase activity in vitro. It has very little action on spinal reflexes. (m-Hydroxyphenyl) trimethylammonium iodide has a much weaker anticholinesterase activity in vitro and a much feebler central inhibitory action in vivo than the parent substances (prostigmine or " meta " methiodide). The central excitatory anticholinesterases are tertiary ammonium compounds; the central inhibitory ones are quaternary ammonium compounds. E. D. WALTER (Chem. Abstr.).

The Existence of an Acetylcholine Complex in the Brain and in Various Organs. Gautrelet, J. [*Bull. acad. méd.*, **120**, 285–91 (1938).]

In determining acetylcholine it is essential to distinguish between the free and bound base. Tables are given presenting the acetylcholine content in various organs of a variety of animal species, including mammals, birds, amphibia, molluscs, crustacea and insects. A. E. MEYER (Chem. Abstr.).

The Cholinesterase Content of Nervous Tissue. Hellauer, H. [*Arch. ges. Physiol.* (*Pflüger's*), **242**, 382–8 (1939).]

Organs in which acetylcholine is presumed to function as a chemical mediator contain acetylcholine and its esterase in proportionate quantities. Adrenergic nerves, on the other hand, contain much esterase in proportion to their small acetylcholine content. ARTHUR GROLLMAN (Chem. Abstr.).

Adenylpyrophosphoric Acid in the Brain at Various Stages of Embryonic and Post-Embryonic Development. Khaikina, B. I., and Epel'baum, S. E. [*Biochem. J.* (*Ukraine*), **13**, 261–8 (*in Russian*, 269–72; *in English*, 272–4) (1939).]

Adenosinetriphosphoric acid (I) was estimated by hydrolysing the Ba precipitant of the nonprotein filtrate of brain for 15 minutes. The values obtained were checked by using adenosinetriphosphatase prepared from liver. It was shown that the I content continually decreased during embryonic existence and for some time after birth. This is correlated with the intensity of glucolysis, which decreases concurrently. R. LEVINE (Chem. Abstr.).

Cerebral Lesions in Hypoglucaemia. III. Experimental Investigations. Baker, A. B. [*Arch. Path.*, **28**, 298–305 (1939); *cf. C.A.*, **33**, 1394[4].]

Rabbits were subjected to repeated hypoglucaemic reactions and their nerve tissues studied months after the last reaction to evaluate the resulting chronic and permanent damage of the brain. Although nerve-cell changes did occur, these were by no means as striking as the cerebral haemorrhages, the areas of demyelination and encephalomalacia and the glial reactions. No correlation

could be found between the total dose of insulin administered and the severity of the damage of the brain. It is suggested that the cerebral damage in hypoglucaemia might be due to a qualitative circulatory disturbance, inasmuch as the blood reaching the brain is deficient in the proper nutritive materials.

HARRIET F. HOLMES (Chem. Abstr.).

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2. Pharmacology and Treatment.

Prostigmine in Neurology. Fortes, A. Borges. [*Hospital*, **14**, 1121–7 (1938).]

The treatment of bulbospinal myasthenia with physostigmine or eserine seems to produce good results. The therapy with prostigmine, however, is better since this substance has no action on the heart. Its oral administration gives the best and most permanent effects. Its combination with other substances (KCl, veratrine, etc.) proves a failure. Vitamin B_1 seems to have an action assisting that of acetylcholine, the liberation of which is deficient in this disease. The use of vitamin B_1, however, seems to be indicated in the treatment of myastheniform syndromes only in addition to prostigmine. GEORGE NACHOD (Chem. Abstr.).

Effect of So-called Extrapyramidal Poisons, Bulbocapnine, Harmine and Harmaline upon the Glutathione Content of the Liver, Spleen and Blood of Rabbits. Asakawa, Hisasi. [*Arb. med. Fakultat Okayama*, **6**, 279–94 (1939).]

The glutathione content (I) of normal rabbits as determined by the Tunnicliff method is on the average 0·031 per cent. for blood, 0·280 per cent. for liver, 0·260 per cent. for spleen in rabbits. Bulbocapnine in small and moderate amounts (1–10 mgm.) diminishes, but in large amounts (20–25 mgm.) increases I in the blood; in moderate and large doses it decreases I of the liver, but increases it in the spleen. Harmine and harmaline in small to large doses (1–15 mgm.) decrease I of the blood and liver, but increase it in the spleen. The decreasing order of action on I of the blood is harmaline, harmine and bulbocapnine, but the last differs from the other two in that it also can augment I. These three drugs act by stimulating the sympathetic nervous centres. The decrease of I of the liver by these drugs depends upon an increased breakdown of glutathione in the liver, which is brought about by stimulation of the sympathetics, followed by increased secretion of adrenaline from the suprarenal gland. The increase of I in the spleen effected by these drugs appears to be due to a compensatory contribution of the spleen in decreasing I of the liver. Forty-nine references.

M. M. RATH (Chem. Abstr.).

The Effects of Adrenaline on the Reflex Excitability of the Autonomic Nervous System. Darrow, Chester W., and Gellhorn, Ernst. [*Amer. J. Physiol.*, **127**, 243–51 (1939).]

The experiments indicate an inhibitory action of adrenaline on mechanisms controlled by both branches of the autonomic system. The effect on reflex excitability is opposite to that of metrazole and the two pharmacologic agents may counteract one another in this respect. E. D. WALTER (Chem. Abstr.).

The Influence of Hypnosis on the Course of Narcosis in Cold-Blooded Animals. Ströder, Josef. [*Schmerz, Narkose-Anesthesie*, **12**, 86–7 (1939).]

From the observation that hypnosis causes vasoconstriction in the frog swim-bladder and viscera, Ströder deducts that it may cause similar vasoconstriction in the brain; this cerebral vasoconstriction is postulated as the means by which hypnosis facilitates urethane narcosis in the frog (cf. Ströder, *C.A.*, **33**, 7896[8]).

MARION HORN (Chem. Abstr.).

The Brain after Nitrous Oxide Narcosis. Horst, L. van der. [*Ned. Tijdschr. Geneesk.*, **83**, 4191–3 (1939).]

Nitrous oxide is more harmful than other anaesthetics. Frogs kept for five-and-a-half minutes in N_2O lose their reflex irritability, whereas in H_2 the irritability is still preserved after one-and-a-half hours. Lowering of the O_2 present below 9 per cent. increases the anaesthetic action. The pathologic lesions which occur after N_2O death are more extended if no O_2 has been added. A rabbit kept under N_2O for 100 hours with adequate O_2 supply showed injection of cerebral vessels, petechial bleeding and vacuolary degeneration of nerve cells. In another rabbit kept under N_2O with only 9 per cent. O_2 the nervous tissue was killed after 100 hours. R. BEUTNER (Chem. Abstr.).

Narcosis and Metabolism. Noyon, A. K. M., and Goor, H. van. [*Ned. Tijdschr. Geneesk.*, **83**, 3962–5 (1939).]

Using the thermic diaferometer, Noyon determines the metabolism of nervous tissue from various sections of the brain; this amounts to 14·88 cu. mm. per min. for the prosencephalon, 14·94 for the mesencephalon, 18·08 for the cerebellum, 8·60 for the medulla oblongata, 5·40 for the medulla spinalis and 2·47 for the nerves. He then determines the depression of this metabolism by some of the well-known soporifics like veronal or chloral hydrate. These drugs do not act alike on different tissues, thus e.g. veronal sodium depresses more strongly the metabolism of the mesencephalon than that of the prosencephalon, while the opposite holds for chloral hydrate. The relationship between drug concentration and the magnitude of the depressing effect is investigated, with the result that a completely different type of curve is needed for veronal and chloral hydrate graphically to represent this relationship. These curves indicate that veronal sodium acts after being adsorbed to the brain tissue, while with chloral hydrate a saturation in the brain tissue occurs. R. BEUTNER (Chem. Abstr.).

Treatment of Acute Narcotic Poisoning with Fatal Doses. Ebes, A. J. H. [*Acta Brevia Neerland. Physiol., Pharmacol., Microbiol.*, **9**, 137–40 (1939).]

The therapeutic effects of strychnine, picrotoxin, piperidine, sparteine, metrazole, coramine, neospiran, cycliton, and combinations of them were determined with 587 white rats poisoned by intramuscular injection of one to two times the fatal dose of sodium barbital. The best results were obtained with the combinations metrazole-strychnine and metrazole-picrotoxin. A complete scheme for the treatment of narcotic poisoning is included.

E. CURZON (Chem. Abstr.).

The Action of Bile Salts and Cholesterol on the Central Nervous System. Köllensperger, F. K. [*Wien. klin. Wochenschr.*, **52**, 593–7 (1939).]

Small doses of Na cholate, decholin and cholesterol, that are in themselves without noticeable effect, sensitize frogs to galvanic narcosis; narcosis is produced at lower current strengths than normally. The narcosis-supporting action of these substances suggests an action on the central nervous system.

D. B. DILL (Chem. Abstr.).

The Rare Earths and the Nervous System. Gehreke, E., Lau, E., and Meinhardt, O. [*Z. ges. Naturw.*, **5**, No. 3, 106–7 (1939).]

Traces of inhaled vapours of the compounds of the rare earth elements had a definite influence on the skin nerves. They caused a heat sensitivity and itching irritation of the skin. A rubbing of the skin with the dry rare earth compounds caused no such effects. The effects (on respiration, heart, blood pressure, etc.) caused by inhaling the vapours of the compounds were different for different individuals. The finely pulverized praseodymium hydroxide (green), when inhaled, caused after only two to three minutes an itching irritation which started first in

the nose, then in different parts of the head, in the arms and legs, etc. Similar effects were observed with neodymium hydroxide (light violet), although to a smaller degree. Lanthanum (white) behaved like neodymium, while erbium (pink) produced (besides the itching irritation) a stronger heat sensitivity and a sharper sense of odour and taste sensation. Samarium (white) showed the least effects: except for a slight influence on the respiration and on the pulse no other irritation was observed. Dysprosium was investigated in the form of its oxide (cocoa-brown), and it caused a pleasant heat sensitivity which lasted for several minutes and re-occurred several times. Cerium in the form of the quadrivalent hydroxide (yellow) caused deeper respiration without any itching irritation. The results of the experiments are explained by the conception of a positive " nervespectrum " which is present in a metal or in some other substance.

W. R. HENN (Chem. Abstr.).

Effect of Thorotrast (Colloidal Thorium Dioxide) on Ependymal Lining and Related Parts of the Brain. Beers, D. [*Arch. Path.*, **28**, 49–57 (1939).]

Thorotrast (colloidal ThO_2) is not readily excreted by the central nervous system and may remain in the ventricular cavity for long periods (in this case, for 27 days), in spite of the absence of obstruction to the flow of the cerebro-spinal fluid. Thorotrast produces extensive inflammatory and destructive changes in the ependymal lining. The source of the macrophages which ingest the granules of thorotrast may be traced in part at least to ependymal cells. The use of thorotrast for the visualization of ventricular cavities is unsafe.

HARRIET F. HOLMES (Chem. Abstr.).

Injury of the Nervous System by Uliron. Kranz, H. [*Z. ges. Neurol. Psychiat.*, **165**, 269–72 (1939).]

Kranz describes five cases in which uliron therapy of gonorrhoea (one to three courses of 20 gm. each) led to nerve injury, consisting of paralysis, loss of reflexes, atrophies and alterations of the electrical excitability of the muscles. One of the patients had indulged excessively in alcohol, another had consumed alcohol regularly and two others had undergone marked physical exertion just prior to or during the period of drug treatment. Kranz concludes that a pre-existent nerve or muscle injury is an important factor predisposing to adverse reactions to uliron.

MARION HORN (Chem. Abstr.).

Carbon Disulphide Poisoning of the Nervous System. Baumann, C. [*Z. ges. Neurol. Psychiat.*, **166**, 568–80 (1939).]

Special sensitivity of cerebellar cells to CS_2 was indicated by neurological studies on a patient and histological studies on a cat, both subjected to CS_2 poisoning.

MARION HORN (Chem. Abstr.).

Experimental Investigation of the Local Action of Thiophene in the Central Nervous System. Upners, T. [*Z. ges. Neurol. Psychiat.*, **166**, 623–45 (1939).]

" Analytically purest " thiophene, injected subcutaneously into dogs, caused greater histological injury in the cerebellum, especially the granulose elements, than in other parts of the central nervous system. Older dogs showed symptoms of thiophene poisoning more rapidly and severely than younger.

MARION HORN (Chem. Abstr.).

The Effect of Poisoning by Strychnine, Cocaine and Chloral Hydrate on the Dehydrogenase Activity of Nerve Tissue. Khvoinits'ka, M. A., and Romanyuk, N. M. [*Biochem. J. (Ukraine)*, **13**, 97–102 (*in Russian*, 103; *in English*, 103–4) (1939).]

Chloral hydrate poisoning leads to a diminution in the intensity of methylene blue decoloration by brain tissue. The other nerve tissues examined were not affected at all by the poisons mentioned.

R. LEVINE (Chem. Abstr.).

The Passage of Arsenic into the Brain Substance after Application of p-Hydroxy-m-Acetylaminophenylarsonic Acid. Tomita, T., and Hozyô, T. [*Folia Pharmacol. Japon.*, **27**, 128–32 (*Breviaria* 15–16) (1939).]

After intravenous injection of a 4 per cent. solution of the drug dissolved in NaOH, As was practically always found in the brain. This was not the case when the drug was given by mouth. The quantities were at a maximum twelve hours after injection. G. H. W. LUCAS (Chem. Abstr.).

Studies on the Subjective Effects of the Cephalotropic Amines in Man. I. β-Phenylisopropylamine Sulphate. Jacobsen, E., and Wollstein, A. [*Acta Med. Scand.*, **100**, 159–87 (1939).]

Cephalotropic amines are phenyl-substituted aliphatic amines which irritate the central nervous system, causing motor unrest. A large number of young male subjects were tested with β-phenylisopropylamine sulphate and the results are described in detail.

II. A Comparison between β-Phenylisopropylamine Sulphate and a Series of other Amine Salts. Jacobsen, Erik. [*Ibid.*, 188–202.]

Tests were made with β-phenylisopropylamine, N-methyl-β-phenylisopropylamine, N-ethylphenylisopropylamine, ephedrine and β-phenylethylamine. All except the last exerted a definite antagonism to hypnotics.

III. The Action of the Cephalotropic Amines on Intelligence Scores. Wollstein, Artur. [*Ibid.*, 203–7.]

No definite objective effects on the intelligence scores of the experimental subjects could be detected. S. MORGULIS (Chem. Abstr.).

The Analeptic Potency of Sympathomimetic Amines. Tainter, M. L., Whitsell, L. J., and Dille, J. M. [*J. Pharmacol.*, **67**, 56–70 (1939).]

The analeptic potencies of 22 representative sympathomimetic amines and four other stimulants were tested in white rats against the hypnotic actions of avertin (I), chloral (II) and pentobarbital (III). The times required for recovery of corneal and righting reflexes and of responses to faradic stimulation were measured. Most of the compounds were ineffective or nearly so. Cobefrine hastened recovery markedly under all conditions. Large doses of benzedrine generally delayed recovery, while small doses hastened recovery of the righting reflex alone under II and III. *l*-Pseudo-ephedrine hastened recovery of all three reflexes after I only. Metrazole was effective after I, but not after II. 2-Phenyl-l-aminopropane and phenylethylamine hastened recovery after II but not after I. No correlation between molecular configuration and responses was found. Some of the amines produced no shortening of recovery time although, when the animals' reflexes returned, violent excitation occurred. This indicates that there are other modes of stimulation than those evidenced by speed of recovery from a hypnotic.
L. E. GILSON (Chem. Abstr.).

A Quantitative Comparison of Different Analeptics. Chakravarti, M. [*J. Pharmacol.*, **67**, 153–74 (1939).]

Picrotoxin, strychnine, ephedrine, benzedrine, cardiazole and coramine were compared for toxicity in mice, power to awaken mice narcotized with nembutal, power to antagonize the toxic action of nembutal, convulsive and emetic action in pigeons, power to stimulate respiration in cats and mice depressed with nembutal and power to increase the carotid sinus reflex. In relation to toxicity benzedrine had the greatest awakening power. Picrotoxin and cardiazole are the only ones which antagonize the toxic action of nembutal. Picrotoxin, cardiazole and ephedrine

cause vomiting in pigeons. Benzedrine and ephedrine stimulate respiration in mice and are similar to lobeline in potency. Compared to lobeline the others are extremely weak. The medullary stimulants increase the carotid sinus reflex when this is depressed but the doses required are too large for therapeutic use.

L. E. GILSON (Chem. Abstr.).

Strengthening by Cyanide of the Convulsant Action of Brucine and Hydrastine. *Bergstermann, H., and Krauskopf, B.* [*Arch. exptl. Path. Pharmakol.*, **191**, 46–54 (1938).]

Combination of subthreshold doses of brucine (I) with subthreshold doses of HCN causes violent strychnine-like convulsions in frogs. With larger doses of I it was found that the paralysing action of I on the motor nerve end-plates is reinforced by subthreshold doses of HCN. Subthreshold doses of hydrastine likewise caused typical hydrastine convulsions when administered in combination with subthreshold doses of HCN. Subthreshold doses of both coramine and HCN are highly toxic. Combination of veratrine and HCN showed no mutual toxicity-increasing action.

EDWARD EAGLE (Chem. Abstr.).

Electro-cardiographic Investigations during (Insulin) Shock and (Metrazole or Azoman) Convulsion Treatment of Schizophrenia. *Schmitt, Doris.* [*Z. ges. Neurol. Psychiat.*, **166**, 108–27 (1939).]

Electro-cardiograms taken in 32 cases of schizophrenia during various stages of insulin hypoglucaemia revealed various abnormalities, including sinus arrhythmia, extra systole, widening of the Q-R-S-interval, diminution of the S-T interval, and flattening or inversion of the T wave. Electrocardiograms taken in 30 cases of schizophrenia after metrazole or azoman convulsions showed either arrhythmia or tachycardia, the response being consistently characteristic in each patient. Generally the cardiac effects of the hypoglucaemia or convulsions were reversible. However, of 60 patients who showed normal hearts before therapy, ten showed myocardial damage after therapy.

MARION HORN (Chem. Abstr.).

Effect of Tetracor (Pentamethylenetetrazole) and p-Methyltetracor on the Central Nervous System. *Issekutz, B.* [*Magyar Orvosi Arch.*, **39**, 582–97 (1938).]

p-Methyltetracor has a stimulating effect on the central nervous system 10–16 times that of tetracor. For rapid injections the lethal dose is eight times that producing convulsions. Subcutaneous injection of p-methyltetracor and tetracor has one-fifth the effect of intravenous injection, and the lethal dose is much nearer that producing convulsions. Both compounds are excreted at the rate of 20–25 per cent. per hour. The therapeutic administration of the drugs in the treatment of schizophrenia and paralysis of the respiratory and vasomotor centres is discussed.

B. C. P. A. (Chem. Abstr.).

Cardiazole in Schizophrenia. *Nyberg, P.* [*Upsala Läkarefören. Förh.*, **43**, 147–68 (1938).]

In the treatment of schizophrenia, leucocytes were increased by 3600 ± 700 per cu. mm. two hours after injection of cardiazole. Changes in the different types of leucocytes are described. The increase in the neutrophile cells is the same whether the patient improves or not and changes in these cells are of no prognostic significance. Blood sugar is increased after injection independently of whether a fit ensues. The range of blood coagulation time is increased in schizophrenia (value obtained, 3–6 minutes; normal, 4–5 minutes). After a cardiazole fit the coagulation time was lowered one hour after the fit with only partial recovery after two hours. This effect was not due to a direct influence of cardiazole on the blood. During treatment the body-weight first diminished with good recovery later. Pathological changes in the heart and central nervous system of rabbits treated with cardiazole are described.

B. C. P. A. (Chem. Abstr.).

The Symptom Complex "Hypoglucaemic Convulsions" in Childhood. Hungerland, H. [*Arch. Kinderheilk*, **117**, 132–8 (1939).]

During severe morning convulsions the blood sugar of a boy aged 4 was found to be 54 mg. per cent. Preconvulsive symptoms appeared at 43 to 47 mg. per cent. A normal rise in blood glucose followed subcutaneous adrenaline, but not oral or rectal glucose. Laparotomy revealed no pancreatic abnormality, but a liver rich in glycogen. Post-operative fasting blood glucose values of 46 to 54 mg. per cent. were not accompanied by convulsions. Hypoglucaemia is considered to be a necessary, but alone not a sufficient, basis for this symptom-complex.

KATHRYN KNOWLTON (Chem. Abstr.).

The Effect of Insulin on Glutathione Content of the Blood in Schizophrenia Patients. Merezhins'kii, M. F., and Kligman, M. I. [*Biochem. J. (Ukraine)*, **13**, 87–94 (*in Russian*, 94–5; *in English*, 95–6) (1939).]

Insulin in doses of 20–150 units produces a rise in the total glutathione content of the blood during the hypoglucaemic reaction. The administration of sugar brings the glutathione content back to normal. These results are not consistent from patient to patient, or in the same patient on different occasions.

R. LEVINE (Chem. Abstr.).

Alterations in Insulin Tolerance and Body Weight in the Course of Insulin Shock Treatment of Schizophrenia. Plattner, P. [*Z. ges. Neurol. Psychiat.*, **166**, 136–48 (1939).]

The beneficial effects of insulin hypoglucaemia in schizophrenia paralleled the ability of the insulin to increase the body-weight. Marked mental improvement appeared less often in patients who became increasingly sensitive to the hypoglucaemic action of insulin during therapy than in the patients who did not. The increase in sensitivity paralleled the original tolerance for insulin and the duration of therapy. Epileptic attacks during insulin hypoglucaemia occurred less often in patients showing habituation than in those showing sensitization.

MARION HORN (Chem. Abstr.).

Relations between Blood-Sugar Changes and Clinical Symptoms and Course of Recovery during Insulin Treatment of Schizophrenia. Hofmann, Ernst. [*Z. ges. Neurol. Psychiat.*, **164**, 531–4 (1939).]

An analysis of 175 blood-sugar curves during wet and dry insulin shocks in 20 schizophrenic patients. The curves generally became less sharp as mental improvement began. MARION HORN (Chem. Abstr.).

The Convulsions of Insulin Hypoglucaemia in Relation to Water Balance. Corwin, W. C. [*Proc. Staff Meetings Mayo Clinic*, **14**, 515–8 (1939).]

Withdrawal of water for 1–8 days failed to alter significantly the response of non-diabetic dogs to insulin, either in the amount of insulin or the length of time required to produce convulsions. A similar failure to influence insulin convulsions followed hydration with water retention amounting to approximately 10 per cent. of the body-weight produced in periods up to 21 days by daily administration of 2 gm. NaCl/kgm. body-weight by stomach tube, and replacement of the drinking water by 1 per cent. NaCl to which the animals had free access.

MARION HORN (Chem. Abstr.).

Effect of Stellate Ganglionectomy on Carbohydrate Metabolism and on Hypoglucaemic Convulsions caused by Administration of Insulin. Corwin, W. C. [*Proc. Staff Meetings Mayo Clinic*, **14**, 374–6 (1939).]

In dogs, unilateral or bilateral stellate ganglionectomy did not prevent convulsions following administration of insulin, and did not alter the fasting blood-sugar values, the results of glucose-tolerance tests or the blood-sugar curves following insulin administration. MARION HORN (Chem. Abstr.).

Action of Vitamin B_1 on Epileptiform Attacks during Insulin-shock Treatment of Schizophrenia. *Ákos, V.* [*Wien. klin. Wochenschr.*, **52**, 39–42 (1939).]

In three cases previous intramuscular administration of vitamin B_1 in 2–5-mgm. doses prevented the occurrence of epileptiform attacks during insulin shock. Flooding the organism with the vitamin is believed to favour sugar oxidation and to prevent accumulation of a hypothetical neurotoxic " N factor."

D. B. DILL (Chem. Abstr.).

The Pharmacology of Acetylcholine. *Vasil'eva, V. V.* [*Bull. biol. med. Exptl. U.R.S.S.*, **3**, 96–7 (1937; *Chem. Zentr.*, **1**, 3359 (1938).]

The action of acetylcholine on frog blood vessels in Fröhlich and Loewen-Trendelenburg preparations was investigated. Almost without exception, contraction of the blood vessels was obtained. At the same time, comparative experiments with adrenaline, caffeine, atropine and histamine were carried out on the same preparations.

M. G. MOORE (Chem. Abstr.).

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Part I.—Original Articles.

MORGAGNI'S SYNDROME: A CLINICAL AND PATHOLOGICAL STUDY.

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IN recent years attention has been drawn afresh to a group of cases in which there is a hyperostosis of the flat bones of the skull, associated with various mental changes and signs of endocrinological disturbances. In 1761 Morgagni mentioned the existence of hyperostosis of the inner table of the skull, and referred to its association with virilism and obesity. Morgagni's brilliant observation was neglected until recently, when it was proposed to name the condition Morgagni's syndrome. F. Morel (1931) published his monograph on frontal hyperostosis of the skull, and expressed the opinion that hyperostosis frontalis interna is a well-defined disease. He suggested that the proliferation of bone is provoked by adhesions between the dura and the inner table of the skull. As characteristics of the syndrome he described obesity, polyphagia, polydipsia, disturbance of sleep, weakness of muscles, loss of sight, headaches, and sometimes epileptic fits. In his opinion a pituitary disturbance is the primary cause of the disease. Shortly before Morel, R. M. Stewart (1928) described cases of insanity with localized calvarial hyperostosis. He found sclerosis of the anterior lobe of the pituitary, which he considered was the responsible cause. Schiff and Trelles (1931) suggested that there might be a

relationship with Dercum's disease. Dressler (1927) and Greig (1928) dealt with the pathology of the bony changes. Greig suggests that a disturbance of the calcium and phosphorus metabolism is the causative agent. Critchley (1931), dealing with the neurology of old age, emphasized the importance of hyperostosis frontalis interna. A very extensive series of skulls taken from the average hospital population was investigated by Sherwood Moore (1936), 6,650 in all. In his case material there was 1·4 per cent. of hyperostosis. He tried to classify hyperostosis into four forms.

Cases have been described by Van Bogaert (1930), Yolton (1930), Pende (1931), Fattovich (1938), Fracassi and Morelli (1936), Cassatti (1936), Levirot (1937), Roger (1938), Carr (1936). Some of these authors have discussed methods of treatment. F. Henschen (1927) has published a monograph on this subject. Of special interest is a contribution by Moniz (1938), who made arteriographic investigations in his cases, and suggested that a considerable degree of inter-cranial pressure was responsible for the physical symptoms. All contributors have stressed the vast predominance of female patients.

A survey of the literature shows that there is unanimity of opinion that a syndrome exists as a clinical entity consisting of changes in the frontal bone, alterations in the mental state, and signs of endocrine dysfunction. However, the character of the disease is still obscure. It appears to have been rarely diagnosed during life without the help of the radiologist, and from the psychiatrical and neurological point of view the disease is still insufficiently defined. There is no doubt that many cases do not show the complete syndrome and remain undiagnosed during life, either because the disease does not develop, or because it is so slowly progressive that death intervenes from some other cause before it is advanced. Many authors have assumed that the disease is one of later years; this statement obviously must be corrected.

Our case material is small, but by reason of its special nature it seems to throw some light on the essential problems. Moreover, we had the opportunity of performing an autopsy and obtaining the pathological material of a patient in whom the syndrome was well advanced.

CASE 1.—Mabel B—, aged 31, married. Admitted 5.i.39.

General appearance.—Emaciated woman, height 5 ft., weight 5 st. 8 lb. Complexion rather sallow.

Skull.—Narrow, with a high forehead, rounded from side to side. X-ray examination of the skull revealed a marked generalized thickening, greatest in the frontal and parietal regions. There were no localized endostoses. In places the skull was more than twice the normal thickness.

Skeleton.—Apart from flat chest and bow legs there was no skeletal abnormality. The teeth were mostly decayed.

Physical examination revealed patches of fibrosis with altered breath sounds in both lungs. Heart sounds were faint. Blood pressure 110/80. Urine: sp.gr. 1020, trace of albumen. Blood count: R.B.C. 3,250,000; W.B.C. 5,937; Hb. 60 per cent.; C.I. 0·9. No abnormal cell forms. C.S.F. without abnormality. Wassermann reaction in C.S.F. and blood negative.

Central nervous system.—Full investigation was rendered difficult by the attitude of the patient. She was hypersensitive all over and was frightened of being touched. There was a certain diffuse tenderness of her skull. Pupils equal and regular, reaction to light and convergence normal. Fundi normal. Her speech was slow and drawling, but there was no typical dysarthria. No affection of the cranial nerves. No stiffness of the neck. Abdominal reflexes present. Upper extremities: no paralysis, tonus normal. Superficial and deep sensibility not obviously disturbed. Tendon reflexes brisk, equal. Slight ataxia in finger-nose test. No adiadochokinesis. Lower extremities: reduction of power with slight spasticity, left worse than right. Deep and superficial sensibility intact. Knee and ankle jerks exaggerated, left more than right. Patellar clonus on both sides. Plantar response: left extensor, right variable. Slight ataxia in heel-knee test. Sensibility: there was no localized loss of any form of sensibility, but there was tenderness along the course of the great nerves of the lower extremities. There was also a diffuse hypersensitivity present as far as could be ascertained on every part of the surface of the body. Kernig's and Lasègue's signs were positive on both sides. Romberg's sign was slightly positive, but inconstant. Gait: shuffling and somewhat spastic. All movements were executed rather slowly and with some difficulty.

Mental state.—On admission she appeared to be dull, sometimes semi-stuporose. She would not reply to questions unless they were repeated and put to her with emphasis. She frequently gave the impression that she did not comprehend questions. She had evidently poor powers of concentration. When approached she cried out: "Don't touch me!" or "Don't hurt me!". She was obviously very much afraid of being touched. At one time she said that any form of touch caused her pain. She was unable to tell her address, or the age or occupation of her husband. She had no idea of time, and imagined that she had been in hospital for several months. She gave her own age as 13. She did not know how long the Great War had lasted, nor the name of the King. At no time while under observation, even by dint of great concentration, could she answer such questions as: What is the difference between a lake and a river? or between a child and a dwarf? etc. Her answer was: "I don't know." She was unable to perform simple calculations.

The patient remained under our observation for ten weeks, when she was transferred to another hospital. During that time her mental condition showed no real improvement. However, she became a little more responsive and co-operative as the members of the staff gained her confidence and as her nutrition improved. At first she was rather difficult to manage, but later, when less apprehensive, she could be dressed without difficulty and would feed and wash herself. At the best, one could say that her conversational powers were much retarded and that her ability to co-operate and concentrate were slight. She would, however, take part in examinations, but soon became fatigued. There were no signs of aphasia, apraxia, or agnosia.

Case history.—As far as could be ascertained she was of a normal standard of intelligence for her station in life. She had worked as a domestic servant in a vicarage for five years, apparently giving satisfaction and holding her post until her marriage in 1935. Menses had been irregular or absent for some considerable time. She had never been pregnant. We were informed that she showed signs of physical and mental changes about two years before admission to hospital. The earliest symptoms complained of appeared to be pains in the limbs. It also appeared that the mental state deteriorated most rapidly just before admission. We were unable to discover any details of the family history of the patient.

Case summary.—The case is a woman, aged 31, who developed within two years a rather rapidly progressive dementia of the organic type, without any signs of antecedent infection, neoplasm, vascular or renal disease. There was no sign of mental disorder or intellectual abnormality before the onset of this

illness. Accompanying the mental changes were signs of an organic lesion of the central nervous system, producing symptoms of a pyramidal disorder and a certain degree of ataxia. Further, there was marked hypersensitivity of the surface of the whole body, greatest on the lower extremities. The characteristic signs of a meningeal irritation were present in the lower limbs. The only possible common cause for the mental and physical symptoms was found in the skiagram of the skull. This skiagram showed that the vault of the skull was enormously and diffusely thickened, most markedly so in the frontal and parietal regions.

CASE 2.—Rosalama R—, aged 65. Admitted 24.iv.39.

General appearance.—Well-preserved woman who did not look her age. Skin and complexion dark, sunburnt colour, with freckles on face and arms. There was an operation scar in the mid-abdomen. She had obviously been fat and had lost weight. She gave the impression of having a serious physical illness. No signs of virilism.

Skull.—Rather narrow forehead, rounded from side to side. An exostosis, the size of a pea, in the midline, 2 in. above the saddle of the nose. No other external skeletal abnormality. Skiagram showed great thickening of the vault of the skull with numerous endostoses in frontal region. The bone was dense, and the thickening involved the parietal bone to some extent. Sella normal. It was impossible to obtain a satisfactory skiagram during life because of the restlessness of the patient. After death X-ray photographs were taken of the skull and of the vault of the skull after its removal at the autopsy. We reproduce only the antero-posterior and lateral views of the latter as they shows most clearly the special nature of the bony change (Fig. 1).

Physical examination revealed advanced fibrotic process in both lungs, considered to be tuberculous. The heart showed no gross abnormality. Peripheral arteries somewhat thickened. Abdomen full and tender.

Central nervous system.—Owing to restlessness and confusion a complete examination was impossible. The fundi could not be examined. A lumbar puncture could not be performed. The skull was very tender, especially in the frontal and parietal regions, less so posteriorly. There were signs of an old iritis with consequent small pupils, bound down by posterior synechiae. No abnormalities of the cranial nerves. Abdominal reflex absent (operation scar). Upper extremities: no paralysis, muscles rather hypotonic. Tendon reflexes: slight response. Pseudo-athetotic spontaneous movements of the fingers on extending arms. Lower extremities: no gross paralysis. Hypotonia of the muscles. Knee and ankle jerks absent on both sides. Plantar reflex normal. Sensibility: a proper investigation was impossible, but no gross disturbances of sensibility were noticed. The gait could not be examined, as the patient was too ill to stand.

Blood pressure 100/70. Wassermann (blood) negative. Urine: sp. gr. 1014, trace of albumen, no other abnormalities.

Mental state.—On admission the patient was somewhat confused. She answered the first questions with "I don't know," but on being pressed she gave her age as 70, and the length of time she had been in hospital as six months. Her orientation in time was considerably disturbed, while her orientation in space was intact. When her attention could be adequately engaged, she appeared to be able to recognize individual members of the staff. She was very depressed, cried and moaned. She accused herself of wickedness and said that she had neglected her duties and that she feared everything. She answered the question: "What have you done?" with: "The most awful things." She said that people were against her because of her wickedness. She was restless and complained that she was unable to sleep. There were no signs of aphasia, apraxia, or agnosia.

Progress.—Her physical state deteriorated rapidly. Her confusion deepened, and towards the end contact could not be established. Four days before her death she adopted a posture in which her legs were drawn up on the abdomen with knees flexed, her arms to a much less degree. Passive flexing and extension of neck met with a definite resistance. At this stage she showed a marked resistiveness to being handled and appeared to experience hypersensitivity to touch and painful stimuli. She died on May 22 after a short period of unconsciousness.

Case history.—She had a normal childhood. She was married at the age of 19. At that time she was a well-built woman, free from any noticeable physical defects or illness, except for the small exostosis described above. She was a self-willed and rather suspicious person. She always suggested that her husband, while he was away—if only for the evening—might be conducting an illicit love affair. As his work sent him all over the world, frequently without her, she found ample grounds for development of her suspicions. At least 20 years before admission to hospital her jealousy had developed into a system of delusions, and if she saw him speaking to any youngish female acquaintance, she concluded that he was speaking to one of his illegitimate children. Some years later she expressed the belief that her husband was trying to poison her, and that he would eventually do so for the sake of some other woman. She interpreted any physical complaint as a sign of poisoning. Her paranoid attitude became more general during the last few years, and for long periods of time she remained in her bedroom. She was always anxious to convince her daughters of the truth of her suspicions. There is no reason to assume that she ever experienced hallucinations, and, apart from her behaviour connected with her paranoid ideas, she appears to have been able to conduct herself reasonably well, until just before an operation in December, 1938, when she was investigated for an attack of cholecystitis, and found to have a small contracted and irremovable gall-bladder. She did not recover fully from her physical illness after the operation, and she continued to lose weight. Her mental state had apparently altered. She now showed the symptoms of deep depression. She refused to take food, and would not use the furniture in the house, believing that it had not been paid for. If left alone she would throw her food at the wall or throw the furniture about. She would strip herself of her clothes and stand naked, crying that she had to be burned for her sins. As she had become impossible to manage at home and was losing strength, she came under our care. According to the statement of her relatives, she had never shown these melancholic features prior to the operation, but her temperament inclined towards moodiness and depression—a characteristic observed in other members of her family.

We were informed that she began to put on weight in her early third decade and was excessively fat until after the operation in 1938. She had borne four children, of whom the first died at the age of four of diphtheria and a second committed suicide two years ago. The other two children are alive.

The family history of this case and of Case 3 are considered together below.

The full post-mortem findings will be considered later.

Summary of the case.—It is evident that psychotic changes had existed in this patient for at least the last 20 years of her life. Earlier in her life she showed a morbid suspiciousness, which had not yet found a definite object. The fully developed case must be regarded as one of pure paranoia (Kraepelin). Severe melancholic symptoms did not appear until six months before her death, after an abdominal operation, when her physical state was deteriorating. When she first came under our care she had, in addition to these psychotic symptoms, signs of definite organic changes in the nervous system, with loss of reflexes of the lower limbs and symptoms of meningeal irritation. During the last six months of her life she suffered from intense headaches, apart

from which there were no other signs of increased intracranial pressure. The skiagram revealed an advanced degree of hyperostosis frontalis interna.

CASE 3.—Thelma M—, aged 32. Daughter of Case 2. Admitted 22.v.39.

General appearance.—Well-made woman, height 5 ft., weight 11 st. 2 lb., fat, the fat distributed over the whole body, reaching its maximum on buttocks and thighs. Fingers and toes small and rather pointed. Pale, greasy skin. High complexion. Growth of dark hair on upper lip and on cheek in front of the ears. No other signs of virilism. Teeth and skeleton normal. External and internal genitalia normal.

Skull.—Forehead rather prominent and rounded from side to side, similar to that of her mother, but with no exostosis. Skiagram: marked hyperostosis of similar degree and distribution to that of her mother (Fig. 2).

No abnormality in heart, lungs, genito-urinary system.

Central nervous system.—Cranial nerves normal. Pupils and fundi normal. Abdominal reflex present. Upper extremities: no abnormalities. Lower extremities: knee and ankle jerks exaggerated. No clonus. Plantar response: left doubtful extensor, right flexor. Oppenheim's both extensor. No paralysis, no ataxia, no disorder of sensibility.

Urine normal. No polydipsia, no polyphagia. Sleep normal. Wassermann and Meinicke (C.S.F.) negative. Water output normal. Blood calcium 11·5 mg. per cent. Inorganic phosphate in blood 3·0 mg. per cent.

Mental state.—The patient was talkative and ready to discuss her case in great detail. The important points of her statement were as follows. She had a normal childhood and girlhood. She had always been accustomed to understand that her father and mother disagreed, that her father was unfaithful and that he wanted to poison her mother. She asserted that she had not been entirely normal for 15 years. She is aware that she suffers from a familial disease of bone. After marriage there were difficulties with her husband. The charges she made against him resembled those that her mother made against her father, and were probably copied. Her sister committed suicide as the result of similar difficulties with her husband.

About three years ago her menstrual life became irregular, and since then she has only an occasional menstrual period with small amount. At the same time she has been growing fatter, losing her looks, and suffering more and more from dizziness and the inability to think clearly.

Before coming to our care she had been treated at two other mental hospitals since February, 1938. She had been becoming increasingly difficult to manage at home. She held a system of delusional ideas against her husband, believing that he was habitually unfaithful to her. These ideas brought her into conflict with female acquaintances of her husband, whom she threatened and attacked. Frequent examination confirmed the impression that she was strongly under the influence of her mother, and that she had always taken her mother's part in any disagreement with her father. According to her, her two sisters also shared all the suspicions of their mother. They had adopted her delusional ideas. From the time of her engagement her mother endeavoured to estrange her from her fiancé, and later suggested to her that her son-in-law, the patient's husband, was unfaithful and going to poison her.

There were no signs of dementia, and apparently no hallucinations. Her intellect was that of a normal woman. After her mother's death she was rather depressed, showing that she had lost the very person to whom she had turned for advice and grievance. In a few days she talked quite dispassionately about her mother's life and character. While in hospital, up to the present, she has shown no initiative nor any desire to occupy herself in any other way than by writing letters. These letters are full of disjointed paranoidal ideas. A very striking feature of her mental state is her childishness and the light-hearted way in which

she laughs as she tells the story of conflicts between her parents, her husband and herself, and the attempts at poisoning.

The patient has one child, 10 years of age.

Summary of the case.—This patient was admitted to the mental hospital on account of aggressive behaviour derived from paranoid ideas. The main features of her mental disorder were morbid jealousy of imagined rivals, and the conviction that poison was being used against her mother and herself. There were no hallucinations and no other psychotic symptoms. Her history and physical state showed that she had gained in weight in the last three years. There was virilism and a history of menstrual disturbances. There was no evidence of a disorder of the central nervous system, apart from exaggeration of tendon reflexes. The blood calcium level was slightly raised. At her present age of 32, X-ray of the skull showed a hyperostosis almost identical in degree and distribution with that seen in her mother at 65. Her delusions corresponded in a remarkable degree with those of her mother. It appears that she did not develop any delusional ideas of her own.

Family History of Cases 2 and 3.

As far as we have been able to ascertain up to the present other cases of mental disorder have occurred in this family. These investigations have not yet been completed, as the family is widely scattered, but it is hoped that it will be possible to do so at a later date. For the purpose of this paper we can produce the following facts:

Case 2: Her father was a man of ability and intelligence, but subject to violent tempers and of a highly suspicious and intolerant nature. His brother died as the result of an accident, and at the post-mortem examination some unexpected condition of the bones of his skull was found. We cannot say what this condition was, but we were informed that an unsuccessful attempt was made to obtain compensation for an old head injury. It is possible that the real condition was hyperostosis.

Case 2 had four daughters. One died in childhood. The second is alive. She has always shared certain of the paranoid ideas of her mother. She frequently writes to her sister (Case 3) letters of similar paranoidal content to the patient's own. She is abnormally suspicious about her husband's behaviour. The third daughter was killed by a railway train in circumstances highly suggestive of suicide. She is stated to have been subject to periodic bouts of depression, but in addition she believed in every respect in her mother's delusional ideas and found it impossible to live with her own husband. The fourth daughter is Case 3.

Amongst the children of Case 2's sister one son has a skull very similar in external appearance to that of Cases 2 and 3, with, in addition, an exostosis on the forehead, similar in position and size to that of Case 2, but with no gross thickening of the internal table.

Case 3 has one daughter, 10 years old. X-ray examination of this child's skull shows early bony changes similar to those of her mother, but naturally very much less marked (Fig. 3). Her grandfather has informed us that the prominent traits of her character closely resemble those of her mother and grandmother. In fact he has said, "She is going to go in just the same way as her mother."

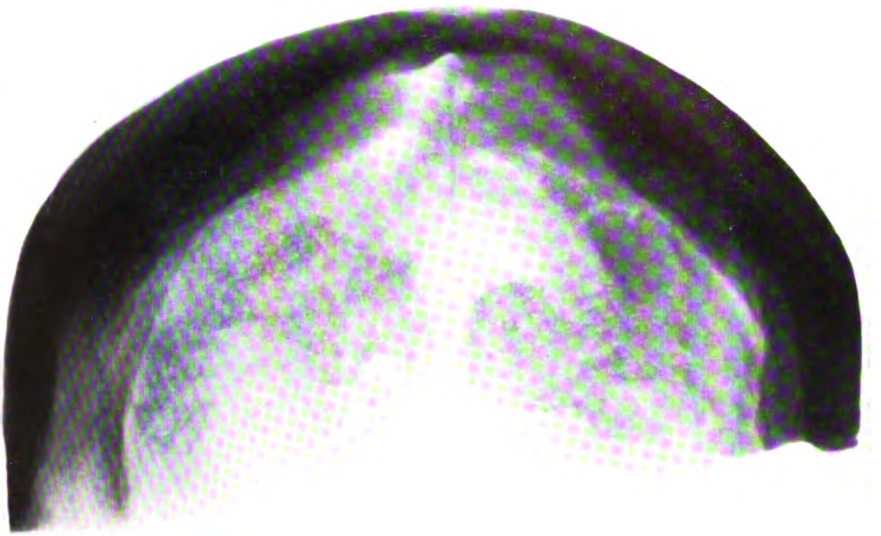
This brief family history is obviously too incomplete to justify any definite conclusions from the point of view of genetics. We feel, however, that it suggests that in our cases heredity is an important factor in the production of the hyperostosis, which appears to be the expression of a dominant gene in this family. Associated with the hyperostosis is a strong hereditary tendency towards the formation of paranoid ideas. We are not justified in assuming that any linkage between the hereditary factors is responsible for these two hereditary conditions.

Discussion of the Clinical Findings.

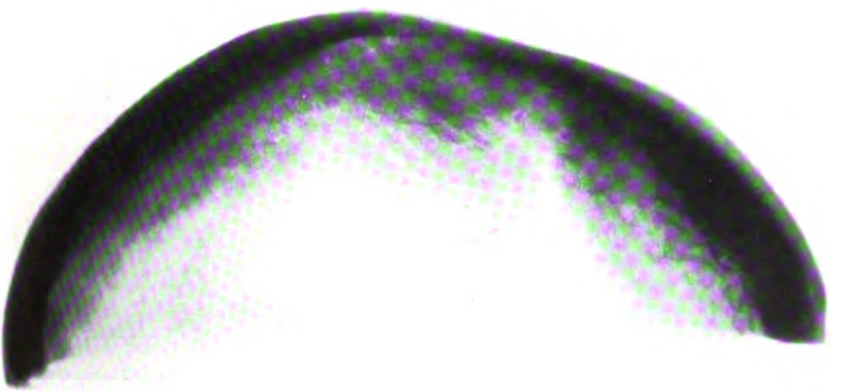
Our case material consists of three cases, of which one has died under observation. In Case 1 the hyperostosis was more diffuse and appeared to be an encroachment on the internal volume of the cranium, without marked local endostosis. This case corresponds with what Sherwood Moore (1936) has described as diffuse hyperostosis. We feel that we are justified in agreeing with Moore's opinion that such a case is one form of calvarial hyperostosis, of which Cases 2 and 3 are another form. It would obviously be incorrect to regard all cases of hyperostosis as occurring solely in connection with the frontal bone, though no doubt, as in Cases 2 and 3, the greatest degree of hyperostosis is seen in the frontal region. We are of the opinion that the proposal by some authors to find a term applicable to all types of this condition is justified, in consideration of the fact that the hyperostosis appears to be but rarely confined to the frontal bone, and that hyperostosis can only be regarded as one part of a syndrome in which there are various other factors. Therefore we have elected to employ the name "Morgagni's syndrome." Our cases, as well as others reported, indicate that a fully developed syndrome is not commonly seen, and that in view of the slowly progressive nature of the disease the great majority of cases present an incomplete picture.

Many authors refer to obesity as the most important single symptom and as indicating an endocrine abnormality. Two of our cases, however, showed that a co-existing wasting disease may mask this feature, so that at the time of the examination the patient presented the opposite appearance. There was in two cases advanced and progressive non-tuberculous fibrosis of the lungs, and in the second, chronic disease of the gall bladder. Our case material is too small to justify any sweeping statement, but we feel that for some reason, perhaps that of an impaired metabolism, these patients are of delicate constitution and might be the subjects of chronic infections.

As to neurological and mental symptoms, the question arises whether they are derived primarily from the pressure of endostosis upon the brain. Our case material is rather special, in that the patients came under care primarily because of symptoms of mental disorder. The neurological disturbances were

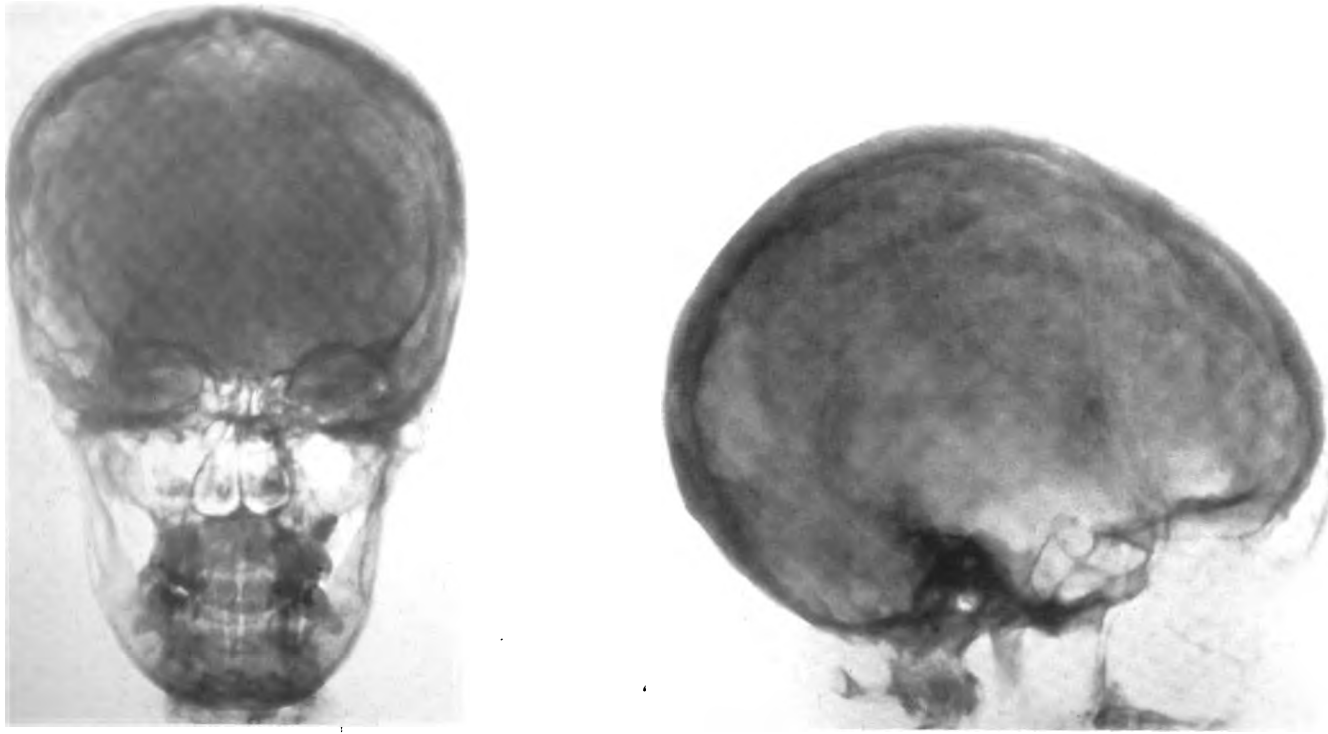


(*a*)



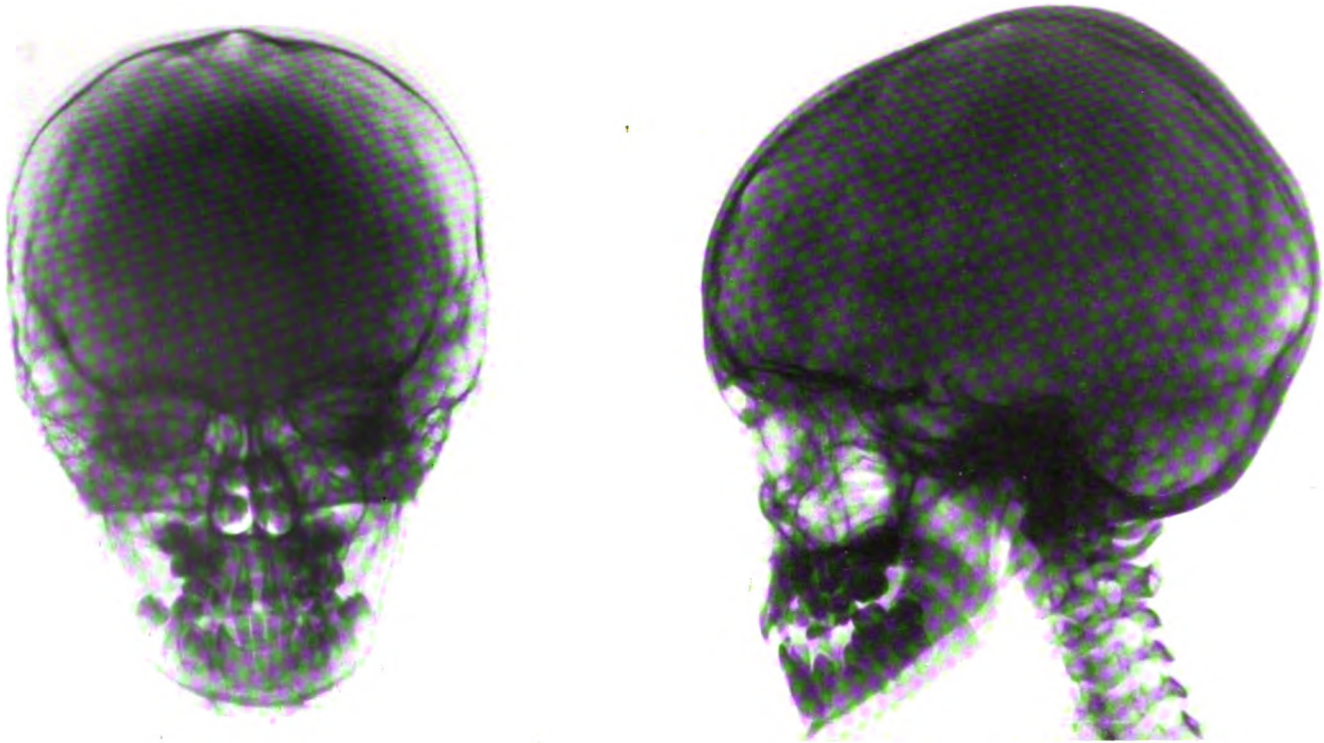
(*b*)

FIG. 1.—(*a*) and (*b*). Antero-posterior and lateral skiagrams of empty vault of skull of Case 2.



(*a*) (*b*)

FIG. 2. —(*a*) and (*b*). Antero-posterior and lateral skiagrams of skull of Case 3, daughter of Case 2.



(*a*) (*b*)

FIG. 3.—(*a*) and (*b*). Antero-posterior and lateral skiagrams of skull of the 10-year-old daughter of Case 3.

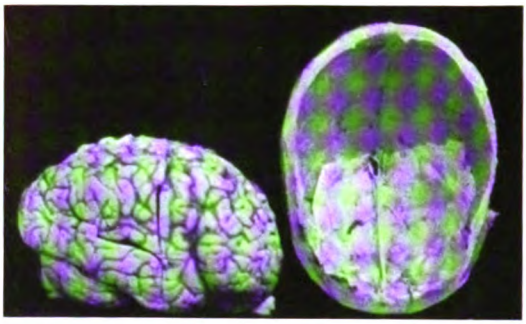


FIG. 4.—Brain and vault of skull with some dura attached of Case 2.

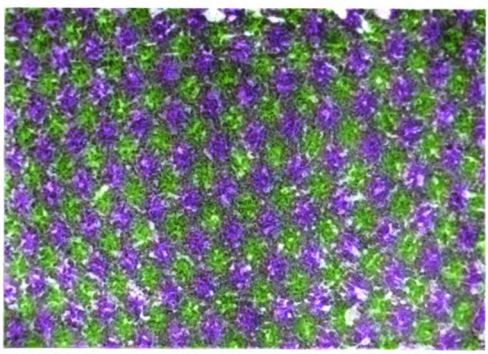


FIG. 5.—Oval body of eosinophil cells in anterior lobe of pituitary, Case 2, H. and E.

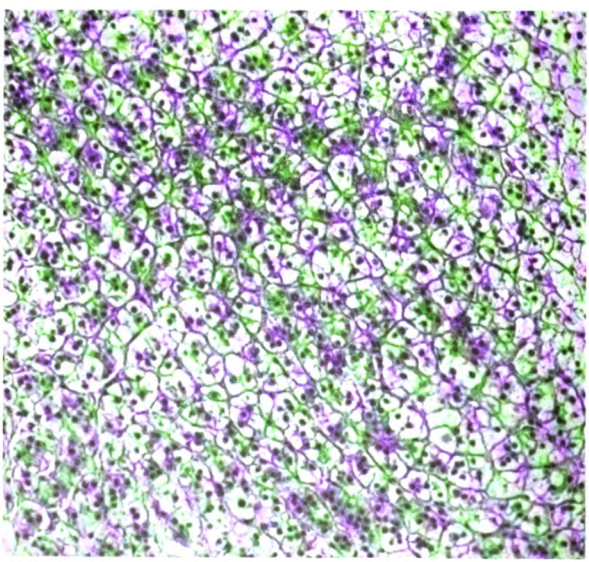


FIG. 6.—Section of upper left parathyroid of Case 2, consisting entirely of large pale oxyphil cells, H. and E.

not prominent in the clinical picture. Nevertheless, it is of importance to ascertain if there are neurological features peculiar to cases of this sort, which might assist in the making of a diagnosis or at least in suggesting that X-ray investigation of the skull should be made, for as far as we know none of the mental changes can be regarded as specific. Even the opinion of the radiologist himself may be uncertain, especially in cases where the hyperostosis is diffuse and without a very definite localization. Furthermore, the ability to recognize such features would be of assistance where the differential diagnosis lay between a meningioma causing hyperostosis and a genuine calvarial hyperostosis.

The neurological symptoms evident in our material were not the same in each case. In Cases 1 and 3 we found pyramidal symptoms, which in the first case produced a spastic gait, while in Case 3 there was no impairment of motor function. In Case 2, however, the most advanced, there was loss of tendon reflexes. The fact that the pyramidal symptoms in Case 1 were the most marked, and that there was a degree of ataxia, might be explained by the fact that the thickening of bone was more extensive and diffuse. The case history suggests that the symptoms developed in a period of not more than two years.

Cases 1 and 2 were more advanced than Case 3, and they had one striking feature in common, namely, signs of meningeal irritation. Furthermore, there was a noticeable hypersensitivity in both cases, resembling what is frequently seen in cases of acute meningitis. Therefore we feel justified in suggesting that where this type of hypersensitivity, with signs of menigeal irritation, is found in patients not suffering from an acute meningitis, calvarial hyperostosis should be considered as a possibility. Probably a chronic irritation of the dura by the attached endostoses produces these symptoms, and it is noteworthy that in Case 3, where headache was absent and neurological disturbances slight, there were no signs of meningeal irritation.

Regarding the mental signs of this syndrome, the existing literature contains no symptom that could be described as pathognomonic, and various forms of mental disorder have been reported. There are obviously four possibilities concerning the relationship between mental disorder and calvarial hyperostosis, namely: (1) that the mental disorder is nothing more than an accidental accompaniment; (2) that the mental disorder is the result of interference with the function of the brain by direct action of the bony condition; (3) that the mental disorder, like the bony changes, results from some common cause responsible for the whole syndrome; (4) that some combination of conditions (2) and (3) may be responsible for the mental changes.

With regard to the first possibility, although it cannot be disproved with absolute certainty, the accidental co-existence suggested is so little in keeping with experience that it must be regarded as improbable. Dealing with the second possibility, one finds that most authors believe that such mental

symptoms as occur are the results of the direct action of endostosis on the brain. For a variety of reasons this simple explanation cannot be accepted without reservation.

It appears justifiable to conclude that in advanced cases some form of mental disorder is a part of the syndrome. This may seem quite obvious if one considers that in this syndrome the endostoses encroach upon the surface of the brain, and especially as the frontal lobes are usually the first and the most seriously to be involved. But if the mental changes were simply the result of this encroachment, one would not expect to find such an enormous variation in the form of the mental symptoms and of the development of some of the ensuing psychoses. We find reliable references to the occurrence of schizophrenic and melancholic states as well as of confusion and dementia, made by various contributors on this subject.

Case 1 of our three cases showed an intellectual deterioration with restriction of knowledge and interest in almost all spheres of life. Not more than two and a half years before she came under our observation she was apparently of normal intelligence. The deterioration of her intelligence greatly resembled that of presenile or senile dementia, although she had not yet reached 30. Nothing in her history pointed in any way to schizophrenia. We therefore regard her case as that of an organic dementia. She consistently showed one special feature, namely, that she was extremely sensitive to any form of approach. Her reaction was one of fear and she cringed away when one approached the bed. This attitude apparently did not result from psychotic fears, but from painful experience through physical hypersensitivity, which, as we mentioned before, resembled that of meningeal irritation. The combination of dementia and fear of being touched gave a picture of an anxious frightened child.

The second case had been the subject of a pure paranoid psychosis for many years. There is no doubt that this psychosis deepened and developed more as she got older, but at the time we saw her first she was physically very ill and features of confusion and melancholic depression were prominent.

In Case 1 the clinical symptoms could perhaps have been explained quite simply by a diffuse damage to the brain surface as a whole. In Case 2 neither the paranoid psychosis nor the melancholic symptoms could be attributed to local pressure. Her intellectual powers were obviously never impaired until shortly before her death, when she was seriously ill and running a temperature. There was no evidence of senile mental changes.

There was only one special feature common to both Cases 1 and 2—an apprehensive attitude with fear of being touched. It is fair to suggest that the hypersensitivity occasioned the same mental attitude, the hypersensitivity itself probably being the result of persistent irritation of the dura. Perhaps this hypersensitivity explains why one author thought that this syndrome was akin to Dercum's disease (Schiff and Trelles, 1931).

The third patient, who showed no signs of meningeal irritation nor of

hypersensitivity, did not display this apprehensive attitude. Although obese, she had no painful deposits of fat.

In this connection it is worth referring to another case under our care. This patient suffers from extensive Paget's disease of the skull and other bones. In her we found considerable hypersensitivity of the meningeal type, and her attitude is childish and apprehensive to a degree, comparable to Cases 1 and 2. We therefore consider that this same hypersensitivity is the result of irritation of the dura. Furthermore, this similarity is of interest, as certain authors take the view that hyperostosis and Paget's disease are akin.

Case 3, the daughter of Case 2, presented paranoid features almost identical with those of her mother. She shared her mother's delusional ideas, and also expanded and transferred them to her own environment. One feels that she developed no delusions of her own. Her psychosis was, therefore, a communicated paranoia. It is likely that her psychopathic constitution is similar to that of her mother, so that she was from the beginning highly susceptible to influences likely to assist the development of the psychosis. We cannot easily estimate how far the constitutional factor and how far the psychological factor of dependency on her mother were responsible; the fact that since the death of the mother six months ago she does not appear to have lost any of her paranoid ideas, suggests that the constitutional factor was the more important of the two.

Having now reviewed the psychiatric aspects of our case material, it seems advisable to consider the third and fourth of the possibilities mentioned above. Our observations as a whole suggest the conclusion that the pathologically abnormal environment of the brain and endocrine dysbalance, producing an alteration in the individual as a whole, activates the abnormal elements in the psychopathic constitution and gives rise to the psychosis, if not actually determining its exact shape. It is reasonable to expect an abnormal but totally different mental picture where the mental constitution is of another type. In this way one can explain the diverse appearances of the mental disorders associated with the syndrome. This hypothesis does not exclude the assumption that in certain cases mental symptoms may be secondary to the mechanical effect of bony changes on the brain, such as has been seen in Case 1.

We will refer to this and to the problem of the influence of the endocrinological factor when the post-mortem findings in Case 2 have been described and discussed.

Post-Mortem Examination of Case 2.

External appearance : A somewhat wasted woman, with a rather dark sunburnt appearance of the skin and many freckles on forehead, face and arms.

Skull : Corresponding to the external boss in the middle of the forehead there was found a well-defined exostosis. The bone as a whole was abnormally dense and offered great resistance to the saw. From within, the inner table of the whole frontal bone and of the adjacent bones, extending back in a fan-shaped fashion as

far as the occiput, was thickened, the maximum thickening occurring round the midline of the frontal bone (Fig. 4). In the affected region the diploë seemed to be absent, and there was a great mass of irregular endostoses with a smooth surface, to which the dura was firmly adherent. More posteriorly, that is from about the vertex backwards, no endostoses occurred; diffuse thickening of the calvarium alone was seen. The dura was only adherent to the endostosis. The calvarium was removed at the average level necessary for extraction of the brain. The weight of this part of the cranium plus the attached dura was 675 gr., that is, almost double the weight of a corresponding area of bone in the average case material. The dura was thickened, its interior surface being smooth; the external, when detached from the bone, presented a rough appearance. There were no other bony changes observed inside the skull. The sella was normal.

Brain: There was a moderate diffuse flattening in the frontal region corresponding with the projections on the inside of the frontal bone, and a certain degree of gyral atrophy in this region (Fig. 4). Otherwise there were no gross pathological features. The vessels were thickened to an extent consistent with the age of the patient. No signs of advanced arterio-sclerosis. No internal or external hydrocephalus. Pituitary gland of normal size and appearance.

The *spinal cord* and its meninges appeared normal.

Skeleton: A small exostosis of the size of half a pea was found on the anterior surface of the body of the third dorsal vertebra. *Lungs:* Both lungs were of uniform mottled grey colour and of almost leathery consistency. They showed an advanced long-standing fibrotic condition, with emphysema in both apices. Enlarged mediastinal glands. *Heart:* muscle flabby, with a degree of fatty infiltration and a slight amount of atheroma of the aorta. No persistent thymus. *Liver:* greasy appearance. *Gall bladder:* small, shrunken. *Pancreas:* smaller than normal. *Kidneys:* no abnormalities.

Adrenals: Both were similar and rather large; the external surface of each rough and nodular. Cut sections showed numerous nodules, 1–2 mm. in diameter, some just outside, others attached to the cortex. The cortex thickened as a whole. Medullae normal.

Alimentary tract: as a whole normal. *Spleen* normal. *Uterus and ovaries:* atrophic according to the age. *Thyroid:* small and hard. *Parathyroids:* four in number, the sizes being—left upper gland 5 : 2 : 2 mm. The three others were unusually small, being about 2 : 2 : 1 mm. in size.

*Histological findings.**

Skull: The examination of the thickened part showed a marked increase of the bony substance. As the result of the increase of the ground substance the lamellae appeared to be increased in size, but the lamellar structure was normal. The inner table was markedly thickened, the diploë being either missing or reduced by thickening of the bony bars. No centres of new bone could be perceived. The lamellae of bone gave the impression of being absolutely quiescent. The external table showed no pathological features except for the exostosis, which showed the same structural features as the inner table, i.e. increase of the ground substance between quiescent lamellae. The pathological character of the thickened parts of the skull was emphasized by the fact that the process of decalcification of even small portions of bone was not complete in less than four months.

Meninges: The *dura mater* related to the bony growths was in many places inseparable from the bone, but there were no elements of dura within the bony tissue. The dura was homogeneous. It was not possible to distinguish between the two layers generally described, of which the outer layer is usually richer in blood vessels. The large venous sinuses which are seen in the normal dura between the two layers were not obvious. They were of small volume and sparsely distributed. The strands of the fibrous tissue ran in all directions. Elastic fibres were

* In the interest of economy the microphotographs for publication have been restricted.

scarce. There was a noticeable increase in the number of connective-tissue cells, especially near the inner surface. There was no marked active proliferation of blood vessels, but as a whole the vascularization seemed richer than usual. The walls of some of the middle and small arteries were thickened; several of them showed early hyaline degeneration. Endothelium of all vessels normal. A number of arteries and capillaries showed a moderate infiltration with lymphocytes. There was no acute disintegration of the dura tissue, but there was a remarkable number of fat cells in the dense connective tissue. There was no calcification of the dura. The parts of the dura mater not adjacent to the hyperostotic parts of the skull showed no abnormality. There was a moderate degree of diffuse thickening of the *leptomeninges*, especially over the frontal parts of the brain. In many places a slight infiltration consisting of lymphocytes and some few plasma cells could be found. These cells were found between the fibres of the leptomeninges and surrounding some of the small arteries and the capillaries. But nowhere could this infiltration be seen to continue to the brain tissue.

Brain: Because there were no clinical localizing symptoms, it was necessary to examine a very large number of portions taken from all the important areas of the cerebral cortex as well as of the other parts of the brain. The staining methods employed were: Nissl's stain (cresyl violet), Kultschitsky-Wolter's and Spielmeyer's stain for myelin sheaths, Mallory's gold-orange aniline-blue stain, Bielschowsky's and Braunmühl's silver impregnation, the modifications of Hortega's silver carbonate and of Cajal's gold sublimate methods for glia staining (Globus, Penfield), the Turnbull blue method for iron deposits, and Herxheimer's lipoid stain. The following are the results of these examinations:

Cerebral cortex: There was no gross lesion in any part of the cerebral cortex. There was no sign of inflammation. But there were signs of a diffuse pathological process. This was found in the frontal region of both hemispheres (less pronounced in the gyrus frontalis anterior), and to a certain extent in the parietal lobes and to a very slight degree in the temporal and occipital lobes.

The pathological changes affected all elements of the nervous tissue. Many of the ganglion cells, chiefly those of the third and fifth layer, to a less degree the small pyramidal cells of the fourth and the cells of the sixth layer, showed a considerable degree of shrinking. Many cells showed an elongated nucleus, sometimes of triangular shape. The nucleus as a whole, or at least the parts surrounding the wall of the nucleus and the wall itself, stained darkly. The tigroid substance appeared more compact. The cellular processes, especially the apical processes of the pyramidal cells, were tortuous. There were no incrustations in the cells. A number of cells showed swelling. In such cells the Nissl bodies appeared fragmented and in parts of the cell body had disappeared. In many of the swollen cells part of the protoplasm was vacuolated. Silver impregnation revealed in the shrunken cells thickening of the intracellular fibres, and in some of the swollen cells fragmentation of the fibrillae. There was no sign of the Alzheimer type of neuro-fibrillary change. There were no senile plaques. There was a considerable quantity of lipofuscin in the cells of the cortex, especially in the larger pyramidal cells. The amount of lipofuscin was considerably greater than one would expect to find in a healthy subject of 65. Clusters of oligodendrocytes surrounded many of the larger ganglion cells. The amount of satellitosis was excessive. In some places there were advanced stages of neurocytophagia. Faintly stained remnants of ganglion cells (cell shadows) could be seen. Small glial elements similar to those forming clusters round the ganglion cells formed long chains parallel to the myelin sheaths, in both cortex and white matter.

A survey of the cyto-architecture revealed that in the frontal and to a less degree in the parietal cortex there was undoubtedly a diffuse loss of ganglion cells, especially in the third, fifth, and to some degree in the sixth layer. In some places a dropping out of ganglion cells was apparent, involving the second to fifth layers and occurring in patches. There were many disorientated cells, especially pyramidal.

The apical dendrite of these cells was not directed radially to the surface, but was sometimes turned through 45°, and even in some cells through 90° from the normal. This alteration in some places made it difficult to distinguish between the individual layers.

The axis cylinders were swollen in many parts of the cortex, most markedly so in the three outer layers. Spindle-shaped enlargements were rather common. The apical processes of the pyramidal cells showed corkscrew shapes and irregular spiral twists. The alteration of the axis cylinders corresponded with the amount of cell affection. In the cornu ammonis axis cylinder changes were not marked.

There were marked pathological changes in the myelin sheaths in the outer layers of the cortex; they were demonstrated in the tangential layer and the supraradial feltwork (lamina suprastriata), and to a lesser extent in the outer Baillarger stripe and lamina interstriata. A great percentage of the fibres showed local distension and swellings, frequently leading to ballooning. In many places a fragmentation into globules of large size could be found. In some parts of the cortex, especially of the frontal lobes, one got the definite impression that the number of the myelin sheaths was reduced, but there were no localized patches of demyelinization.

There was a considerable increase in the number of all glial types, most markedly of the fibrillary and protoplasmatic astrocytes, which were increased not only in the white matter but also in the deeper layers of the cortex. The number of the protoplasmatic astrocytes attached to the external walls of the smaller vessels was definitely increased. Fragmentation of the processes of the protoplasmatic astrocytes (clasmatodendrosis) could be seen in a limited number of cells in the deep cortical layers. Many of the astrocytes revealed a swelling of the cell body. The number of the oligodendrocytes was increased, more especially in the white matter. In the cortex one could find many swollen oligodendrocytes. Their appearance as satellites has been described above.

There was a moderate proliferation of microglial cells, some cells showing a marked hypertrophy and signs of disintegration, and some being distended by globules of fat (gitter cells). Some of the enlarged microglial cells contained granules of iron pigment. These pathological changes were greatest in the frontal and to a lesser extent in the parietal lobes.

Other parts of brain: There were no marked changes in the walls of the *blood vessels*, except where some of middle size showed slight signs of early arteriosclerosis, about the average for the age. There was only a small degree of iron pigment in the walls of the smaller blood vessels of the cortex, and inside the bodies of the microglial cells. The *thalamus, corpus striatum* and the *globus pallidus* did not show marked pathological changes, except an increase of lipofuscin in the larger cells, with satellitosis of these cells and a proliferation of glial elements, especially of the protoplasmatic astrocytes. There was no considerable loss of cells. The substantia nigra was normal. The walls of the medium-sized blood vessels of the globus pallidus were degenerated, and were in part replaced by a homogeneous material which stained darkly with haematoxylin. This was the pseudo-calcium commonly seen in the walls and smaller vessels of the globus pallidus in patients past middle age. In the neighbourhood of these vessels balls of a similar material were seen in ganglion and glia cells and free in the tissue.

No pathological changes were found in the immediate neighbourhood of the *third ventricle* and the *aqueduct*. These regions were investigated carefully, as disturbance of sleep has been described as a characteristic symptom in these cases. The cell groups of the *tuber cinereum* were studied in serial sections. There were noticeable degenerative changes in the supra-optic nuclei, especially in the anterior and middle parts. These cells showed diffuse tigrolysis and some were shrunken. The distribution of the tigroid peculiar to the cells of this nucleus was not to be seen. The cell wall was ill-defined, the cells—normally round or oblong—showed a variety of atypical shapes, some being polygonal with regular or irregular angles. The cells were obviously reduced in number. In places cell-shadows could be seen and advanced neurocytophagia. There was a marked increase of small glial elements in the vicinity of the ganglion cells of this nucleus. Both sides of the tuber were

equally involved. The other nuclei of the tuber showed a slight degree of similar cell changes, but without obvious loss of cells.

There were no pathological changes of importance in the *medulla* and *cerebellum*. The cells of the inferior olives showed an increase of lipofuscin.

Spinal cord : Representative specimens were taken throughout the spinal cord. There were slight signs of meningeal irritation, as shown by infiltration of some of the meningeal vessels. Some nerve roots at various levels showed slight lymphocytic infiltration, but there was no degeneration of root fibres. There was no systematic or diffuse loss of myelin sheaths. A number of the large ganglion cells of the anterior horns showed a considerable degree of dissolution of tigroid, so that in some cells the protoplasm was quite homogeneous. However, there were no signs of damage of the nucleus. The deposit of lipofuscin into the protoplasm of these cells was very substantial.

Endocrine organs.

Pineal body : Normal size. No cavum pineale. The epithelial cells formed a syncytium, partly of trabecular structure. The ill-defined protoplasm of the cells showed granulation, chiefly of basophil and to less degree of oxyphil character. There was a moderate amount of calcareous concretions.

Pituitary gland : Normal size. It was examined in serial sections, stained either with haematoxylin and eosin, or Mallory's aniline-blue-gold-orange. Anterior lobe : acidophil and basophil cells were well stained and of various sizes. The majority of both types, but more especially of the acidophil, were of large size with well-defined cell walls, typical granular protoplasm, and darkly stained nucleus. In many cells there was a vacuole near the nucleus. The basophil cells were irregularly distributed, but the acidophil cells tended to occur in homogeneous groups, especially in the lateral parts of the anterior lobe, where there was a vast predominance of these cells. These areas were less vascular than elsewhere. In some places there were small vesicles containing colloid.

In the left posterior quadrant of the anterior lobe there was a conspicuous circumscribed area, well defined from the surrounding tissue (Fig. 5). It was an oval body, about 3 mm. long, and with a cross section of 2 mm. and 1 mm. It was composed exclusively of eosinophil cells, smaller and more compactly arranged than those of the surrounding tissue. The arrangement of these cells was not very well defined but, on the whole, they tended to form columns radiating approximately from the centre towards the periphery of the body when viewed in cross section. Between some of these columns there was a homogeneous colloid substance, which stained pinkish with eosin and light blue with Mallory's stain. In the centre of the body in the cross section was a small irregular space containing droplets of colloid. The outline of this body was distinct, and there were circular connective fibres surrounding it, while inside there was no connective tissue. The tissue immediately surrounding the periphery of the body was rather loose and showed signs of pressure, as can be seen in Fig. 5. This body could be seen quite clearly with the low power and even with the naked eye in the stained sections.

There were large groups of nuclei set in dense heaps, situated chiefly in the centre of the anterior lobe and along its periphery, and to a lesser degree between the chromophil cells. These nuclei were embedded in a syncytium of protoplasm which stained pale, and in some places showed no cell walls. In some of the cell heaps, however, small cells with distinct walls, some of which contained acidophil granules, could be distinguished. The densest concentration of these cells was at the centre of the anterior lobe, where they occupied the whole space intermingled with thick strands of fibrous tissue. The amount of protoplasm in these dense cell heaps was small considering the size, and most of these nuclei were obviously the nuclei of chromophobe cells, of which the protoplasm was pale and the cell body ill-defined. A few lymphocytes were seen.

With regard to the proportion of the number of these types of cells, it is not possible to make more than approximate statements. It is quite certain that the

eosinophils were greatly in excess of the basophils, and the impression was given that what is considered to be the normal ratio of 3 to 1 was exceeded. The chromophobe cells appeared to be at least as numerous as the chromophils together, or even more so.

The vascularization of the gland was rich. There was a marked increase of connective tissue, especially in the centre of the gland, where the groups of glandular cells were separated by thick connective tissue, rather poor in fibroblasts. Connective-tissue fibres radiated towards the periphery, where they formed a loose tangential layer between the gland cells. These fibres merged into what appeared to be a normal capsule. In spite of the considerable amount of connective tissue, one did not get the impression that there had been a reduction in gland substance as a result of proliferation of connective tissue.

The pars intermedia was well developed, showing a number of large vesicles containing colloid which stained partially blue and partially purplish-red with Mallory's stain. In the periphery of the anterior lobe adjoining the pars intermedia were masses of colloid substance between the anterior lobe cells, which seemed to drown these cells in colloid. These concentrations of colloid were free and were not contained in vesicles with any discernible wall. The colloid in this part of the anterior lobe appeared to be the same as the colloid of the pars intermedia. The posterior lobe was rather small. It showed no pathological changes. In one place *a group* of small basophil cells was seen in the tissue of the posterior lobe.

Parathyroid glands: As described above, there were four glands, three of which were unusually small, and the left superior of normal size. The structure of the three smaller glands was similar and was as follows: There was a dense mass of cells with darkly stained small round nuclei and rather indistinct cell walls. The protoplasm of these cells, stained with haematoxylin and eosin, was faintly bluish or not stained at all. In many cells of the latter type a halo of unstained protoplasm could be seen next to the nucleus. The cells described showed all characteristics of the so-called chief cells, being either clear or what has been described as *Wasserhelle cells*. In some places these cells formed small vesicles, but on the whole they formed a compact uninterrupted mass. Colloid was present between many of the cells in small droplets. Among these cells were single cells, rather small, with well-defined walls and a granular protoplasm which stained distinctly with eosin. These cells resembled the smaller eosinophil cells of the anterior lobe of the pituitary. Furthermore, there were large well-defined cells arranged in groups of various sizes. The size of these cells exceeded not only that of the chief cells but also that of the oxyphil cells described above. Their protoplasm was granular and stained rather pale with eosin, so that they could be easily distinguished from other oxyphil cells. These two types of oxyphil cells (Welsh cells) obviously represented what was described as the dark and pale oxyphil cells. While the number of the dark oxyphil cells was not very large, the amount of cell groups composed of pale oxyphil cells definitely exceeded what is usually found in the normal individual of this age. These cell groups were more numerous and larger than normally. As many as 50 to 80 cells could be counted in one group. There was no colloid between the cells in these groups. The gland tissue was interrupted in many places by globules of fat consisting of typical large fat cells. Strands of fibrous tissue interrupted the compact tissue.

The upper left parathyroid showed a structure quite different from that of the three others. It consisted entirely of large oxyphil cells of considerable size with very well defined walls (Fig. 6). The protoplasm of about half of these cells was densely granular and stained pale red with eosin. The other cells showed fewer granules, which in many cells were concentrated around the nucleus, and in others loosely distributed in the cell body. There was a number of cells without granules, so that the protoplasm appeared to be quite empty. The walls of all these cells were well defined and appeared to be thickened. This thickening was more obvious in those cells which contained little or no granular protoplasm. No cells contained vacuoles. The tissue of this gland was not interrupted by fat, so that the whole

gland presented a homogeneous appearance and was constructed of large cells, which obviously represented pale oxyphil cells in different stages of disintegration of the protoplasm. There was no colloid between or in the cells. The vascularization of this gland was poor. There was no proliferation of connective tissue.

Adrenals : The three layers of the adrenal cortex could be easily distinguished. The numerous nodules described in the macroscopic findings were composed of cells of the glomerular and fascicular cortex. The majority of these cells were of normal size; some of them, however, were enlarged. They were all of normal structure. These cortical growths were sufficiently numerous to produce a considerable increase of cortical tissue, which could be assessed as about one-quarter of the normal cortex. The medulla did not show pathological changes.

Thyroid gland : There was a considerable diminution in total colloid. The vesicles were comparatively small, many of them atrophic, and the number of vesicles with signs of activity reduced. There was an increase of interstitial fibrous tissue, which seemed to invade the rather atrophic vesicles.

Ovaries : There were the usual signs of atrophy corresponding to the age of the patient. No pathological changes.

Pancreas : No pathological changes. The islets of Langerhans showed a normal structure.

Other organs.

Lungs : The lung tissue appeared to be completely disorganized. There was a massive proliferation of fibrous tissue between the alveoli, which were grossly distorted. In many places there was a reversion to the foetal type of epithelium. In the fibrous tissue there was an intense diffuse infiltration with lymphocytes and plasma cells. The bronchial cartilage showed calcification in places. From the microscopic picture it was difficult to imagine how the patient had conducted the normal function of respiration adequately.

Liver : As a whole much diffuse fatty degeneration observed, with a chronic infiltration of the portal ducts.

Kidneys : No significant pathological changes.

Summary of the Pathological Findings.

1. *Macroscopical findings.*—The significant pathological features were the following: Diffuse hyperostosis of the vault of the skull, especially of the frontal and parietal parts of the calvarium with nodular frontal endostoses. The bone was eburnated, the diploe reduced, the frontal dura thickened. There was a flattening and a moderate atrophy of the frontal lobes of the brain. The lungs showed a diffuse fibrosis. There was agranular hypertrophy of the cortex of the adrenals. Three of the four parathyroids were unusually small.

2. *Microscopical findings.—Skull and meninges :* There were no signs of an active process in the hyperostotic bones. The dura mater corresponding to the thickened bones showed proliferation of fibroblasts and slight signs of inflammation. The dura tissue was in some places replaced by fat. The leptomeninges in the same areas were slightly thickened and showed a moderate infiltration. *Brain :* Diffuse degenerative changes, involving all elements of the cortical tissue, throughout the frontal and to a lesser degree in the parietal cortex. The changes were slight in the gyri centrales. In many places the ganglion cells were disorientated. There was dropping out of ganglion cells,

especially of the third and fifth layers. A great number of ganglion cells showed signs of chronic disease with shrinking, lipoidosis, and neurocytophagia, and there was marked swelling of the myelin sheaths, with signs of disintegration. The associated axis cylinders were swollen. In the frontal and parietal lobes there was a proliferation of all glial elements, but chiefly of the protoplasmatic and fibrillary cells, many of which showed degenerative changes. The basal ganglia did not show any noteworthy pathological condition. In the hypothalamus there were chronic cell changes in the anterior parts of the nuclei supraoptici with a considerable amount of neurocytophagia.

Endocrine glands: In the anterior lobe of the pituitary the number of acidophil cells appeared to be greater than normal. There was a well-defined area within the anterior lobe, differentiated from the surrounding tissue, composed of small acidophil cells with a special arrangement. This cell concentration must be regarded as an adenoma of acidophil elements. The basophil cells were normal. The chromophobe elements formed dense concentrations in the centre of the gland, with amongst them a small number of lymphocytes. There was a marked proliferation of connective tissue without a noticeable reduction of gland tissue. Of the parathyroid glands, three showed an increase of pale oxyphil elements, definitely greater than what is regarded as normal for individuals of the age of the patient. The fourth gland was formed exclusively of large pale oxyphil cells. In the adrenals there was a considerable number of small adenomata consisting of cells of the glomerular and fascicular layers of the cortex. There was a moderate atrophy and fibrosis of the thyroid gland.

Discussion of the Pathological Findings.

With regard to the condition of the brain, it has been regarded hitherto by most authors as a matter of course that the pathological changes of the brain are merely the result of the pressure exerted on the surface of the brain by the thickened internal tabula of the skull. This explanation is only satisfactory in so far as it explains the clinical signs of endocranial pressure and local brain injury, such as might accompany any condition where a bony mass encroaches on the brain, e.g. Paget's disease. It has also been suggested that the action and pressure of the endostoses upon the meninges produce local accumulations of cerebro-spinal fluid, most marked in the frontal regions, and in some measure responsible for the symptoms. In our case there was no evidence to support this hypothesis. The dura showed thickening and a little infiltration which appeared to be secondary to and the result of the growth of the inner bony table. There was no sign of serious reaction in the leptomeninges.

Contrary to what has been suggested, there was no evidence that outgrowth of bone was a response to some dural activity of bone cells. In our case the

changes of the brain cortex were of the order of a chronic degeneration and seemed to correspond in extent and in severity with the nature and distribution of the hyperostosis, these changes being greatest in the frontal and parietal regions. At first sight it would seem quite obvious to relate the changes of the brain to the changes of the contiguous bone. But it is equally true that the frontal and parietal lobes are the most heavily involved in any of the chronic degenerations of the cortex, so that a similar distribution of degeneration is the rule in many cortical disorders where there is no question at all of an external mechanical or irritating agent. The distribution of the cortical changes is not in itself conclusive proof that pressure of endostoses alone is responsible for these changes, nor were there any special signs of tissue injury characteristic of the results of immediate and direct pressure.

We do not regard these changes as a result of senility. Apart from the fact that the patient showed no clinical symptoms of a senile psychosis, there were no changes in any element of the nervous tissue pathognomonic for senile degeneration. The lipoidosis was only moderate, and the basal ganglia, which in typical senility show marked degeneration corresponding to the cortical damage, were practically unaffected. The dropping out of ganglion cells recalled what is sometimes found in schizophrenia, where, however, the degeneration is not diffuse as in our case. The pathological findings in the brain, therefore, suggest that the changes found in the cerebral cortex might be partially unrelated to the bony interference.

In the deeper regions of the brain there were noteworthy changes only in the nuclei supraoptici. In these nuclei there was evidence of a chronic degeneration of ganglion cells with reduction of the number of cells, especially in the anterior parts of the nuclei. Other nuclei of the hypothalamus appeared unaffected. This finding is of special interest, as the nuclei supraoptici are regarded as having an influence on metabolism, and as it has been shown that nerve fibres arising from these nuclei end in the posterior lobe of the pituitary, which, however, in this case did not show any marked abnormality. Our findings, therefore, seem to confirm the assumption that the infundibulo-hypophyseal system is affected in this disease.

Some authors (Yolton, 1930; Geschickter and Copeland, 1931; Dressler, 1927) took the view that the reduction of the volume of the brain—especially of the frontal lobes—in old age stimulates the growth of the bone. Greig (1928) tried to explain the fact that the frontal bones are the ones chiefly involved by pointing out that in an old and sick person the recumbent posture tends to relax the mechanical approximation of structures, thus favouring the proliferation of bone. Our investigation produced no evidence in support of such a view. The fact that hyperostosis can be found in young people makes this theory untenable, at least in a proportion of cases, and our case material proves convincingly that hyperostosis is not due to senility. Apart from these objections, it is quite obvious that the common forms of brain atrophy do

not provoke any bony reaction of the nature of cranial hyperostosis. Some proliferation of bone occurs occasionally in the conditions associated with old age. Such bony changes, however, cannot be regarded as part of Morgagni's syndrome.

The diffuse non-specific fibrosis of the lung, with the rarely observed calcification of the small bronchioli, demands special consideration. The origin of the fibrosis is obscure. There was no history of pneumonia and no signs of tuberculosis. The condition of the lungs in Case 2 is all the more interesting, as there were also in Case 1 clinical symptoms of a diffuse fibrosis of the lungs. It is possible that the association of a chronic fibrosis of the lungs with cranial hyperostosis in two of our cases is not merely a coincidence and may reflect some general constitutional or metabolic disturbance responsible for both. It is possible that the tendency to calcium retention and deposition, which favours an increase in the deposition of bone, has produced the calcification of the bronchioli. It is, however, unlikely that this calcification played an important part in the causation of the fibrosis.

Turning to the endocrine glands, changes in the pituitary alone have been recorded in the literature. Stewart (1928) found in one of his cases a marked sclerosis in the anterior lobe, and a deficiency in the chromophil elements. In a second case he found increased connective tissue, the cells of the anterior lobe shrunken and reduced in number. F. Henschen reports reduction of the chromophil cells with increase of the acidophil and basophil elements. Fattovich (1938) found a chronic productive interstitial inflammation of the pituitary. The findings in our case do not correspond with those quoted. It is true that there was in our case a certain degree of proliferation of connective tissue in the anterior lobe, but not enough to justify us in naming it a sclerosis of the anterior lobe. However, there appeared to be some increase of the chromophobe elements in the centre of the gland. A small number of lymphocytes were seen. A similar finding might have induced Fattovich to speak of interstitial hypophysitis. There was certainly no increase in the basophile elements. The eosinophils were very numerous, and there was a small eosinophile adenoma, which did not lead to an enlargement of the gland. We believe that in our case the abnormality of the eosinophile elements alone was sufficiently marked as to be regarded as significant.

Investigation by serial sections of pituitaries taken from a large number of elderly subjects free from any obvious endocrinological disorder shows that there is a great variation in their histological structures. These variations are seen in the distribution and ratios of the different cell types, in the accumulation of fibrous tissue (which is not found in the same degree in younger individuals), and in the number of lymphocytes present. There is hardly any pituitary which does not show some degree of abnormality, and caution must be observed in interpreting these findings. It is, for instance, very difficult to be sure if an increase of one of the cell types is the cause of a certain disorder.

Rasmussen (1928) has shown that there are very great variations in the percentages of the cells of the anterior lobe in normal individuals. Simonds and Brandes (1925) found lymphocytic infiltration in 21 of 200 cases without clinical signs of endocrine dysfunction, and regard it as a sign accompanying chronic infections of some distant organ or of chronic intoxication. We cannot, therefore, do more than make a guarded assumption that in our case dysfunction of the eosinophile apparatus, indicated by an eosinophile adenoma, has acted in part or entirely as the causative factor of this syndrome. This finding compels us to remember that a thickening of the flat bones of the skull is a regular symptom in acromegaly. One can imagine that a localized hyperostosis as in our case is associated with a comparatively minute disorder of the function of the eosinophile cells. In any case, some such suggestion seems to be more in keeping with the features of Morgagni's syndrome than that such a process could have had an inflammatory origin.

The histological investigation of the parathyroids has apparently been neglected in cranial hyperostosis. Disturbance of the calcium and phosphorus metabolism has been suggested by some authors (Greig, 1928; Sherwood Moore, 1936). There is no doubt that the parathyroids of our case showed pathological changes. Probably the unusually small size of three of the four glands can hardly be regarded as important in the present state of knowledge of parathyroid conditions. There was, however, an unusual increase of oxyphil cells in these three glands, otherwise of normal structure, and the fourth gland consisted entirely of oxyphile cells with signs of disintegration of the protoplasm. These findings doubtless indicate an abnormal functioning of the parathyroid apparatus. Investigation of normal parathyroids by Welsh (1898), Erdheim (1903), and the most recent studies by Gilmour (1939) have shown that no normal parathyroid is composed entirely of oxyphile cells, although these elements are increased with advancing years, especially in females. On the other hand, according to Hunter and Turnbull (1931), where there is a definite hyperplasia of the parathyroids with tumour formation the affected gland is frequently composed of oxyphile cells alone. It has been demonstrated that changes suggestive of hyperplasia are often confined to one or two of the parathyroids, the remainder being normal (Albright, Bloomberg, Castleman and Churchill, 1934). It may therefore be concluded that since in our case one gland consisted entirely of oxyphil cells and in the others the number of these cells was obviously abnormally high, there was a parathyroid hyperfunction at some time during life. We are unable to show whether this hyperfunction had existed for a short period during the patient's life, or was still active at the time of her death. Against this assumption it may be argued that in cases reported with a hyperfunction of the parathyroid, the hyperplasia observed has usually amounted to the formation of a parathyroid tumour many times larger than the normal gland. It seems to be reasonable to assume that unless the evidences of hyperactivity of the parathyroid are great, no great

increase in the size of the gland need be expected. Reiss has observed certain rare cases in which there was hyperfunction without obvious enlargement of the gland. It might also be argued that if there were a hyperfunction of the parathyroid, the calcium and phosphorus metabolism would be affected. It was not possible to estimate the blood calcium and phosphorus in Case 2. No evidence of recent osteoblastic activity was found at the post-mortem investigation, so that it seems probable that active bone formation was arrested or had come to an end some considerable time before death. In Case 3 there was a very slight increase in the blood calcium. Normal levels of calcium and phosphorus have been reported in the literature. It is by no means certain that the blood calcium level at the time of the investigation, when incidentally the bony changes were well established or possibly stationary, represented the calcium level during the active stages of the disease, and even in some cases of typical osteitis fibrosa cystica the calcium and phosphorus level has been found normal (Cuthbertson, 1927). It is possible that the calcium retention in the tissue prevents a rise of the blood calcium. It is not necessary to postulate a continuously high blood calcium, as the bony changes evidently take place slowly and over a long period, and the actual weight of new bone laid down, although striking in the skull, is not in itself very great.

In cases of established parathyroid hyperplasia, two sorts of bony changes are commonly seen—formation of new bone and destruction. In cranial hyperostosis there is no destruction of bone. This cannot be held as an argument against parathyroid hyperfunction, in view of the work of Selye in Collip's laboratory. He has shown that the prolonged injection of very small doses of parathyroid hormone into rats produces an increased bone formation due to multiplication of osteoblasts, but only if the dose is sufficiently increased is there a multiplication of osteoclasts, resulting in destruction of bone, thus producing the complete picture of osteitis fibrosa cystica. It seems very probable that in cranial hyperostosis there is only a slight degree of parathyroid hyperfunction, sufficient to stimulate the action of osteoblasts, but not great enough to cause osteoclasis.

Erdheim (1903) has put forward the suggestion that hyperplasia of bone of any etiology causes compensatory hyperfunction and hyperplasia of the parathyroids. Since Mandl (1926) and others have demonstrated that in osteitis fibrosa cystica the calcium metabolism returns to normal after the removal of the parathyroid growths, the validity of Erdheim's theory is doubtful. (Hadfield and Rogers, 1932, and others). In cranial hyperostosis the demand of calcium is comparatively small and probably is spread over a long period of life. One could scarcely expect, therefore, that there would be any noticeable compensatory hyperplasia of parathyroids.

There is another mechanism which could be responsible for the pathological changes of the parathyroids, i.e. the action of a parathyrotrophic principle of the pituitary, for which there is some experimental evidence. It must be

considered that in our case an abnormal function of the pituitary may have influenced the function of the parathyroids. It is of interest that in another pituitary disorder—pituitary basophilism—osteoporosis is a common symptom.

With regard to the changes of the adrenal cortex, it must be admitted that similar changes are not rare in adults without signs of endocrine disorder (Goldzieher, 1929). However, according to Cushing and Davidoff (1927), hypertrophy of the cortex, with or without the formation of adenomas, is found consistently in all the various forms of hyperpituitarism. It is not unlikely that in our case the adrenotrophic hormone (Collip, Anderson and Thompson) is responsible for the hyperplasia of the adrenal cortex, although a primary hyperplasia cannot be excluded, especially as virilism, which is an important part of the complete syndrome, occurs in hyperplasia of the adrenal cortex.

It is possible that the moderate atrophy of the thyroid was part of the polyglandular disorder which existed in our case, although it must be remembered that similar changes are sometimes observed in individuals of this age without special endocrine symptoms. Considering the relationship of the thyroid to other glands, especially to the pituitary, it is highly probable that the changes observed in the thyroid in our case are associated with the abnormal function of the pituitary and other endocrine glands.

The pathological findings can be related to some of the clinical symptoms of the case. It is very likely that the symptoms of meningeal irritation were caused by changes in the meninges which, although not of an acute character, were probably still active until the death of the patient. The diffuse degenerative changes of the brain cortex did not produce dementia. It is hardly possible to explain the character of the psychotic symptoms of the patient by reference to the pathological findings in the brain. We were unable to find a satisfactory explanation for the loss of tendon reflexes of the lower extremities. Possibly the slight irritation in the leptomeninges and around the posterior roots of the spinal cord may have been responsible. It is improbable that the small exostosis found in the body of the seventh dorsal vertebra had any pathological effect on the spinal cord. This loss of tendon reflexes, however, may possibly be attributed to some general toxic process, perhaps connected with the severe physical illness from which the patient suffered in the year before her death. Adie has shown that loss of tendon reflexes sometimes appears in various diseases in which the central nervous system is not primarily involved.

The changes in the endocrine glands are no doubt related to the obesity which was a remarkable feature of this patient for many years. We suggest tentatively that her psychotic attitude towards her husband was influenced originally by abnormal changes in her sexual life. These changes might very well be attributed to dysfunction of the pituitary and perhaps of the adrenals.

SUMMARY.

Three cases have been described in which there was a hyperostosis of the flat bones of the skull with mental changes and signs of endocrine disorder (Morgagni's syndrome). The first case was a young woman in whom there was a diffuse hyperostosis of the vault of the skull with the mental changes of organic dementia. In the second and third cases the hyperostosis was more localized, being especially marked in the frontal and parietal bones. The psychosis in these cases was of the type of a pure paranoia. Both these cases belonged to a family in which the disease appeared to be due to a dominant Mendelian gene. In Case 3 the syndrome was well developed at the age of 31, and in her daughter there was some evidence of hyperostosis at the age of 10.

Clinical signs of meningeal irritation, causing a general hypersensitivity of the surface of the body, were observed in Cases 1 and 2. They are to be regarded as symptomatic of pathological changes in the meninges resulting from the encroachment of the bone.

A fibrosis of the lungs was found in Cases 1 and 2, and may be related to the whole syndrome.

The pathological investigation in Case 2 revealed diffuse degenerative changes of the brain cortex, affecting mainly the frontal and parietal lobes. It is suggested that these changes are largely due to some primary process correlated to the other symptoms of the disease, and the pressure upon the brain surface only contributes secondarily. A certain amount of cell degeneration was found in the region of the nuclei supraoptici.

Pathological changes were found in the pituitary, the parathyroids, the adrenals and the thyroid. The most marked finding in the pituitary was that of an increase of eosinophil cells with a small eosinophil adenoma. There were definite signs of hyperfunction in the parathyroids. The adrenals showed cortical hyperplasia. There was some atrophy of the thyroid.

The opinion is expressed that the variety of forms of mental disorder seen in Morgagni's syndrome is due to the interaction between the mental constitutions of the individuals, and the disorder of the brain and endocrine glands. The distribution and degree of this disorder is in itself subject to great individual variation.

We should like to express our gratitude to Dr. J. J. B. Martin, Medical Superintendent of Bristol City and County Mental Hospital, for his interest and for permission to conduct these investigations, to Dr. A. L. Taylor, Consulting Pathologist, for advice in matters of general pathology, and to Dr. S. B. Adams, Consulting Radiologist to Bristol Mental Hospital, for his valuable assistance. We are indebted to Prof. Golla for providing facilities at the Burden Neurological Institute for some of the radiography and biochemical examinations in Case 3.

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THE CONTRIBUTION OF THE RORSCHACH METHOD TO WARTIME PSYCHOLOGICAL PROBLEMS.

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IN his book, *Psychology and the Soldier*, which gives a critical estimate of the psychologist's contribution during the last war, Bartlett (1) makes an interesting statement which takes on new meaning at the present time. Commenting on the fact that intelligence tests may safely "rule out a man" from participation in activities which may endanger the group, he queries whether a man can as simply be "ruled in" for filling a responsible position. "For practical purposes," Bartlett says, "temperament is a more important factor in success than intelligence, as the latter is understood in the mental test movement. Slight variations in temperament may make a bigger difference to a man's practical value in any social organization, such as an army, than large variations in intellectual processes. No doubt much can be done by psychological examination to discover a man's real temperamental qualities; no doubt a psychologically skilled or a psychologically trained observer can detect such qualities speedily and with reasonable accuracy. But the satisfactory direct temperament test has yet to be devised, and very likely never will be found."

The questionnaire type of temperament test, which has become so popular with psychologists since Bartlett's publication, does little, it would seem, to alter his prediction. For direct questions to the subject concerning his own feelings, emotions, worries and psychosomatic sensations give us at best the subject's picture of himself, and may, in some cases, lend itself to a frankly false estimate of a person's temperamental qualities.

In contradistinction to this type of test, and test situation, the great value of the Rorschach method lies in the fact that the subject cannot do other than report that which he sees in the ten ink-blots. There is no artificial personality ideal to which he can attempt an approximation, while indications of neurotic behaviour, or emotional instability, are evidenced in ways quite beyond the subject's control or remotest knowledge.

As those with experience with the Rorschach method will realize, it is obviously dangerous to emphasize types of personalities when the great value of the method lies in its sensitivity to the individual personality picture. We

feel, however, that certain questions which may arise at the present time are sufficiently important to warrant a certain over-simplification in discussion and consideration of various groups of persons investigated by this method.

Briefly we feel that this method may be used in the following situations, if and when the psychologist may again be participating in wartime activities:

1. The Rorschach may be used to supplement the intelligence test scores in the finding of those persons of exceptional mental and emotional balance for positions of responsibility and peculiar strain.

2. Conversely it may be used to weed out the obviously emotionally unstable not necessarily from the fighting forces, but from those positions of responsibility for which they are not fitted.

3. It may be used as a means of differentiating between the frank malingerer of mental symptoms and the individual with genuine dementia and disorientation caused by physical injury to the brain.

4. Since the personality structures, as evidenced in the Rorschach, of the hysteric, the compulsive and the anxiety neurotic are recognizably different from those of the normal individuals, this method might be used by the psychologist to supplement the differential diagnosis of the psychiatrist in cases which have somewhat indiscriminately fallen under the classification of "shell shock."

With a view to illustrating these uses of the Rorschach method, we have presented here the composite pictures and individual records of various types of personality structures, in order that certain outstanding differences may come to light. As a simple method of epitomizing these results, we have employed a graphic method of presentation. The subject's responses to the ten ink-blots are scored according to the system used in the Rorschach Research Exchange, and are tabulated so that certain important relationships and factors concerning the records stand out.

Fig. 1 illustrates a (hypothetical) normal individual, in whose record various scores are given in optimal ratios. The W : D : d : S ratio is that in which no special emphasis is given to any one mode of approach.

The M : FM : m ratio indicates the higher incidence of the integrated creative responses (M) over the more primitive drives (FM) and the repressive tendencies (m).

Similarly the FC : CF : C ratio illustrates the preponderance of the adjusted emotional responses over the egocentric and impulsive ones. The F plus responses are 100 per cent. of the F responses (F plus : F minus). The F responses constitute fewer than 50 per cent. of the total number of responses (R : F).

The ratio of W : M is approximately 2 : 1.

Figs. 2 and 3 illustrate composite pictures of two groups of subjects, each of ten individuals, from very different educational and social levels. These will be seen to differ from the hypothetical picture in varying degrees.

Fig. 4 illustrates the composite picture of 28 cases of infiltrating cerebral tumour, i.e. widespread cerebral destruction. The marked deviation of this psychogram from the various normal ones is a striking indication that, following extensive organic cerebral damage, the personality picture is uniformly

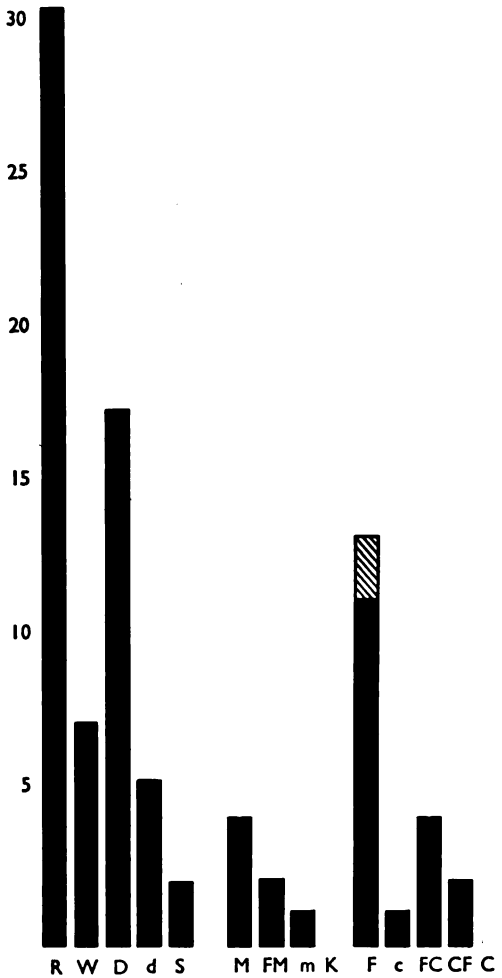

Fig. 1.—Hypothetical normal record showing ratios of W : D : d : S ; M : FM : m ; FC : CF : C; F + : F − ; R : F; W : M ; M : ΣC.

restricted and constricted to an astonishing degree. As has been pointed out elsewhere (3), the similarity between a group of records from tumour patients and the diversity which is shown among an equal number of normals is very striking. A "typical" personality picture emerges for the patients with cerebral tumours.

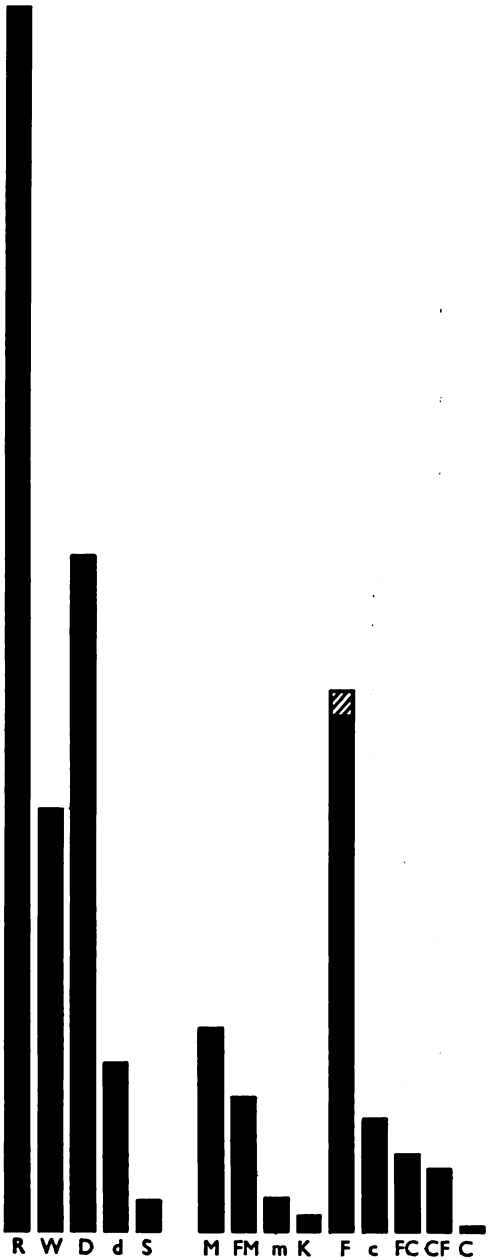

FIG. 2.—Composite record. Ten scientists.

Figs. 5 and 6 illustrate two cases of patients who were disoriented and obviously affected mentally following a cerebral injury.

Figs. 7 and 8, in contradistinction, are records given by persons who were *afraid* that they had been affected mentally following head injury, although actually they had not been so affected. Several points of difference should be noted:

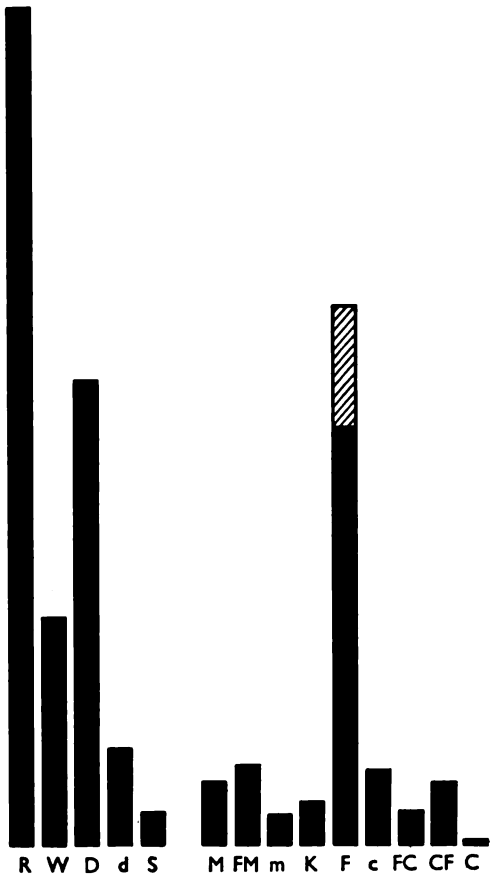

FIG. 3.—Composite record. Ten hospital employees.

1. The poor form (F minus) of the actually deteriorated patients, the high F plus of those only anxious about their condition.

2. The wide range of reactivity of the normals, the undifferentiated and meagre reactivity of the deteriorated patients.

3. The high m and K scores indicating inner difficulties in the anxious patients, and more than all else, the high c score in their records, indicating the excessive sensitivity, "exposure" to the environment.

Fig. 9 illustrates a typical case of compulsion neurosis. The high F plus, showing the rigid intellectual control, the virtual lack of all other types of responses, is striking.*

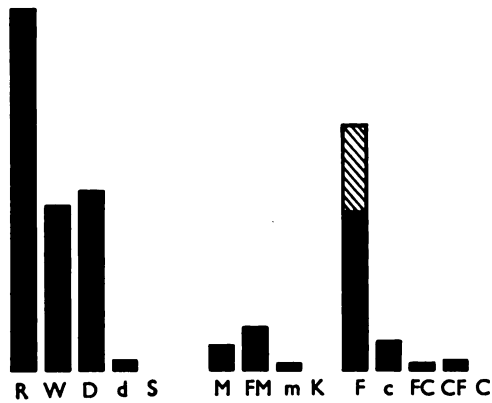

FIG. 4.—Composite records. Twenty-eight tumour cases pre- and post-operative; all locations.

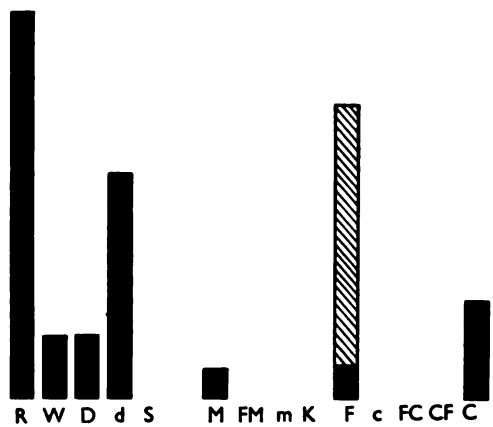

FIG. 5.—Records taken during periods of disorientation and mental confusion following head injury.

Fig. 10 illustrates a case of anxiety neurosis. It will be seen how the original performance is restricted, but the additional responses given in the inquiry (indicated by the broken lines) give a superimposed picture, allowing of an interesting comparison with the original responses.

We have given no graph for the hysterical personality structure, for as

* The discussion of the neurotic and emotionally unstable personality is an outgrowth of a joint study by the author and F. R. Miale, made possible by the National Research Council of Canada.

yet a sufficient number of cases has not been investigated to allow of generalizations or composite pictures. However, we may offer the following suggestions in the light of the cases studied :

1. FM greater than M.
2. CF greater than FC.
3. ΣC greater than M.
4. Several F minus anatomical responses.
5. A low F score.
6. A dilated rather than constricted personality structure.

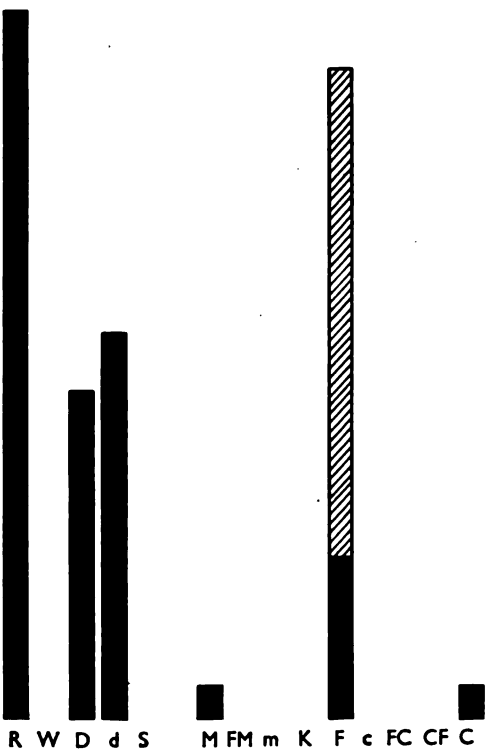

FIG. 6.—Records taken during periods of disorientation and mental confusion following head injury.

In the light of these records, we may make more explicit our suggestion that the Rorschach method be used in the situations already outlined :

1. When the Rorschach method is used to give further information concerning an individual with high intelligence, it may be said that the more closely the record approximates that of the hypothetical normal (particularly in the ratios of M : FM : m, and FC : CF : C) the more likely is this individual to be exceptionally well balanced.

Furthermore, the particular *qualities* of this high intelligence may become clearer when the mental approach (the W : D : d : S ratio) as indicated in the Rorschach record is considered. For example, an individual with a predominantly theoretical abstract approach (a preponderance of good W responses at the expense of D) is not likely to prove a useful administrator, if such work involves concern with an essentially practical handling of details.

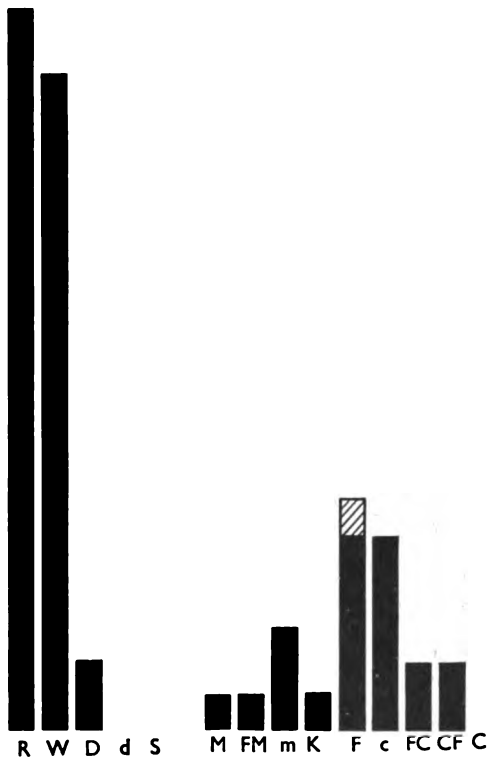

FIG. 7.—Patient apprehensive concerning mental ability following head injury.

2. Concerning the weeding out of the emotionally unstable from positions of responsibility, the following characteristics of a record may be considered as "danger signals":

(*a*) More than 60 per cent. F responses (an undue and unhealthy constriction).

(*b*) No responses on the right-hand side of the graph, i.e. no response to affective stimuli. (The F column constitutes the centre of reference.)

(*c*) No responses on the left-hand side of the graph.

(*d*) If the optimal M : FM ratio is reversed, so that FM overshadows M by more than 2 : 1.

(*e*) If the record contains more than one pure C response except in records of very richly endowed extroverts who have high FC and CF scores in addition.

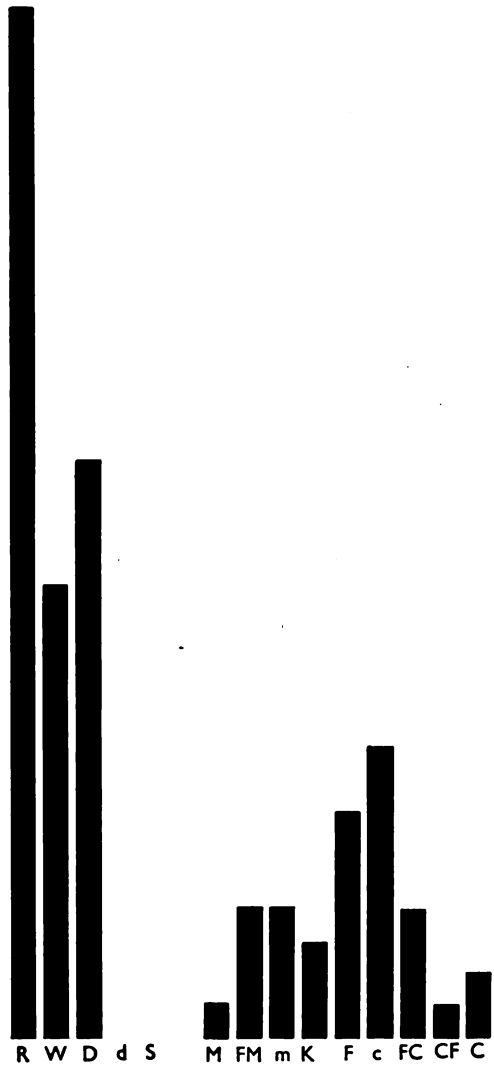

FIG. 8.—Patient apprehensive concerning mental ability following head injury.

(*f*) A total of more than three K responses (except in records with so many responses that these are a negligible proportion).

(*g*) A record with no M response.

3. The records of patients with actual cerebral damage, whose personalities and mentalities are altered (either as a result of infiltrating tumour, as in Fig. 4, or following cerebral trauma with a concomitant disorientation and mental confusion, as in Figs. 5 and 6) are outstandingly different from the

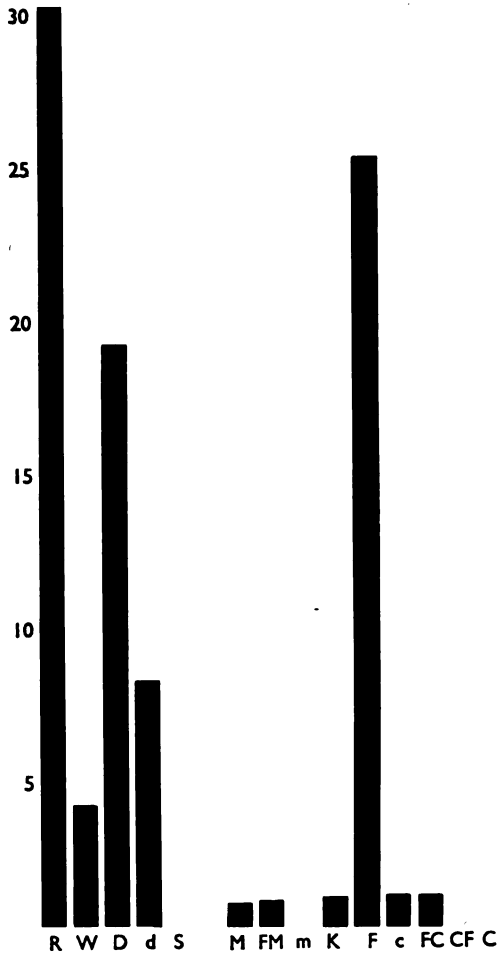

FIG. 9.—Record typical of compulsion neurosis.

records of normals, from those of the anxiety neurotic, and from those of persons merely apprehensive about their mental ability (see Figs. 7 and 8).

Our suggestion that the Rorschach method may be used to discover persons simulating mental disorientation or confusion rests on the fact that the chances of such persons producing a record which is characteristic of a cerebral condition which they do not possess is extremely unlikely. Moreover, the most obvious

attempt to "fail" on the Rorschach examination, that is the refusal to see, or the claim to be unable to see, anything in the cards at all, in itself makes the presence of widespread organic cerebral damage unlikely. In examination of over fifty cases of cerebral tumour and various kinds of traumatic cerebral injuries where the cerebral destruction is considerable, and where frequently the patient's physical condition is not of the best, not a single person failed in all the cards.

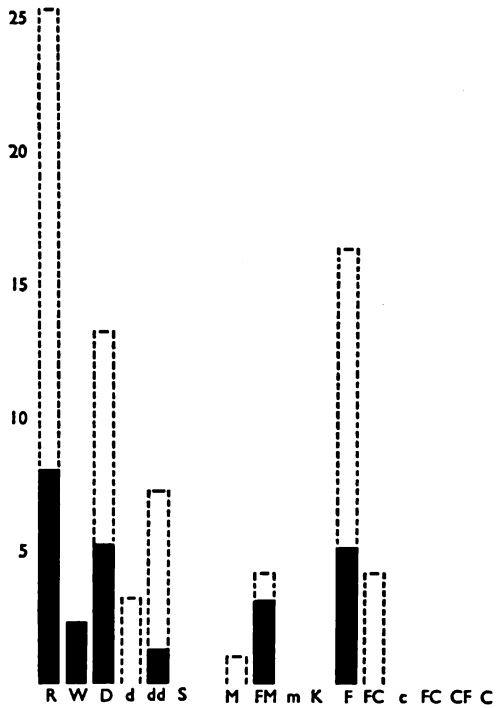

FIG. 10.—Record typical of anxiety neurosis.

While one cannot say, therefore, that those who fail in this way are malingerers, one must at least question the presence of some unusual psychogenic factor.

4. Although the responsibility for the clinical diagnosis concerning the psychoneurosis obviously rests with the psychiatrist rather than with the psychologist, the Rorschach method in the hands of the psychologist may throw light on doubtful cases, or may epitomize a psychological condition in a short space of time when a full psychiatric examination is not possible.

The compulsion neurotic, for example, whose picture is easily recognized by the Rorschach, may make an excellent subordinate, but, as Prados (4) has reported, may fear responsibility so greatly that he will commit suicide rather

than serve in the capacity of an officer. The recognition of compulsive trends in those considered for responsible conditions would therefore seem important.

Since the hysterical and the over-anxious personality are in many cases recognizable through the use of the Rorschach, before situations of strain produce physical symptoms, it would seem that the Rorschach method might be used to distinguish such unstable personalities before physical symptoms make them major medical problems.

In conclusion, we cannot emphasize too strongly that this presentation of types of records cannot be of help to those who have had no individual training and experience in the use of the Rorschach method. Our tabulated results are not meant to provide a short cut, or to be a substitute for the necessary training in the use of the method. Mere tabulation of a record never does more than epitomize certain aspects of it, so that it may be more readily held in mind. In view of the fact, however, that the present war situation may provide an opportunity for the trained Rorschach worker to make a contribution, we have presented these results in the hope that perhaps they may indicate lines along which this contribution may best be made.

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* In a recent article, Benjamin and Ebaugh (2) have given evidence of being able to distinguish the malingerer by means of the Rorschach method (one case diagnosed as "psychoneurosis, hysteria, *with malingering*"). Unfortunately, however, no details are given in the publication, so that the particular characteristics of the record which led them to such a conclusion are not known.

PROGNOSIS IN SCHIZOPHRENIA.*

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IN the world of mental diseases schizophrenia may well be termed "the sickness that destroyeth in the noonday." Although the replacement of Kraepelin's nomenclature of "dementia praecox" by Bleuler's term, "schizophrenia," has carried with it a general recognition that the chance of recovery is better than had been originally anticipated, the doom of those who do not recover is amongst the most dreadful meted out by any disease. It so frequently means a body apparently fully alive with a mind permanently impaired or virtually dead. Despite the obvious desirability of assessing the prognostic chances of the individual case, the statistical works published up to date have failed to establish agreement as to how this may be done. The object of this paper is to combine a detailed examination of the literature with a personal study of the histories of over 100 cases of schizophrenia in an effort to reach a definite conclusion in this matter. The paper will be divided into the following parts: I, a detailed survey of the literature; II, the outcome of 120 cases studied by myself; III, a comparison of remission rates and prognostic factors in cases treated by cardiazol.

Prognosis, which means the possibility of forecasting the course of a disease, may be viewed from two different points of view: firstly, the chances of recovery or progress indicated by statistical figures; and secondly, the significance of various signs and syndromes in estimating the prognosis of the individual case. In this thesis both aspects of the subject will receive attention.

PART I.

A Critical Survey of the Literature.

A. VARIATIONS IN THE CRITERIA OF DIAGNOSIS AND RECOVERY.

The necessity of comparing the remission rates of cases treated by cardiazol and insulin with those treated by the ordinary mental hospital methods of a routine life, good food, attention to physical health, occupational therapy, etc., has revived interest in various statistical studies of the remission rates in the latter. It is usual for the champions of the modern therapies to quote merely

* An M.D. thesis approved by the University of Cambridge, February 23, 1940.

the figures of such previous studies with little reference to the angles from which the various authors have approached their subjects, the result being that the comparatively wide discrepancies in the figures renders reliable deductions impossible. It has seemed to me that a more detailed examination of the articles concerned, with particular reference to the individual author's standpoint, might lead one to effect a synthesis on a common basis from which valid conclusions might be deduced. That this cannot be done by mere quotation of figures is due to the differences in the criteria employed by the authors concerned in diagnosing the incidence and remission of this disease. As a preliminary to a survey of literature on the subject, it will be well, therefore, to discuss briefly what forms these differences take.

(a) *Diagnosis.*

Fully to comprehend the varying criteria of diagnosis necessitates a knowledge of the evolution of Kraepelin's conception of dementia praecox to Bleuler's conception of schizophrenia, and also an understanding of the implications of the "reaction" types of Adolf Meyer, the "biological" types of Kretschmer and Mauz, the "temperamental" types of Jung, etc. For a detailed discussion of this subject the reader is referred to the comprehensive articles of Adolf Meyer (1929) and James V. May (1932) on the subject. In the meantime a brief survey of certain basic facts would not be inappropriate.

Bleuler (1936) states: "Schizophrenia does not appear to us as a disease in the narrower sense, but as a disease group. It is characterized by a specific kind of alteration of thinking and feeling, and of relations with the outer world that occur nowhere else." Aubrey Lewis (1935), says: "Schizophrenia may be regarded for diagnosis and other clinical purposes as a form of maladaptation in which there are certain characteristic defects of inner harmony and consistency in behaviour, thought and emotion." Bleuler (1936), summarizing what is included in the term "schizophrenia," says: "Under schizophrenia are included many atypical melancholias and manias of other schools (especially nearly all 'hysterical' melancholias and manias), most hallucinatory confusions, much that is elsewhere called amentia (the continental term for the confusional syndrome), a part of the forms consigned to delirium acutum, motility psychoses of Wernicke, primary and secondary dementias without special names, most of the paranoias of the other schools, especially all hysterically crazy, nearly all incurable 'hypochondriacs,' some 'nervous people' and compulsive and impulsive patients. The diseases especially distinguished as juvenile and masturbatory forms all belong here, also a large part of the puberty psychoses, and the degeneration psychoses of Magnan. Many prison psychoses and the Ganser twilight states are acute syndromes based on a chronic schizophrenia. If we still come across reactive psychoses included under this head, then it is due to defective diagnoses, not to the classification of a system.

" *Latent schizophrenias* are very common under all conditions, so that the ' disease ' schizophrenia has to be a much more extensive term than the pronounced psychosis of the same name. This is important for studies of heredity. At what stage of anomaly anyone should be designated as only a ' schizoid ' psychopath, or as a schizophrenic mentally diseased, cannot at all be decided as yet. At all events, the name latent schizophrenia will always make one think of a morbid psychopathic state, in which the schizoid peculiarities are within normal limits. Social uselessness, catatonic symptoms, hallucinations, delusions make certain the practical diagnosis of the acute mental disease."

A little later he continues :

" Schizophrenia may be combined with other psychoses ; it may undoubtedly originate on top of oligophrenias, and may be followed by senile psychoses. Occasionally also a paresis, more frequently alcoholism, eventually with delirium tremens or hallucinosis, complicate the picture. There is probably also a mixture of manic-depressive insanity, and of epilepsy with schizophrenia. The associations of these two diseases with dementia praecox are undoubtedly multiform and not at all clear, nó more than the delimitation of the combined from the simple forms with only apparent mixture symptoms."

May (1932) comments on Bleuler as follows :

" To insist, moreover, as Bleuler apparently does, that a mere schizophrenic colouring in a given psychosis automatically forces it into the dementia praecox group is no more logical than it would be to assign every excitement or depression to the manic-depressive one, or call all deliria alcoholic in origin. Marked schizophrenic colourings often appear in manic-depressive insanity, in genuine involution melancholia, and in many other psychoses. A careful study of the history of these cases will show that they were originally psychopathic, intellectually defective, or showed some other complicating factor unrelated in any way to dementia praecox."

May further points out that Bleuler insists that dementia praecox and schizophrenia are synonymous, but differentiates the two himself in the following manner :

" Patients are often brought to the hospital with a positive diagnosis of dementia praecox and show a fully developed schizophrenic syndrome which clears up entirely in a few weeks or in several months at the outside. Investigation shows that these individuals were in some instances feebleminded from birth, a condition which is found to be unchanged in any way after the recovery from the schizophrenic episode which was responsible for their coming to the hospital. There is no logical reason for the assumption that this is a combination of two diseases, mental deficiency and dementia praecox, or that the latter psychosis has been engrafted upon the former condition. There are at this time few, if any, reasons for thinking that the feebleminded ever develop a genuine dementia praecox. They are often subject to schizophrenic episodes just as they frequently develop other transitory attacks which are expressions

of their fundamental deficiency and are not disease entities such as schizophrenia. That the feebleminded are subject to psychotic episodes has been known for centuries. Schizophrenic episodes occur, moreover, in psychopathic personalities, in epilepsy, hysteria and other psychoneuroses, alcoholism, senility, toxic and exhaustive states, and even in pellagra. They are very common in the involution period of life in individuals who have never before shown any suggestions of dementia praecox. This is no more late schizophrenia than syndromes of the same kind in epilepsy are dementia praecox. . . .

"That these episodic affairs do not belong in the dementia praecox group is shown by the fact that there have been no previous evidences of that disease in the patient's history, which does show early suggestions of complicating factors such as psychopathic personality or mental deficiency, etc.; that the syndrome completely disappears in a very short time; that it is followed by no definite evidences of dementia praecox later and may never show any further schizophrenic suggestions; that the episode on close analysis is nearly always atypical in character; and finally that the recovery made is nearly always complete."

If the above passages are quoted liberally and fully, it is because they illustrate so well the nature of the problem. Reading between the lines, it is easy to comprehend that there are those who follow Bleuler in a very broad interpretation of the term "schizophrenia" (see reference to Burghölzli Hospital admissions below); those who have merely replaced the term "dementia praecox" by that of "schizophrenia," while retaining Kraepelin's conceptions; and thirdly, those who, although they agree largely with Bleuler, are not prepared to extend the diagnosis of schizophrenia to all cases tainted with schizophrenic symptoms.

The attitude which the various schools of psychiatry have adopted in this matter has been largely determined by the views they have held as to the aetiology of schizophrenia. The tenets of the so-called "biological" school, which is that adhered to by most continental psychiatrists, is based mainly on the teachings of Kraepelin and Kretschmer. Kraepelin's original conception of dementia praecox was confined to a group of so-called endogenous psychoses. Long before Bleuler embraced this conception in the term "schizophrenia," psychiatrists had sought to unravel its aetiology. Work had been done by Rüdin, Kahn and others on the factor of heredity; Jung had shown that the introverted temperaments were particularly liable to this disease, and investigations into other factors of constitution had been made. The latter work culminated finally in Kretschmer and Mauz's work claiming that the asthenic, the athletic and the dysplastic types of bodily build are more prone to develop schizophrenia than the pyknic build. This school would seem to consider schizophrenia as essentially an endogenous disease whose presence in a patient is signified by certain definite mental symptoms called process symptoms, and whose degree of severity may be gauged to a certain

extent by the form which the symptoms take. They also stress that these process symptoms occur in persons prone to the disease through constitutional factors. Psychoses with this type of symptoms are called true or process schizophrenias. The existence of schizophrenic types of mental disintegration is recognized, however, as occurring in many other cases who are thought not to be particularly liable by virtue of constitution to true schizophrenia. These latter cases are grouped together as the so-called atypical or reaction schizophrenias or 'schizophreniform' psychoses. A few quotations may illustrate the beliefs held by this school.

Strauss (1931) describes the process symptoms thus:

"The cardinal pathognomonic indication of this process is the subjective experiencing of an awareness of his illness by the patient as a change in himself, as a threat to his ego and its unity, as an experienced withdrawal of something from his personality, as a conscious disintegration of individuality and as a diminished sense of personal activity. The general frame of mind is therefore one of doubt, anxiety and perplexity accompanied by weird feelings of approaching dissolution. Pathognomonic of this group are also purely physical sensations experienced by the patient—peculiar and often bizarre paraesthesiae such as feeling that one half of the body has expanded or shrunken, that the genitals are being tampered with, that the forehead is made of glass, and so on. Sometimes these sensations make their appearance before the general sense of menace and approaching disintegration makes itself felt at the psychic level. Symptoms of this kind are not in themselves referable to anything occurring at the psychological level, the more clear-cut and simple the more pathognomonic they are of schizophrenic process."

Langfeldt (1937) says:

"Whatever it may be which renders possible the exciting of the latent schizophrenia, whether endocrine, vegetative, autointoxications (teeth, tonsils, intestines, etc.) or exogenic intoxications and infections, it is probable that both the onset and the further development depend not only on the qualitative and quantitative relationship between genes and noxes, but also in a high degree on the manner in which the individual organism tolerates the various exogenic factors. In this connection a number of humoral biological circumstances probably intervene. . . .

"Among the isolated symptoms in acute process psychosis Mauz especially found *autochthonous ideas* (a sign of passivity), acts of the will and impulses, remoteness from reality, ideas of influence and schizophrenic confusion of thought, but the author expressly calls attention to the fact that these individual symptoms scarcely play any noteworthy prognostic role *by themselves* if they cannot be deflected by the actual fundamental symptom: the experience of the change as such. The process symptom is regarded as a palpable sign of a malady of an organic character, and this is often revealed at an early stage by a number of physical paraesthesiae and nervous irradiations which should

therefore be followed as being prognostically important. The organic character of the symptom also emerges from the fact that it cannot be deflected and is not comprehensible psychologically. The symptom is there isolated and *plain*. The clearer and plainer the symptom is, the more process-organic it is. It has less process-character if it is encased in acute confusion, ecstasy and psychic reactivity.

" According to Mauz the process-character signifies nothing more than that the complaint *tends* in the direction of schizophrenic deterioration. How far such deterioration occurs Mauz has now found to be dependent, *inter alia*, on the age at which the psychosis commences and the bodily form of the particular individual. The process may develop as a schizophrenic catastrophe or in attacks (schub)."

Again, remarking on the atypical " schizophreniform " mental diseases, Langfeldt says :

"Analyses show that in the majority of cases one or more of the following pathogenetic or pathoplastic (or both in union) factors can be demonstrated :

" (1) *Hereditary conditioned junction* with manic-depressive insanity . . . expressing itself by depressive or manic features in the symptomatology.

" (2) *Psychogenic factors* (particularly in a feeling of inferiority as an origin of self-reference and conflict-accentuated absorption in sexual questions . . .).

" (3) *Exogenic factors* (abuse of alcohol, septic angina, toxicosis, overstrain, childbirth . . .).

" Of the 17 cured cases out of the 100 in his katamnesic follow up, 11 presented an *atypical schizophreniform symptomatology marked by strong admixtures of manic-depressive, psychogenic (self-reference tendencies) and symptomatic (cloudiness, incoherence) trends and pathoplastic symptoms*, in contrast to the process psychoses in which the acute mental symptomatology is entirely dominated by process symptoms (massive primary persecution ideas, sensations of influence, depersonalization and derealization, massive katatonic-stuporous symptoms)."

The psycho-biological school is founded mainly on the teachings of Adolf Meyer. It stresses the reaction of the individual as a combined psychological and biological entity. He does not consider schizophrenia as of purely organic origin, but as the result of the interaction of the person's combined psycho-biological make-up with his environment. The essence of this view is expressed in Henderson and Gillespie's *Textbook of Psychiatry* (1936), in the following passage : " Schizophrenia is not a disease but a congeries of individual types of reaction having certain general similarities. While recognizing that the individual may be loaded in various ways—by inheritance, by physical defects of an endocrine disorder or some grosser kind, by intellectual deficiency or what not—none of these is in itself a sufficient cause for schizophrenia."

It is only when the subject has to battle with life's problems that reactions appear which cumulatively lead to one of the conditions included under schizo-

phrenia. Meyer concluded that " schizophrenia is the end result of an accumulation of faulty habits of reaction." This school therefore particularly stresses the prepsychotic personality and the ability of the individual to deal with life's problems in a direct and confident way. Consequently little attention is paid to the question of pure endogenous process symptoms, classification being made only according to the symptoms of the acute stage.

From the foregoing description it should be easy to see how the criteria of diagnosis vary, and how certain cases that might be considered true schizophrenics by some authorities would not be so by others.

(b) *Remission Rates in Cases Treated by the Usual Routine Hospital Methods, other than Cardiazol, Insulin or Prolonged Narcosis.*

There has been a great deal of loose talk about the word " remission " and its implications. It is quite a favourite habit among cardiazol and insulin therapeutists, in comparing their results with those obtained by other methods of hospital treatment, to make the statement that " so-and-so gives a remission rate of 50 per cent. or 20 per cent.," or whatever the figure may be, with no further details. Reference to the Oxford Dictionary (1934) gives the following definition of the word " remission " : " Diminution of force, effect, degree, violence, etc. : the act of remitting." (Remit, v. = " abate, slacken, partly or entirely to cease from or cease ".) The difference of interpretation is contained in what degree of improvement or abatement is implied by the authors concerned. Some would appear to talk of the term " remission " as applying to all cases whose course is arrested before progressing to ultimate dementia ; others would appear to apply it only to those who make sufficient improvement to attain their discharge ; and others again seem to confine the term almost exclusively to the cases which recover sufficiently to carry on in their original employment and environment, although many of these are admitted not to have attained complete recovery. Some authors consider that no case of true schizophrenia ever recovers ; others find a high rate of complete recovery. In this respect it is interesting to note Bleuler's ideas on the subject :

"*This disease may come to a standstill at every stage and many of the symptoms may clear up very much or altogether ; but if it progresses, it leads to a dementia of a definite character.*" And again, " The disease at times runs a chronic course, at times in shifts ; it may become stationary at any stage or may regress a certain distance, but probably does not permit of a complete *restitutio ad integrum.*"

The reason for these discrepancies is to be found in the fact that there are no commonly recognized definitions of the various gradings of improvement. We shall see, when reviewing the literature, the use of such terms as " recovery," " complete recovery," " social recovery," " recovery with deficit," " much improved," " improved," etc., varying in number and meaning from one

article to another. Combine with the above inconsistencies in diagnosing the disease and estimating the remissions the fact that there is comparatively little effort to assess the prognostic factors in the cases dealt with, and the reasons for variations in statistical results are patent.

There is one other point of importance that must be borne in mind when considering remission rates, namely, the type of hospital from which the figures originate. In this country we have two separate hospital systems, one for rate-aided patients and one for paying patients. For the former we have the county and borough mental hospitals, which in the past took certified patients only and which, despite the advent of voluntary patients, still take much the same type of patients from the point of view of prognosis. Connected with these are the mental observation wards in the corresponding county or borough general hospitals, which act as centres of distribution. Apart from the county hospitals most of the general voluntary hospitals have out-patient departments or clinics for psychotic patients, but very few have in-patient beds available.

On the Continent each university has attached to it what is known as the University Clinic—a self-functioning psychiatric unit with both in- and out-patients' departments. Each clinic corresponds more closely to the Maudsley Hospital than to anything else in this country and it is obvious that the material of these clinics will be much better as regards immediate prognosis than that received in one of the State mental hospitals.

In the United States of America clinics usually resemble the continental system. Some of them exist as part of a large hospital, not particularly associated with a University; and others in definite relationship with a University. There are also private mental hospitals for the paying patients.

B. Statistics of Remission Rates in Cases Treated by Methods other than Cardiazol, Insulin or Prolonged Narcosis.

One of the favourite methods of reaching conclusions in this respect is to represent figures of various authors in combination in tabular form. Tables I, II and III represent efforts in this respect by Strecker (1938), Hunt, Fieldman and Fiero (1938) and Jorgen Ravn (1934). It is my intention briefly to survey the articles from which these figures were taken and then to go on to individual articles not included in these tables.

1. The two series of figures quoted from Lemke occur in his article on the value of encephalography as an aid to progress in schizophrenia.

The first is a katamnesic follow-up in 1935 of 255 cases admitted to Jena University Clinic in the years 1918 to 1923 inclusive. This was effected by means of a questionnaire. Only 126 cases were traced. In these he found the following results:

TABLE I.—*Spontaneous Remission Figures in Schizophrenia* (*Strecker*, 1938).

Author.	When published.	Cases. Total.	Cases. Traced.	At home. Well or improved.	At home. Not improved.	At mental hospital.	Died.	Period under review.
1. Lemke	1935	132		48	14	29	9	1933/35
2. Faurbye	1936	72		42% more or less recovered			..	1935
3. Mayer-Gross	1929	328	294	35	3·4	19	42·5	1912/13
1. Lemke	1935	255	126	34	19	27	20	1918/23
4. Otto-Martiensen	1921	527	312	33·7	7·4	21·1	31·4	?
5. Otha	1936	?	179	29% complete remission			..	?
6. Dussik	1936	94		20% complete remission			..	?
7. Arnesen	1937	815	772	18·5% recovered			..	1915/28
8. Menzies	1935	17		5·9% recovered			..	1928/30
9. Stearne	1912	? 315		5	4·5	64·1	23·8	?
10. Ederle	1937	147		3–4% complete remission			..	1935
Total		2,460		23·6%				

FIG. 1.

At home and employed	43 = 34%
At home, unimproved	24 = 19%
In mental institutions	35 = 27%
Dead	24 = 19%

In the second series he has traced 132 cases admitted to the same clinic during the two years prior to his article (written in 1935). His results were as follows:

TABLE II.—*After Hunt, Fieldman and Fiero* (1938).

TABLE IIA.—*Recovery Rates, from the Literature.*

Author.	Number of cases.	Number recovered.	Per cent. recovered.
9. Stearne (1912)	395	51	13
11. Rosanoff (1914)	213	25	11
12. Bond (1921)	20	0	0
13. Bond (1921)	34	3	8·8
14. Pollock (1925)	19,927	?	6·4*
15. Strecker and Willey (1924)	186	38	20·4
16. Levin (1931)	592	35	5·9
17. Wootton *et al.* (1935)	95	18	20
18. Whitehead (1937)	90	14	15·5
19. Bond and Braceland (1937)	116	12	10·3
Total (excludes the figures of Pollock)	1,741	196	11·3

TABLE IIB.—*Amelioration Rates, from the Literature.*

Author.	Number of cases.	Number ameliorated.	Per cent. ameliorated.
Pfersdorff (quoted by Kraepelin)	150	23	15
20. Coles and Fuller (1909)	109	27	25
9. Stearne (1912)	395	95	24
11. Rosanoff (1914)	213	62	29
12. Bond (1921)	20	3	15
13. Bond (1921)	34	3	8·8
21. Williams and Potter (1921)	200	46	23
14. Pollock (1925)	19,927	?	40†
17. Wootton *et al.* (1935)	95	31	32·6
18. Whitehead (1937)	90	32	35·5
19. Bond and Braceland (1937)	116	37	31·9
Total (excludes Pollock's figures)	1,422	359	25·6

* Number discharged as recovered per 100 admissions during the same period.
† Number discharged as recovered or improved per 100 admissions during the same period.

TABLE III.—*From Jorgen Ravn* (1934).

Author.	Date.	Diagnosis.	Cases.	Cured. %	Cured with defect. %	Unchanged. %	Died. %
Kraepelin	..	Catatonia	?	13	27	59	..
		Hebephrenia	?	8	17	75	..
E. Meyer	1903	Dementia praecox	46	30	..	..	..
,,	1909	,, ,,	142	21·8	19·1	69	..
Albrecht	1905	,, ,,	693	2	17	81	..
Kahlbaum	1902	Catatonia	27	30	15	55	..
Raecke	1910	,,	171	15·8	11·1	55·5	17·4
Schmidt	1911	Dementia praecox	455	16·2	15·5	57·9	10·2

FIG. 2.

Cured and employed	19 = 14%
At home and improved	45 = 34%
At home and not improved	18 = 14%
In mental institutions	38 = 29%
Dead	12 = 9%

2. Faurbye's (1936) figures appear in an article on "Some Statistics Concerning the Prognosis in Schizophrenia." The first part of the paper deals with the total number of schizophrenic patients in the mental hospital with reference to the percentage of beds they occupy and the proportion of the various subdivisions (catatonia, hebephrenia, etc.). The second part pays particular attention to recent cases. A follow-up was made in November, 1936, of such cases who were admitted to hospital at least a year previously. It is not clear for what length of time each case was followed up. It would appear that they were admitted somewhere between 1932 and 1935.

FIG. 3.

Diagnosis.	Dementia praecox simplex.	Dementia praecox katatonica.	Dementia paranoia.	Unascertained group.	Total.
Patients with new psychosis and admission of at least one year ago	31	21	15	5	72
Discharged total	16	11	8	5	40 (55·5%)
,, with remission	11	9	6	4	30 (41·7%)
,, without remission	5	2	2	1	10 (13·8%)
Readmitted	3	2	1	0	6

He presented his results in tabular form as above, and commented upon them thus:

"The 42 per cent. (i.e. discharged with remission) occupy an intermediary position, but the figure certainly will grow, as none of the patients had been in hospital so long that no remission could be expected. The figures are too small to enable us to calculate the percentage of the remissions in the respective clinical sub-groups, but the relatively greatest remission percentage seems to

lie—as others find it too—in the katatonic group; it appears that the best quality remissions are found in this group also—there are six of the remitted patients whom we considered better or practically better, and four of those are katatonics.

"Of the 72 patients admitted with recent schizophrenia at least a year ago, at present 39 are in hospital—32 have been here since their admission; 6 have been readmitted and 1, who had been discharged unchanged, is amongst the readmitted. The fate of these patients has not yet been decided upon. The end result—improvement or stationary—in most cases comes only after three to ten years. As the hospital is only four years old, such an investigation had not been made.

"With 'recovery,' 'social recovery' was meant, i.e. the patient can return to society and appear well (often, it is true, under easier conditions than before), but in the majority of cases with some persistent signs of defect."

This article is frequently quoted with reference to the high percentage of recoveries, and it is therefore interesting to note what exactly the author means by "recovery."

3. Mayer-Gross (1929) published the results of following up 294 cases admitted to the Heidelberg Psychiatric Clinic in the years 1912 and 1913. They were followed up over ten years or more and a personal re-examination was made of each case at the time of the follow-up. The results are represented in the following table:

FIG. 4.

	Number.	Percentage.
At home recovered (i.e. employed and full social recovery)	89	32·4
At home improved (employed)	14	4·8
At home not employed and obviously ill . .	10	3·4
In mental hospitals	56	19
Dead	125	42·4

The importance of this article (and the reason which makes it probably the most often quoted of all) lies in (*a*) the large percentage of cases traced, (*b*) the length of time covered, and (*c*) the personal re-examination of cases by the author. Braatoy (1936) criticizes the lack of information as to how long the completely cured group had been out of the hospital (i.e. duration of psychosis before discharge, number of relapses, etc.), and this deficiency renders the picture incomplete.

4. The article from which Otto-Martiensen's (1921) figures are taken is written from a specialized point of view, being "A Katamnesic Investigation of 312 Cases of Schizophrenia with Special Reference to their having taken

part in the War." The latter fact brands the cases as having undergone an ordeal not common to the ordinary schizophrenic. Moreover, the 312 cases represent the only ones from whom an answer to a questionnaire sent to a series of 527 cases previously treated at the Jena Clinic was obtained (i.e. only 59 per cent.). The author pays particular attention to the question of readmission (see table below):

FIG. 5.

	Complete remissions.	Improved.
After one readmission only	1	52
After two or more readmissions	3	10
After transfer to another mental hospital	11	28
Total	15 (4·9%)	90 (28·8%)

At present in a mental hospital	21·1%
Dead	31·4%

5. The reference to Otha's (1937) figures is merely a passing one of two lines in an article by Roggenbau, quoting the bare facts that from 179 cases Otha had observed 52 (or 29 per cent.) with full remissions with no other details whatsoever.

6. Dussik (1936) states that out of 94 cases of schizophrenia (with psychosis of not more than six months' duration) treated at the Vienna Clinic in 1936 with methods other than insulin (and of course excluding cardiazol) 20·2 per cent. of complete remissions were obtained, whereas in cases treated with insulin under similar conditions, the complete remission rate was 70·7 per cent. The average duration of stay in hospital was in the former case 202 days and in the latter only 62.*

7. Arnesen (1937) (*British Medical Journal* extract, 1937) investigated the subsequent careers of 815 patients treated at the Gaustad Asylum in Norway over the period 1915 to 1929: 42 could not be traced, 143 had been discharged and were out of hospital, and 630 were dead or still in hospital. Thus, allowing for probable recoveries among the 42 not traced, 20 per cent. of patients had been discharged. Of the 143, 1 was discharged as well, 106 were discharged improved, and 36 discharged not improved.*

8. Menzies' (1935) figures (the only British figures quoted in Strecker's series) occur in an article entitled, "Pyrotherapy in Dementia Praecox," and refer to the remission rates during the three years 1928 to 1930 inclusive, used

* Original articles were unobtainable in this country.

as a control for a similar number of cases treated with pyrotherapy during the years 1932 to 1934 inclusive. Below is the table of results obtained:

FIG. 6.

	Number of cases. 1932–1934. Treated.	1928–1930. Untreated.
Recoveries	1	1
Partial remissions	2	..
Transferred	4	..
Died	1	2
Chronic	11	14
Total	19	17

No explanation is given as to what criteria are used for the grading, "recoveries," "partial remissions" and "chronic." The total number of cases is seen to be very small, and referring to this "untreated" group (i.e. not treated by pyrotherapy), the author remarks, "Most of these are still resident with all symptoms well established, so that the original diagnosis can hardly be doubted," which points to the cases being of a severe type. In these circumstances the quotation of a recovery percentage of 5·9 can hardly be considered of much significance.

9. Stearne, A. W. (1912), reported in 1912 on 395 cases admitted to Dasuvas State Hospital, U.S.A., during the years 1901 to 1905 inclusive. Of these, 315 were traced by questionnaire. It was found that of the 315, 187 had been discharged from hospital, their condition on discharge being given in Fig. 7.

FIG. 7.

	Male.	Female.	Total.	Percentage.
Not improved	42	50	92	47
Improved	8	36	44	23·5
Much improved	9	29	38	20
Capable of self-support	11	2	13	7
Total	70	117	187	47% of total number of cases.
Readmitted				44
Readmitted twice				9

In 1912 the distribution of traced cases was :

FIG. 8.

	Male.	Female.	Total.	Percentage.
Now in hospital for the insane	80	122	202	64·1
Dead	27	48	75	23·8
Boarding out	..	8	8	2·5
At home apparently well	8	8	16	5
At home demented	8	6	14	4·5
Total	123	192	315	

Of the 202 cases now in hospitals for the insane, 98, or 24 per cent., have had a continuous hospital residence. The large percentage of relapses among the cases discharged is obvious from a comparison of the two tables.

As regards the patients apparently well, the author states, " After analysis of the fairly well group, Dr. H. W. Mitchell, who was familiar with the patients themselves as well as their records, was of the opinion that they were not cases of dementia praecox, but were for the most part atypical depressions." It seems apparent, therefore, that the type of case being dealt with was severe, and in its course corresponded broadly to the old conception of the almost unfailing downhill progress of dementia praecox.

10. In Ederle's (1937) article again there is only a bald statement of the remission rate he found in 147 cases. A translation of this runs as follows : " The number of spontaneous remissions is given by Bumke as 22 per cent. It is doubtful whether these are really full remissions comparable with those obtained by insulin treatment. Only 3·7 per cent. of the 147 schizophrenics admitted to the Tübingen Clinic in 1935, and who were not treated with insulin, have been discharged as really full remissions." The reference to full remissions in this passage presumably means in the sense described by Müller as a criterion in insulin shock. No other details of the cases are given.

11. Rosanoff (1914) followed up all cases of past admission to King's Park State Hospital for the year ending September 30, 1908, and determined their condition five years later. His findings are revealed in the following statistics taken from his article. It is to be noted that the cases were divided into the " Dementia Praecox group " and " Conditions allied to Dementia Praecox group."

FIG. 9.—*Subsequent Fate of Admissions.*

	Cases admitted.			Repatriated and deported.		Died.		Discharged.		In hospital.	
	M.	F.	T.	Number	Percentage.	Number.	Percentage.	Number.	Percentage.	Number.	Percentage
D.P. group	92	77	169	8	2·2	23	13·6	39	23·1	99	58·6
Allied conditions	34	19	53	1	1·9	4	7·5	31	58·5	17	32·1

FIG. 10.—*Conditions at Time of Discharge.*

	Total number of cases.		Recovered.		Improved.		Unimproved.	
	Admitted.	Discharged.	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.
D.P. group	169	39	..	..	32	18·9	7	4·1
Allied conditions	53	31	25	47·2	5	9·4	1	1·9

FIG. 11.—*Subsequent Course of the Discharged Cases.*

	Total.	Number discharged.	Readmitted, now in hospital.		Readmitted, eventually discharged.		Not known to have been readmitted.	
			Number.	Percentage.	Number.	Percentage.	Number.	Percentage.
D.P. group	169	39	10	25·6	1	2·6	28	71·8
Allied conditions	53	31	2	6·5	3	9·7	26	83·8
Total	222	70	12	17·1	4	5·7	54	77·1

Rosanoff comments upon the "allied" group thus: "Nearly half of the patients in this group allied to dementia praecox have been discharged as recovered, many of these being placed in this group instead of straight dementia praecox for no other reason than that of their eventual recovery. Moreover, a percentage of these patients higher than average find their place at the end of five years under the heading 'not known to have been readmitted'."

12. Bond's article (1921) is entitled "A Review of the Five-year Period following Admission in 111 Mental Patients." He traced out the histories of all the 111 female patients admitted to the Department for Mental and Nervous Diseases of the Pennsylvania Hospital (a private hospital) in the year 1914 for five subsequent years. Of the twenty cases of dementia praecox in the group all remained continuously in hospital except one, who remained outside, improved, but with no insight and retaining her delusions. We see that the three cases quoted in Table IIB as ameliorated had not left hospital. Bond also gives summaries of the histories of twenty unclassified cases. As many as fifteen of these might well fit into the modern conception of schizophrenia, and of these six recovered; one remained at home improved, and one at home not improved; six were still in a mental hospital and one had died. If these cases are included, we see that a different picture is presented, namely, 17·1 per cent. recovery, 11·4 per cent. improved, 5·7 per cent. at home not improved, and 71·4 per cent. continuously in hospital.

13. The above findings are substantiated in Bond's second article (1921): "Results in 251 Cases Five Years after Admission to a Hospital for Mental Diseases." In this article he has followed up 251 consecutive admissions (again females) to the Pennsylvania Hospital for the five years following. It appears that Hunt, Fieldman and Fiero have made a misquotation in their table, as Bond's figures are:

FIG. 12.

	Number.	Recovered.	Recovered minus.	Died.	Unimproved.
Dementia praecox	47	1	9	3	34
Unclassified	44	14	17	5	8
Total	91	15	26	8	42

The figures of the unclassified group are again quoted because of the possibility that some cases are included which would nowadays be considered as schizophrenia.

Bond does not define "recovered," but regarding the recovery minus group he says, "they show as striking a tendency to improve (i.e. as do the "recovery" group) but are as strikingly differentiated by coming to a partial or poorly maintained adjustment."

14. Pollock (1925) described the findings of a special census of mental hospitals by the Federal Census Bureau. The census covered the number of first admissions, readmissions, discharges and deaths during the calendar year 1922 and the total number resident on January 1, 1923, in all hospitals and institutions treating mental disorders. His findings regarding dementia praecox are shown in Figs. 13, 14 and 15. The total number of dementia praecox patients resident on January 1, 1923, in such places was 60,153 males and 53,587 females, a total of 114,240.

FIG. 13.—*The Movement of Patients in Hospitals for Mental Diseases, 1922, by Psychosis and Sex.*

Psychosis.	1st admissions.			Readmissions.			Discharges.			Deaths.		
	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.
Dementia praecox	8,950	6,576	15,526	2,479	1,922	4,401	6,785	4,659	11,444	1,930	2,018	3,948

FIG. 14.—*Rates per* 100 *Admissions with the Same Psychosis of Patients Discharged from Hospitals for Mental Diseases during* 1922, *Classified by Sex and Condition on Discharge.*

Psychosis.	Total percentage discharged.			Percentage recovered.			Percentage improved.			Percentage not improved.		
	M.	F.	T.	M.	F.	T.	M.	F.	T.	M.	F.	T.
Dementia praecox	59·4	54·8	57·4	6·3	6·6	6·4	33·8	33·3	33·6	17·6	13·7	16·0

FIG. 15.—*Percentage Distribution of Patients Discharged as Recovered or Improved from Hospitals for Mental Diseases during* 1922, *by Psychosis and Length of Hospital Residence.*

Psychosis.	Condition on discharge.	Total.	Under 4 months.	4–6 months.	7–11 months.	1 year.	2 years.	3 years.	4 years.	5 years or over.
Dementia praecox	Recovered	100	28·8	22·1	17·0	15·0	6·0	3·0	1·6	6·4
	Improved	100	30·7	16·2	15·5	16·8	6·8	4·0	2·3	7·7

Recovery he defines as " the condition of a patient who has regained his normal health so that he may be considered to have practically the same mental status as he had previous to the onset of his psychosis." After tabulating the results according to the findings in the various States, he says : " Some States seem to have adopted a conservative policy in regard to discharging patients as recovered ; their recovery rates, therefore, are out of line as compared with those of most of the other States. As would be expected, many States that have low recovery rates have relatively high improvement rates."

The large number of cases dealt with in this article make it of particular interest.

15. The figures compiled by Strecker and Willey are taken from an article on " prognosis in schizophrenia," which will be referred to in more detail later. They found that of 186 consecutive female admissions to Pennsylvania Hospital for Mental and Nervous Diseases, 38 recovered, and 148 improved, remained stationary, or deteriorated. The average symptom-free period for the recovered cases is five years, and therefore no relapses are reported.

16. Wootton and Armstrong (1935) published a follow-up study of cases of dementia praecox admitted during the years 1928 to 1931 inclusive to St. Ebba's Hospital, Epsom, which at that time was taking certified cases only. Their results, of the dementia praecox group, are represented in tabular form thus :

FIG. 16.

Year.	Number admitted.	Number discharged.	W.	S.	T.	R.	I.	U.
1928	36	13	6	1	..	2	2	2
1929	28	18	7	..	1	3	3	4
1930	21	7	3	..	..	2	2	..
1931	19	9	2	..	2	2	..	3
Total	104	47	18	1	3	9	7	9

W. = Completely well since discharge.
S. = Has remained well in sheltered environment.
T. = Minor relapses without mental hospital treatment.
R. = One or more major relapses in a mental hospital.
I. = Certified insane at inquiry.
U. = Unchanged.

These figures are significant in that they consider not only the rate of discharge, but the fate of the discharged cases during the following years. The large number of relapses is interesting. The authors comment on the period after discharge at which these tend to occur : " The same tendency to relapse at the end of a year exists in the dementia praecox group (i.e. as in the manic-depressive group), but these cases seem to suffer another danger period towards the end of two years." The authors are unable to provide any explanation for this, and the suggestion entailed is one which requires confirmation by a considerably larger number of cases.

17. In Duncan Whitehead's article on "Prognosis in Schizophrenia" (1937), he traces up the subsequent histories of 90 cases of dementia praecox admitted to the Utica State Hospital in 1935–1936, and analyses them from the point of view of duration of psychosis and clinical subtype of the cases. He represents his findings in tabular form (Figs. 17 and 18):

FIG. 17.

Duration of psychosis.	Recovered.		Much improved.		Improved.		Unimproved.	
	Total.	Percentage.	Total.	Percentage.	Total.	Percentage.	Total.	Percentage.
Less than 6 months .	8	22	1	3	7	25	18	50
6 to 18 months . .	0	..	3	23	2	15	8	62
Over 18 months . .	0	..	0	..	9	23	29	77
Total . .	8	..	4	..	18	..	55	..

FIG. 18.

Total.	Type of psychosis.	Recovered.		Much improved.		Improved.		Unimproved.	
		Total.	Percentage.	Total.	Percentage.	Total.	Percentage.	Total.	Percentage.
88	All types of dementia praecox combined .	8	9	6	7	18	20	56	62
48	Hebephrenic type .	4	8	3	6	8	16	33	67
25	Paranoid type .	0	..	2	8	5	19	18	69

Regarding catatonic and simple types, the total number of cases here was too small to be of value for statistical purposes.

18. In Bond and Braceland's article (1937) entitled "Prognosis in Mental Diseases," they publish the result of five-year follow-up studies on 710 consecutive admissions to Pennsylvania Hospital (a private hospital). Of these, 116 were cases of dementia praecox, and their condition at the end of five years was as follows:

FIG. 19.

Total number.	Recovered.		Improved.		Not improved.		Died.	
	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.	Number.	Percentage.
116 .	12	10·3 .	37	31·7 .	57	49·1 .	10	8·69

No definition of recovery is given.

The authors state: "These percentages may be increased if to the cases diagnosed dementia praecox there are added those which at the time of admission had symptoms which strongly suggested the diagnosis. In the manic-depressive group there are 7 of these, in the unclassed group 16, and in the paranoid group 5, making a total of 28. Of these, 17 recovered, 3 improved, 3 were unimproved and 3 were lost. By combining these cases of suggested dementia praecox with those which seem fully to warrant the diagnosis, the percentage of full recoveries is 20 per cent. and of recovery and improvement is 40 per cent."

A further very significant comment is made in this paper on the apparent differences in the criteria of diagnosis in such countries as Switzerland. A report quoted regarding the Burghölzli Hospital gives the following statistics for 1936: All admissions were 990, of which 11 were manic-depressive and 375 schizophrenia, and the deduction is made that the diagnostic criteria are so different in Switzerland (and ? Vienna) from those in the United States that due allowances must be made.

19. Meyer, E. (1903) followed up 46 cases of definite catatonia who had presented themselves at the Tübingen Psychiatric Clinic. He found that 14 (i.e. 30·4 per cent.) of these cases had "a favourable outcome," 11 (23 per cent.) were cured with defect, and 21 (45 per cent.) had an "absolutely unfavourable" course. With regard to specific factors, he mentions acute onset, early stupor and slow disappearance as favourable. It is not clear for how long each case was followed up, and for how long cases with a favourable outcome or cured with defect were in the clinic or back at home. Regarding the implications under the group, "a favourable outcome," Kraepelin remarks, "Meyer evidently does not make the very strictest claims."

20. Albrecht (1905) investigated the histories of the 693 cases admitted to the Provincial Institution between April 1, 1900, and April 1, 1904, inclusive. Of these, 202 were cases of dementia praecox. He found "cures" in only 4 (2 per cent.) of cases and "cure with defect" in only 32 (17 per cent.), moderate dementia in 93 (48 per cent.) and severe dementia in 63 (33 per cent.) cases. He follows with observations of rather doubtful value on such factors as heredity, exogenous factors, age of onset, etc. The duration for which each had been ill, cured, relapsed, etc., is not mentioned.

21. Kahlbaum (1902) reported the results of investigating the histories of 27 patients admitted to the Frankfurt Mental Hospital some years previously suffering from catatonia. He found that 9 (33 per cent.) of them had been completely cured, 7 (25 per cent.) had incomplete cures, and 11 (42 per cent.) had not improved or had become worse; but he adds later that the "ultimate outcome" is unfavourable in about 70 per cent. of the cases. By "cure" is meant "no mental defects of any kind: ability to go about their business just as before; no signs of stereotypy and nothing that attracts particular notice to them as different from other people." In cases of "incomplete cure" there is ability to work to a certain extent, but affected behaviour, irritability and a tendency to temporary states of stupor and stereotypy remain. Nothing is said regarding the duration of the psychosis before admission, or the duration of hospital residence in cases eventually discharged.

22. Raecke (1910) made inquiries in the spring of 1908 regarding the histories of 200 cases of catatonia admitted to the Kiel University Clinic for

Neurology and Psychiatry between November, 1901, and December, 1905. It was only possible to obtain useful reports from the relatives of 171 cases. No personal examination was made, for the stated reason that it was not intended to discuss the unprofitable question of the possibility of a cure in the strict scientific sense. A " cure in the practical sense " was accepted if the relatives considered that the patient was " restored to health," that is, if the patient gave laymen the impression that he had recovered, if he followed his profession in the same way as before, if he did not complain of any disturbances and if he no longer appeared strange in any way.

The term " improvement " was used if it was reported that the patient was not quite the same as before, that he had less energy, was more irritable or generally nervous, but that he was no longer mentally disturbed.

On this basis the author found that 27 patients (15·8 per cent.) could be said to have attained a practical cure, 19 (11·1 per cent.) " improvement," and the remaining 125 (73·1 per cent.) to be uncured. Of the latter, 30 had died, 86 were still living in institutions, and 9 were being looked after at home.

The author goes into the question of the relationship of heredity, age and symptoms to prognosis, but the question of duration of psychosis and the time the patients were in hospital or in the outside world is not dealt with in any detail.

23. Schmidt, H. (1911), collected the subsequent histories of 455 cases of dementia praecox admitted to the Waadt Mental Hospital during the ten years previous to his investigation. He found cures in 16·2 per cent. of cases, cure with defect in 15·5 per cent. and dementia in 57·9 per cent. The criterion of cured cases is not so strict as some, since he does not rule out cases in whom such minor symptoms as irritability, tendency to tire frequently, etc., are still present. He examined 68 of the " cured " cases himself. He notes that some of the cases with a catatonic aspect showed similarity to pictures of acute confusion, and that it was remarkable how often the latter syndrome was present in cured cases, and how seldom in those not cured.

24. Meyer, E. (1909), in a further article on the prognosis in schizophrenia, followed up 170 cases admitted to the Königsberg Clinic from 1904 to 1906. He found that 13 (= 7·6 per cent.) of these cases had " recovered with defect " and 14 (= 8·2 per cent.) had improved. By recovery with defect was meant that " these cases support themselves wholly or in part, but show some mental abnormalities or have had to change their occupation. The ' improved ' are still capable of earning something, but are mentally diseased even in the eyes of the layman."

The works discussed henceforth have not been included in Tables I, II and III, or in any other such table to the best of my knowledge. Each is discussed on its individual merits.

25. Braatoy, T. (1936), published an article on " The Prognosis in Schizophrenia with Some Remarks Regarding Diagnosis and Therapy." He commences with a preliminary discourse on the difficulties encountered in diagnosis, and the poverty of literature on the factors governing prognosis in schizophrenia. He then declares himself fully aware of the various shortcomings of the katamnesic follow-up by the questionnaire method, but despite these shortcomings, considers it worth while publishing the results of such a follow-up by himself on 208 cases with " certain " and 90 with uncertain schizophrenia admitted to the University Psychiatric Clinic, Vinderen, Oslo, during the three-year period September, 1926, to August, 1929. The follow-up lasted from autumn, 1932 to February, 1935. The conditions of the patients at the end of this time are summarized by the author thus :

FIG. 20.

	Certain schizophrenics.		Uncertain schizophrenics.	
	Male.	Female.	Male.	Female.
Died	11	4	6	2
In institutions	48	49	20	10
In private care	14	20	8	6
Improved	9	13	6	5
Recovered	21	19	14	13
Total	103	105	54	36

Particular emphasis is placed on the tendency of remissions to relapse and on the importance of prognostic assessment of the possible duration of each remission. He gives the following definitions :

" Recovered = the patients registered as such are those regarding whom we have received statements to the effect that they are just as well and at full work.

" Improved = comprises the patients who are half or entirely at work, but about whom the report contains hesitations of one kind or another.

" In private care comprises patients who are practically unfit for work but who can be taken care of outside an institution, whether at home or in special colonies.

" In mental hospitals means in one of those at the time of the follow-up."

The fate of cases subsequent to admission he gives in a graph, but it only deals with the total time in or out of the mental hospital, and the author states that no attempt has been made to give expression on the graph (or in numbers) to short remissions within the period of five years involved in the investigation.

26. Langfeldt (1937) produced in a paper sufficiently lengthy to be published as a special supplement to the *Acta Psychiatrica et Neurologica* the results of a katamnesic follow-up of 100 cases of schizophrenia. These cases had been admitted to the University Psychiatric Clinic, Vinderen, during the years 1926 to 1929 inclusive, and their condition had been ascertained by personal re-examination by the author in 1936 (at periods varying from one case to another from six to ten years following admission). Of these 100 cases, 90 were cases of unmistakable process schizophrenia and 10 were cases of atypical schizophrenia (in the senses we have already seen—pp. 381–383), included for comparative purposes. The condition of the cases at the time of the investigation he summarized in the following table :

FIG. 21.—*Clinical Conditions of Patients and their Places of Residence in* 1936.

	Total.		Completely cured.		Cured with defects.		Improved.		Unimproved.	
	M.	F.	M.	F.	M.	F.	M.	F.	M.	F.
In institutions . .	22	24	..	..	...	..	1	1	21	23
In private care . .	10	15	..	..	..	..	2	5	8	10
At home . . .	14	15	9	8	2	2	1	3	2	2
Total . . .	46	54	9	8	2	2	4	9	31	35

All of the 66 per cent. of uncured, 13 per cent. of improved and 4 per cent. of cured with defect were true schizophrenics, but of the 17 per cent. of complete cures 14 were found to be cases of atypical schizophrenia (i.e. the 10 cases deliberately included plus another 4 allotted to this group after reconsideration), leaving only 3 per cent. of " process " schizophrenias in this category. " Completely cured " cases are defined as those who have responded in a normal fashion to the all-round psychologico-psychiatrical examination by the author ; " partially cured " are those who, although retaining a few symptoms, have adjusted themselves to these changes in their own worlds ; " improved " are those cases more or less cured, and " uncured " are all the rest.

27. Fromenty (1937) wrote an important paper entitled " Les rémissions dans la schizophrënie—Statistiques sur leur fréquence et leur durée avant l'insulin thërapie." The material consists of cases admitted to the department for mental diseases at the Tours General Hospital. 271 cases were carefully selected, the author pointing out that all cases in the following categories were eliminated in order that no doubtful cases should be included :

(1) All schizophrenics in whom the first manifestations had not been observed (e.g. immigrants, transfers from another hospital, or cases who had previously been in a mental hospital).

(2) Cases carrying the recognized diagnosis of " délire des dégénérés," although according to G. Heuyer and Dublineau attacks of dementia praecox arise quite frequently in this group.

(3) Puerperal psychosis cases who have turned into dementia praecox and, on the other hand, puerperal cases who, having had a variable number of remissions, had had the most recent attack preceded by pregnancy.

(4) Cases of chronic hallucinatory psychosis, or progressive hallucinatory deliria, which German authorities consider as late cases of schizophrenia with comparatively little downhill progress.

The chief interest in this work consists in accurate information of histories subsequent to discharge with special reference to the duration of first attack, remissions, subsequent attacks, and tables revealing the details of each of these are given (Figs. 22 and 23). Unfortunately it is not stated what is meant by "remission" (i.e. whether recovered or merely improved to varying degrees).

FIG. 22.—*Numerical Results.*

Category according to subsequent histories.	M.	F.	Total.	Percentage.
Number of cases	127	144	271	..
1. Schizophrenics having progressively deteriorated from the first	87	103	190	70
2. Schizophrenics having deteriorated after a variable number of remissions	20	20	40	15
3. Complete and durable remissions after a varying number of schizophrenic attacks and cures	20	21	41	16

FIG. 23.—*Summarizing Table of the Number and Duration of Remissions.*

A. In 2nd Category (i.e. above, Fig. 22).

Number of remissions.	Under 6 months.	6–12 months.	1–2 years.	2–3 years.	3–5 years.	5–10 years.	10–15 years.
1st	6	4	9	3	9	4	3
2nd	3	..	4	1	1	1	..
3rd	3	..	1	..	..	..	..
4th	3	..	..	..	..	..	..
5th	1	..	..	..	..	..	..

B. In 3rd Category.

1st	1	5	10	7	13	7	..
2nd	..	2	1	2	..	..	..
3rd	..	1	..	..	..	..	..

No prognostic findings or remarks are mentioned, other than that the hebephrenic type is less liable to remissions than other types.

28. In their survey of cases of dementia praecox discharged from the Psychiatric Institute and Hospital, Horwitz and Kleinman (1936) dealt with cases discharged from there between January, 1930, and January, 1933, inclusive. Of the 193 such cases 23 were untraceable, but the other 170 were followed up and their condition in August, 1935, determined. Of the 170 cases discharged before 1933, 124 had been rehospitalized in August, 1935. Seven of these were dead, 77 were still in mental hospitals unimproved, 30 were improved (12 in hospital still and 18 discharged), and 10 were discharged not improved. Of the remaining 46 who had remained continuously out of hospital, 1 was dead, 14 unimproved, 22 improved (10 improved and 12 much improved) and 9 recovered.

FIG. 24.—*Summarizing Table.*

Condition on discharge.	Number of cases.	Present condition.				
		Recovered.	Much improved.	Improved.	Unimproved.	Dead.
Recovered	5	3	1	..	1	..
Much improved	10	..	5	1	4	..
Improved	50	6	7	10	26	1
Unimproved	105	..	16	12	70	7
Total	170	9	29	23	101	8

The exact meaning implied by the gradings, recovered, much improved, improved, unimproved, was not given.

The authors also endeavoured to determine any prognostically favourable factors, and state: "In comparing the group that required re-hospitalization with the non-re-hospitalized group to find what factors made for continuous adjustment in one and subsequent re-hospitalization in the other, we find that the mode of onset, age on admission, institution, family background, social work done and pre-psychotic personality showed no significant differences in the two groups.

29. R. G. Fuller (1935) followed up 947 cases discharged from the New York State Hospital ten years prior to the investigation, and published his findings in an article called "What Happens to Mental Patients after Discharge from Hospital?" Of the 947 cases traced, 242 were cases of dementia praecox, and their position at the end of the ten years was as follows:

FIG. 25.—*Dementia Praecox 242 Cases.*

	Percentages.		
	Male.	Female.	Total.
In the community after ten years . .	40·3	46·4	43·8
In a mental hospital after ten years . .	47·1	40·6	43·3
Died in the ten years' period . . .	12·5	13·0	12·8
In the community continuously . .	29·8	41·3	36·4
Readmitted to a mental hospital . .	61·8	50·7	85·8

"In the community after ten years" includes patients in the community at the time of the study who had been in a mental hospital at some time within the ten years. Unfortunately there is no indication of how many times each of these cases had been readmitted, or for how long. "In a mental hospital after ten years" refers to any mental hospital, not necessarily to a civil State hospital. "Readmitted to a mental hospital" means that the patient was either in a mental hospital at the time of the study, or had been in a mental hospital one or more times within the period of ten years.

30. Hunt, Fieldman and Fiero (1938), in an article entitled "Spontaneous Remissions in Dementia Praecox," deal with the subsequent fate of 641 consecutive admissions to the Rochester State Hospital, U.S.A., between July, 1927, and June, 1934, paying particular attention to such factors as sub-type of the disease, duration of psychosis before admission, time spent in hospital, number of relapses, etc. They classify their results into three grades—much improved, improved, and unimproved—and justify themselves thus: "All cases showing significant remissions were classified as either much improved or improved. No attempt was made to separate recoveries from the much improved group—a difficult task at the best (Lewis and Blanchard, 1931). Furthermore, in our hospital the designation 'recovered' was almost never applied to a case of dementia praecox during the period of this study. Our "much improved" group contains all cases showing a disappearance of all active psychotic manifestations, and returning to a substantially normal life in the community with or without scarring of the personality and with or without good insight. The 'improved' group contains all those who showed enough improvement of conduct to warrant release from hospital, but fell short of being much improved because of residual psychotic trends or conduct, or because of such severe personality scarring as to require a definitely sheltered environment. All other cases were considered unimproved."

Fig. 26 shows their results in tabular form according to sub-type of manifestations and duration of psychosis expressed in percentages.

Fig. 27 shows the number of relapses.

Fig. 26.

	Total number.	1–5 months.				6–18 months.				Over 18 months.				Total.			
		No.	M.I.	I.	U.I.	No.	M.I.	I.	U.I.	No.	M.I.	I.	U.I.	No.	M.I.	I.	U.I.
Catatonics	111	54	48·2	14·8	37	29	47·5	10·5	42·0	28	25	10·7	64·3	111	41·6	12·7	45·5
Hebephrenics	151	38	39·5	26·3	34·7	38	29·0	10·5	60·5	75	4·0	22·7	73·3	151	19·2	20·5	60·3
Paranoids	218	29	24·1	24·2	51·7	50	10·0	22·0	68·0	139	7·9	17·3	74·8	218	10·5	19·3	78·2
Unclassified	161	38	23·6	13·1	63·3	41	17·3	17·7	75·6	82	13·4	7·3	79·3	161	14·3	11·2	74·5

Because there were only 10 cases of simple schizophrenia, their results were not tabulated.

Fig. 27.—*Relapses.*

Condition on discharge.	Number of cases.	Relapse percentages.			
		No relapses.	Temporary relapse.	Permanent relapse.	Not traced.
Much improved	118	56·8	12·7	12·7	17·8
Improved	107	41·1	12·2	31·8	14·9
Total	225	49·4	12·4	21·8	16·4

In the temporary relapse group the relapse came on after an average length of remission of 22 months; 10 of the 28 patients had two or more relapses.

Fig. 28.

Sub-type.	Number of cases.	A.				B.				
		Rec.	M.I.	Imp.	Unimp.	Rec.	M.I.	Imp.	Unimp.	Hosp.
Simple	24	4·2	41·7	37·5	16·7	8·3	29·2	8·3	4·2	50·0
Hebephrenic	206	6·3	25·7	20·9	46·1	1·0	7·8	6·8	14·1	68·4
Catatonic	356	17·4	25·6	27·0	29·5	7·9	13·2	6·2	3·9	61·4
Paranoid	448	12·7	28·1	25·7	31·5	·7	10·2	8·5	7·3	68·3
Unclassified	5	20·0	40·0	0	40·0	20.0	..	20·0	30·0	40·0
Total	1,039	12·9	27·1	25·3	33·4	3·5	11·2	7·4	7·5	68·8

A. = Insulin-treated group.
B. = Non-insulin-treated group.

Rec. = Recoveries.
M.I. = Much improved.
Imp. = Improved.
Unimp. = Unimproved.

} Expressed in percentages.

Commenting on the time of remission the authors say: "Most of the group seem to strike about the same average, except the paranoid group in which there is a relative delay before remission. There is still a slight but quite consistent tendency for remissions to develop earlier in the cases of shorter duration. The general average of 9·5 months of hospital residence before remission is, of course, considerably larger than the two or three months required for the new therapies. It is noteworthy, however, that over a quarter of the spontaneous remissions occur within six months, and three-quarters within a year." Their table showing the number of relapses which occurred is interesting and is reproduced in Fig. 27.

31. Benjamin Malzberg (1938) produced a statistical survey of "The Outcome of Insulin Treatment of One Thousand Patients with Dementia Praecox," in which he compared rates of remission and improvement in 1039 cases treated with insulin in the New York State Hospitals in 1937, with those of a similar number of first admissions to the same hospitals from July, 1935, to July, 1936. The "condition of the patient" in the insulin group referred in each case to a period approximately one month after the date of treatment. The non-treated group consisted of the same number per hospital, per sex and per type as the insulin-treated group. Although we are particularly concerned with the non-insulin-treated group at present, Fig. 28 represents both groups, as reference will be made to the comparison later on.

Malzberg also produces tables to show that the rate of recovery is inversely proportionate to the length of insulin therapy required and also to the previous duration of hospital residence.

32. Guttmann, Mayer-Gross and Slater (1939) have recently produced an important paper on the "Short-distance Prognosis of Schizophrenia." This paper is written with the deliberate object of forming a criterion against which the claims of the modern insulin and convulsive treatments may be weighed, and from this point of view material which is prognostically comparatively favourable is selected. This selection is based first of all on the fact that "the Maudsley Hospital admits only those who prima facie have a favourable outlook," and is further limited by the exclusion of all cases whose illness antedated admission by more than 12 months, and of all cases over 45 years old, and of those on whose diagnosis the authors did not all agree. The material from which the selection was made consisted of all schizophrenics discharged from the Maudsley Hospital between January 1, 1934, and December 31, 1935, inclusive, and the investigation determined their state on January 1, 1938. The work was carried out with the aid of a social worker, who visited the majority of the patients' homes, and in cases where there was any doubt regarding the patient's condition, examination at the hospital by one of the authors was, when possible, carried out.

This work is of value not only because of its thoroughness, but because of the manner in which the results are represented in tabular and graphical form. The classification in this case is into the following groups, as suggested by Müller:

(T.R.) *Total recovery* = freedom from symptoms and signs, return to previous social environment and to previous or to an equivalent occupation.

(S.R.) *Social recovery* = return to previous social environment and to previous or equivalent occupation, in spite of persistence of minor signs and symptoms, such as irritability, shyness, shallowness of affective response, etc.

(S.D.) *Social defect* = presence of minor symptoms as above, incapacity to carry out work of previous level and failure to maintain self in the same degree of social adaptation.

(F.I.) *Family invalid* = presence of well-marked symptoms, incapacity to carry out any useful occupation, but manageable at home.

(H.I.) *Hospital invalid* = inmates of mental hospitals, some continuously since discharge from the Maudsley Hospital, some relapsed after a temporary recovery.

(D.) Dead.

(U.) Untraced.

The table in which they give their final results is given in Fig. 29.

FIG. 29.

	Male.		Female.		Total.	
	Number.	%.	Number.	%.	Number.	%.
H.I. with free intervals	10	12·7	15	13·8	25	13·2
H.I. without free intervals	24	30·4	28	25·7	52	28·0
F.I.	9	11·4	9	8·3	18	9·7
S.D.	8	10·1	7	6·4	15	8·3
S.R.	8	10·1	17	15·6	25	13·2
T.R.	13	16·5	29	26·6	42	21·5
D.	5	6·3	2	1·8	7	4·1
U.	2	2·5	2	1·8	4	2·2
Total	79	100·0	109	100·0	188	100·0

Thus, after an average period of observation of slightly more than three years, 41·2 per cent. were in mental hospitals and 9·7 family invalids—a total of 50 per cent. deteriorated to the extent of requiring full support; 34·5 per cent. were in the community able to fend for themselves and as good as they were before from a purely social point of view; and 8·3 per cent., while not

recovered, were able to fend for themselves to a certain extent and not require mental hospital treatment.

The question of relapses is dealt with in the following table :

FIG. 30.—*Table.*

Of 69 males, 44 were discharged from hospital	= 64%
,, these 44, 14 were subsequently readmitted .	= 31%
,, these 14, 4 were, at the end of 3 years, out of hospital	= 28%
Of 98 females, 73 were discharged from hospital	= 75%
,, these 73, 21 were subsequently readmitted	= 29%
,, these 21, 9 were, at the end of three years, out of hospital	= 42%

The authors also produce graphs and tables which show (*a*) that the prognosis is better in females than in males ; (*b*) that the total recoveries and social recoveries have an average period of hospitalization of about six months ; (*c*) curves of recovery show that the maximum number of patients are out of hospital in some category of recovery or improvement (i.e. T.R., S.R., or S.D.) at the end of 18 months ; (*d*) age statistics suggest that those whose illness begins at an age of twenty or less have a better prognosis than those who fall ill at a later age ; (*e*) the low fertility of discharged schizophrenics : 1 of the 44 discharged men married and had three children ; 9 of the 73 women discharged married and had 12 children between them.

33. Stalker, Millar and Jacobs (1939) compared remission rates obtained by insulin and cardiazol treatment with those treated by the normal routine methods. Their group of routine treated patients consisted of all first admissions during the five years August 1, 1932, to July 31, 1937, inclusive, a total of 133 cases, of whom 4 were untraceable, leaving 129 followed up in September, 1938, at least 14 months after admission. Their results in tabular form are as follows :

FIG. 31.

Group.	Number of cases.	Percentage.
Complete remission	15	12
Social remission	11	8
At home improved	12	9
Remitted and relapsed . . .	27	21
Unimproved	64	50
Total	129	

"Complete remission" is defined as patients showing an absence of all symptoms and having insight into their illness.

"Social remission" is applied to patients who are leading a normal social life and following their normal occupations, but who continue to show some schizophrenic symptoms varying from lack of insight to hallucinations.

"At home improved" refers to patients who have shown some definite improvement and been able to return home.

"Readmitted and relapsed" refers to patients who have had a remission of any degree which has allowed them to be at home at least three months, but who have now relapsed.

"Unimproved" refers to those patients who have not had a remission of at least three months.

Of the 15 cases of complete remission, 12 patients had kept well for two years and 1 for one year; 2 had a second attack from which they again recovered. Two cases of the complete remissions had suffered from an acute schizophrenic illness which could not be fitted into any of the standard sub-groups.

34. Briner, O. (1938), published an article dealing with the frequency and quality of remissions in schizophrenia with special reference to prolonged narcosis and "Frühentlassungen" (the latter meaning the discharge of patients from hospital at the earliest moment possible, which often means before waiting until the patient has reached maximum improvement). The cases dealt with were all those of not more than one year's previous illness who were admitted to the Waldau Clinic, Berne, between April, 1933, and July, 1936. His figures given here are the most favourable of any, but in view of the extensive use of prolonged narcosis and "Frühentlassung" they are not strictly comparable with previous ones of the series (and therefore not included in the table below):

Total number of cases	245
Discharged and since then having had at least one year without relapse	144 (58·7%)
Made up as follows:	
Complete remission	16
Social recovery	56
Able-bodied (i.e. employable) but with slight defect	39
Only partially employable and obviously ill	15
At home, unemployable or capable of only very limited efforts	18
Detained in mental hospitals	64 (26·1%)
Dead	37 (15·1%)

The classification of remissions into so many subdivisions is inclined to confuse the issue. The author defines the various gradings thus:

" ' Complete remission ' includes only cases in which personal examination failed to reveal the least trace of schizophrenic defect. We are fully aware that even then one cannot speak of a true medical cure, for, as Bleuler says, the determination of a cure depends on psychological skill and the time available for examination. We have no doubt that in the cases with full remissions something abnormal would be found after prolonged observation.

" Under the heading of ' social recovery ' are included patients who have regained the condition they were in before the onset of the disease and are capable of working, but have some peculiar characteristics in the schizoid sense.

" ' Slightly defective ' is used for patients who, though fit to work, show distinct symptoms of disease."

The other terms explain themselves.

Perusal of the articles described above reveals the extreme difficulty of any reasonable synthesis. Nevertheless, certain facts stand out.

To estimate the prognosis of schizophrenia from the point of view of remission rates necessitates knowledge of (*a*) the short distance prognosis, (*b*) the ultimate prognosis, (*c*) the incidence of relapses. Alternatively, it may be considered from another angle, namely, (*a*) continuous hospitalization, (*b*) continuous remission after discharge, (*c*) relapses. Considering the matter from these aspects, and always allowing for discrepancies as revealed in the text, I have compiled the table below (Table IV).

To understand the table recourse to the previous text is essential.

Diagnosis, from the point of view of this article, may be taken in each case to be based on Bleuler's ideas as opposed to those of Kraepelin. This has allowed me to include in this picture various so-called atypical groups (cf. Bond (1921), Rosanoff (1914) and Langfeldt (1937)).

Regarding the articles which deal with " recovery " rates as distinct from improvement, I have done away with such artificial barriers as are used by many authors to divide the recoveries into numerous categories, and have considered " recovery " to be synonymous with " much improved " in the sense quoted by Hunt, Fieldman and Fiero, namely, " All cases showing a disappearance of all active psychotic manifestations and returning to a substantially normal life in the community with or without scarring of the personality and with or without insight." " Improved " is also used with their meaning, which is as follows: " The ' improved ' group contains all those who showed enough improvement of conduct to warrant release from hospital, but fell short of being much improved because of residual psychotic trends or conduct, or because of such severe personality scarring as to require a definitely sheltered environment." Bearing these criteria and the previous review of the various articles in mind, it is easy to see how the present figures have been completed. In the figures of Guttmann, Mayer-Gross and Slater (1939), for

TABLE IV.—*Remission Rates.*

Author.	Number of cases.	Period in years.	Ment. hosp. or clinic.	Percentages. Recovered.*	Improved.	Recovered + improved.	Not improved.	Dead.
Lemke (1935)	132	1/12–12	C.	14	34	48	43	9
Whitehead (1937)	90	1–2	M.H.	13·3	20	33·3	61	..
Guttmann, Mayer-Gross and Slater (1939)	188	2–3	C.	34·7	18	52·7	41·0	4·1
Faurbye (1937)	72	1–4	M.H.	42·0		42·0	58·0	..
Rosanoff (1914)	222	5	M.H.	32·4		32·4	48·1	12·6
Bond (1921)	91	4–7	Priv. M.H.	45·5		45·5	46·8	7·7
Bond and Braceland (1937)	134	5	Priv. M.H.	20·0	40·0	20·0	56·9	4·1
Stalker, Muller and Jacobs (1939)	129	1–6	M.H.	20·0	19·0	39·0	50·0	..
Wootton and Armstrong (1935)	104	4–7	M.H.	23·0	22·0	45·0	55·0	..
Schmidt, H. (1911)	455	1–10	M.H.	16·2	15·5	31·7	57·9	..
Braatoy (1936)	298	7–10	C.	26·0	16·0	42·0	48·3	7·5
Langfeldt (1937)	100	7–10	C.	21·0	13·0	34·0	56·0	..
Mayer-Gross (1932)	294	10	C.	32·4	4·8	37·2	22·4	42·4
Fuller, R. G. (1935)	242	10	M.H.	43·8		43·8	43·3	12·8
Hunt, Fieldman and Fiero (1938)	641	4–11	M.H.	18·4	16·7	35·1	64·9	..
Totals	3,192	1–11	M.H. or C.	..	..	40·1	53·3	6·6

* For definition of recovery see text.

instance, the "total recovery" and "social recovery" groups are included in the "recovery" group of this table and the "social defect" and "family invalid" groups in the "improved" group.

In some cases it was only possible to represent a figure which combined the recovery and improvement rates together, and in order to tally with these figures, the combined result is placed in a separate column in the cases dealing with recovery and improvement separately.

We see from this table that the total rates of recovery and improvement combined vary within the comparatively narrow margin of 31·7 per cent. and 52·7 per cent., with a total average of 40·1 per cent. These figures show considerably less variation than previous compilations, especially as they are not selected in any way beyond the already-mentioned requisites of criteria of diagnosis and degree of remission.

The average for the "Clinics" is 40·7 per cent. and for the mental hospitals 38·78 per cent.—a very small difference. The interesting fact that there is comparatively little variation between the figures dealing with short histories and those with long histories is probably due to many relapses being only temporary, and the permanent ones being to a large extent counter-balanced by late improvements of a sufficient magnitude to warrant discharge.

In the case of the articles differentiating "recovery" from "improvement," we find that the average recovery rate (as opposed to "improved") varies from 13·3 per cent. to 34·7 per cent., with an average of 21·7 per cent. The average for the Clinics in this case is 25·6 per cent. and the hospitals 17·98 per cent.

If we accept these averages and examine the widest discrepancies from them, reasons for these become apparent. Lemke's figure of only 14 per cent. recoveries for cases of two years' history (i.e. two years since they first attended the Clinic) is countered by an improvement rate of 34 per cent., and it is probable (since exact definitions are not given) that in the sense in which we are using the word "recovery," many cases might on detailed analysis require to be transferred to the recovery group.

The comparatively low figure of Langfeldt, 21 per cent., is probably due to the fact of his rigid diagnosis. He considers that of these 21 recoveries themselves, 11 were atypical cases. If we included in this group a certain number of the "schizophreniform" or atypical schizophrenias he describes later, and which might be diagnosed by many of the adherents of other schools as "schizophrenia" in the simple sense of the word and with no appended adjective, the average rate of recovery would increase.

The high recovery rate of 34·7 per cent. of Guttmann, Mayer-Gross and Slater may be due to the fact that their cases are exclusively of a maximum history of one year. This would appear to be confirmed by the high recovery rate in short distance prognosis given by Briner (1938), whose cases are also of not more than one year's history.

Mayer-Gross's figure of a 32·4 per cent. recovery rate after ten years is remarkable. The contrasting small percentage of improved cases (only 4·8 per cent.) is worthy of note, however, and one wonders whether this batch of cases may not by a stroke of chance have been prognostically more favourable than the average.

Relapses.

To try to reach a reasonable synthesis regarding the incidence and outcome of relapses is considerably more difficult. Table V represents a synthesis of the various articles dealing with relapses. The average percentage of relapses in the discharged cases is 35 per cent. Fromenty's figures are based on admissions and not discharges, and a total of 30 per cent. of admissions (approximately) relapse. Although there is a considerable discrepancy of findings as to the percentage of relapses which recover or deteriorate, it is seen that roughly speaking (if all the figures are considered together) about 50 per cent. of the total number of relapses are temporary and 50 per cent. permanent. This is what one would infer from the fact that in the figures of remissions previously referred to, there is comparatively little difference between the short-distance and long-distance outcome. It is also obvious, broadly speaking, that single remissions are the most common, double cases less common, and that more than two remissions are comparatively rare.

Summary.

We may summarize the result of this investigation of the literature dealing with remission rates in schizophrenia by the conclusion that an average of 40 per cent. of cases admitted to mental hospitals (including clinics in the continental sense of the word, which has been explained on p. 385) recover or improve, whereas the other 60 per cent. fail to improve or deteriorate. Of these cases the average number of " recoveries " (as defined above) is about a half, i.e. 20 per cent. of all cases admitted. For various reasons the percentage varies considerably from one author to another, but the rate is higher for clinics (26 per cent.) than for mental hospitals (18 per cent.)

Relapses occur in about 20 per cent. of the cases discharged as recovered or improved, of which approximately half are permanent and half temporary.

C. The Relationship of Various Specific Factors of Constitution and Disease Manifestation to Prognosis.

Of the colossal bulk of literature dealing with dementia praecox and schizophrenia comparatively little has dealt with prognosis. Schizophrenia is a disease of a protean symptomatology and a protean course, and the difficulties of assessing prognosis according to individual factors in the patients' constitutions and histories are profound. The most that can be said to have been

TABLE V.—*Relapses.*

	Period (years).	Number of cases.	Number of relapses.	Temporary relapses.			Permanent relapses.		
				1.	2.	More than 2.	1.	2.	3.
Rosanoff (1914)	5	70 D.	16 (22·2%)	4 = 5·7%			12 = 17·1%		
Otto-Martiensen (1921)	3–7	312 D.	105 (33·7%)	53 (16·9%)	13 (4·1%)		39 = 11·7%		
Wootton and Armstrong (1935)	4–7	47 D.	14 (29%)	9 = 18%			5 = 10%		
Hunt, Fieldman and Fiero (1938)	3½–11	225 D.	77 (34·6%)	18 (8%)	10 (4·4%)		49 = 21·8%		
R. G. Fuller (1935)	10	242 D.	55·8%	7·4%			48·4%		
Fromenty (1937)	6–7	271 A.	81 (30%)	38 = 14%			43 = 15%		
				28	6	4	38	4	1

D. = Discharged (total number of cases). A. = Admitted (total number of cases). All percentages are expressed as percentages of the total number of cases discharged, except in Fromenty's article, where they are of the total number admitted.

established so far are certain general prognostic indications, but it has to be borne in mind that prognosis based on these must always be guarded. This especially applies if too much emphasis is placed on the individual factors and the picture as a whole must always be considered.

I propose to enter into a brief survey of the literature on this subject and follow on with a summarizing synthesis. The specific prognostic factors will be divided into two groups: (i) those of constitution, (ii) those of disease manifestations.

GROUP I.

The Constitutional Factors.

Heredity.—Kraepelin is reported by Henderson and Gillespie to have found hereditary abnormalities in 53·8 per cent. of 1,054 cases. Bleuler (1936) states: "Great importance is undoubtedly to be attached to hereditary burdening. Among the direct ancestors of the patients, psychoses, especially schizophrenia, are much more numerous than with the healthy. Most frequently one finds in families schizoid characters, people who are shut in, suspicious, incapable of discussion, people who are comfortably dull, and at the same time sensitive people who, in a narrow manner, pursue vague purposes, improvers of the universe."

Rüdin's (1916) work showed that only 4·48 per cent. of the siblings of parents, one of whom had suffered from dementia praecox, were affected with a similar trouble. The incidence was very much higher where both parents were schizophrenic, 53 per cent. of the offspring being schizophrenics and 29 per cent. psychopaths.

Barrett's (1928) work confirms that of Rüdin in proving that direct inheritance of schizophrenia from one parent is rare, but from two is common. He also shows that tainting of the family tree with psychosis is about equal to that occurring in the manic-depressive group, and in psychoses as a whole; mental abnormalities are much less in the parents of schizophrenics, but greater in the grandparents and greater still in the collateral relations than they are in manic-depressive psychotics.

Myerson (1917), in the study of the family history of 97 cases, concluded that dementia praecox in an ancestor tends to be followed by a similar disease in the offspring.

Leonhard (1936), dividing schizophrenics into typical and atypical in accordance with ideas already reviewed, points out that heredity seems to play a smaller part in the typical than in the atypical group. Langfeldt's (1937) investigations support this.

Luxemburger (1937), Humon (1935) and Rosanoff (1931) established the importance of the heredity factor in the inheritance of schizophrenia in twins.

On Mendelian principles one may quote Devine (1933), who says: "It cannot be claimed that Mendelian studies on the psychoses are in any sense

conclusive." Rüdin, who has worked according to the statistical methods formulated by Weinberg, makes only one positive statement, viz. that certain forms of dementia praecox follow the recessive type of inheritance, and he states very soberly later on that no one can, on the basis of research up to the present time, state that Mendelian laws cannot apply to the inheritance of mental disease. Lewis (1935) states that " apart from the indications afforded in rare instances by two affected parents or by an affected uniovular twin, hereditary guides to prognosis are dubious : in no instance can one prognosticate with certainty from them regarding the present attack."

Age.—The prognostic significance of age is only really intelligible when considered in conjunction with symptomatology, and more especially with reference to the various divisions, i.e. (i) hebephrenic, (ii) catatonic, (iii) simple, and (iv) paranoid. In this respect it is well to point out that the simple and hebephrenic forms occur at slightly younger average ages than the catatonic, and at a considerably younger one than the paranoid form.

Strecker and Willey's (1927) results regarding this age question are interesting. Of 186 cases they found the results expressed in Fig. 32.

FIG. 32.

Sub-group.	Number of cases admitted.	Number of cases recovered.	Average age of onset.
Catatonic	45	18	28
Hebephrenic	49	8	24
Paranoid	85	12	35
Simple	7	0	?

Kraepelin (1919) points out that forms which begin in the earlier years tend to be associated with excitement and depression, and have a better prognosis than those developing later as far as possibility of improvement, although the latter seldom progress to such complete disintegration. " It could therefore be approximately said," he states, " that with advancing age the ability to restore the equilibrium and repair the damage generated by the disease gradually diminishes, but at the same time the work of destruction appears to spread less deeply."

Mauz (1930) declares that the catastrophic* form of the disease appears almost exclusively between the ages of 16 and 25.

Langfeldt (1937) found that of his 100 cases, 35 commenced before 23, 14 of whose course was catastrophic and 5 of whom were cured ; 39 occurred between the ages of 24 and 30 inclusive, of whom 11 were cured ; and 19 occurred from 31 to 40 inclusive, about half of which were catastrophic or

* For a description of the meaning of this term, see later in the text.

chronically progressing. He concludes that "a young age is not always synonymous with an unfavourable prognosis, and a high age does not always protect against an unfavourable course."

Guttmann, Mayer-Gross and Slater (1939) find results suggesting that " those whose illness begins at an age of 20 or less have a better prognosis than those who fall ill at a later date," but add that from a statistical point of view, nothing certain can be said about the effect of age on prognosis. Braatoy (1936) also finds an early onset favourable.

Sex.—Kraepelin (1919) says that men have a larger share in the unfavourable silly dementia (hebephrenia), while women predominate in the paranoid group, but adds that there are not nearly enough statistics to hand to be of any conclusive value, and this may be said still to be true. Guttmann, Mayer-Gross and Slater (1939) draw attention to the distinctly more favourable course of the psychosis in the female than in the male sex, but they do not make clear what are the proportions of men and women in the various subdivisions.

Pollock (1928), in a statistical study of many patients (based on the general census of institutions for mental diseases), finds that schizophrenia is commoner and tends to occur earlier in life in the male sex than in the female. Bowman and Raymond (1928), on the other hand, find no differences in the incidence of each sex.

Bodily build.—The importance of bodily build has been emphasized by the work of Kretschmer (1921) and Mauz (1930). Efforts had been made before those of Kretschmer to classify types of bodily build, but the observations of Kretschmer on this subject revitalized it from a psychiatric point of view. Kretschmer's approach, as Raphael, Ferguson and Searle (1928) point out, was impressionist rather than strictly anthropometric, but work on more exact anthropological lines has tended to confirm his ideas. Briefly, Kretschmer's divisions were as follows :

(1) *The asthenic type*—slender, narrow and thin, with a small trunk and long limbs.

(2) *The pyknic type*—(the reverse of the asthenic) short, thick-set, well-nourished, with large trunk and body and comparatively short limbs.

(3) *The athletic type*—tall, broad-shouldered, wide-chested, with small waist.

(4) *The dysplastic type*—due to or associated with endocrine changes, e.g. thyroid, pituitary, genitals, etc.

Kretschmer claims that schizophrenia occurs for the most part in people of asthenic, athletic and dysplastic build. It is rare in people of pyknic build, who, on the few occasions when it does affect them, seem to do much better than the other builds. Mauz's work confirmed this belief. Schmidt (1919), however, in his study of 18 schizophrenic cases with pyknic build, found among them both cures and dementias. He found that some cases went downhill from the very beginning in a typical schizophrenic manner, and

concluded that in some cases of pyknic build schizophrenia seemed to thrive in a malignant form.

Raphael, Ferguson and Searle (1928) go into the whole matter very thoroughly from an anthropometric point of view, and conclude that "Kretschmer's hypothesis seems to be essentially valid in spite of possible criticisms which may be raised relative to his method of classification."

Kolle (1926) produces a table (Fig. 33) which is of interest in showing the discrepancy of figures by various authorities :

FIG. 33.—*Table Representing the Percentage of the Various Types of Bodily Build in Schizophrenia, according to Different Authors (Kolle).*

Investigator.	Number of cases.	Asthenic.	Athletic.	Dysplastic.	Pyknic.	Mixed.
Kretschmer . . .	175	46·2	17·7	19·4	2·8	13·7
Sioli	43	16·3	16·3	9·2	23·0	34·0
Olivier. . . .	64	42·2	12·5	12·5	13·4	9·4
Henckel . . .	100	34·0	25·0	11·0	2·0	28·0
Moellenhoff . . .	140	15·7	2·9	20·7	5·0	55·7
Mickel and Weeber .	141	43·3	20·5	5·0	17·1	11·2
Wyrsch . . .	192	42·7	14·6	8·8	9·3	24·4
Kolle (Schweren) .	100	18·0	8·0	4·0	30·0	40·0
Kolle (Jena) . .	100	11·0	8·0	4·0	36·0	41·0
Jakob	168	14·3	33·3	4·8	14·8	28·1
Range . . .		11–46	2·5–33·3	4–20	2–36	9·4–55

The wide variations in this table make one realize the inconclusive nature of their findings. Particular significance may be found in the large number of "mixed" builds found by certain authors. Failure to give comparative figures of the so-called normal population to act as controls is also conspicuous among articles on this subject, combined with divergences of opinion as to the exact proportion of builds in schizophrenics as represented above. These facts all point to the failure to establish statistical conclusions, with the result that at present nothing more than certain general tendencies has been established.

Temperament and mental make-up.—The importance of the temperamental and mental make-up of schizophrenic personalities has long been recognized. Adolf Meyer (1903) as long ago as 1903 pointed out the frequency of previously shy and seclusive personalities among schizophrenic patients, and Hoch (1910) soon after described this oft-occurring type of pre-schizophrenic personality as the "shut-in" personality. Jung, in studying temperaments, had divided them into two main classes, the extravert and the introvert temperaments, and had shown how much more frequently the latter occurs in pre-schizophrenic personalities. These foregoing ideas were finally crystallized into the conception of the schizoid and cycloid mentalities. Kretschmer (1921) made a great effort to correlate the mental sides of personality with his types of bodily build, but although he showed that frequently pyknic build

and extravert temperament or asthenic build and introvert temperament were combined, the correlation is far from absolute.

One thing which has been almost universally agreed on amongst the various authors is the comparatively favourable outlook in the "extravert" type of temperament to the "shut-in" or "introvert" one. Langfeldt (1937) has recently confirmed this, and claims that the outlook in cases with a combination of introvert temperament and asthenic or leptosomatic build is of particularly ominous significance, as had already been pronounced by Kretschmer and Mauz.

The previous history of the pre-psychotic personality.—Kraepelin (1919) says: "Bleuler considers those cases more unfavourable in which from childhood up abnormal qualities have appeared, and Zablocke also thinks that there is in them a stronger tendency to profound dementia. That becomes intelligible if one assumes that in such cases, through an inferior disposition, either there exists a lesser power of resistance to the morbid process, or the morbid process itself, developing insidiously from childhood, has already generated the abnormalities."

Bleuler (1936) states: "In probably three fourths of the cases the personal disposition already expresses itself during youth in a dereistic character inclined to seclusion." "Dereistic" is a word coined from "de" and "res," and meaning "away from reality." Elsewhere, discussing phantasy, he states: "The principal trend of thought is determined by the impulses and the affects. We wish to reach a definite aim. But even in the individual elements of thought we can see the influence of affective needs. It accounts for daily disturbances and even direct falsifications of logic which manifest themselves to a slight degree in normal persons and to a much greater extent in the insane. The material taken up forms new combinations in phantasy whereby different degrees of detachment from experience become possible." An excessive indulgence in the habit of satisfying instincts, sentiments and wishes by refuge in phantasy as opposed to reality lead to dereistic thinking.

The importance of this tendency to day-dreaming and phantasy in schizophrenic personalities is generally well recognized, but in considering it from a point of view of prognosis, certain facts must be borne in mind. Bleuler points out that humans think dereistically (*a*) whenever our knowledge of reality is insufficient for practical needs; (*b*) whenever reality becomes unbearable; (*c*) in dreams and deliria. It is well known that puberty and adolescence are times in everybody's life where the former two conditions are very liable to be stressed, and dereistic thinking is common; and Mapother (1926) has pointed out the difficulty of differentiating between these reactions among so-called normal people and those of the milder schizophrenics. Sullivan (1928) has also emphasized this narrow dividing line between normal adolescent mental activities and those of the onset of schizophrenia.

We may say, therefore, that although phantasy and dereistic thinking of an extreme nature may be prognostically unfavourable factors in schizophrenia, it must always be remembered that they exist in a slight or even a moderate degree in so-called normal people.

The main tenets of Adolf Meyer and his followers have already been cited. This school emphasizes, as we have already seen, the reactions of the individual as a psycho-biological entity, so that from the point of view of prognosis in schizophrenia, its adherents consider the main point to be the previous reactions of the personality to the difficulties and problems of life, rather than the other specific factors of prognosis.

Henderson and Gillespie express their view thus: "The emphasis must be placed more on an attempt to estimate how the individual met his difficulties in his prepsychotic period. If he handled them for the most part in a satisfactory way and if his general interests have been well maintained, then he has a very much better chance of re-adjusting himself than the shut-in or introverted individual."

Psycho-sexual history.—Another point of interest about which much has been said but little proven is the pre-psychotic sexual activities of the patient. Sexual maladjustment would appear to be common in schizophrenia. Lewis and Blanchard (1931) found numerous sexual abnormalities among the 100 recovered cases whose history they investigated: namely, prolonged masturbation in 68 per cent., overt homosexual tendencies in 17 per cent., incest in 3 per cent., bestialism in 1 per cent. and exhibitionism in 1 per cent.

Langfeldt (1937) finds that interest in the other sex seems to have been strikingly little. He says: "In a number of cases the special column in the anamnesic questionnaire circulated to relatives was not filled in; in some it was answered by 'quite normal,' but in quite half of the cases the reply has been 'no particular interest in the other sex.'" He also found that the number of married people in whom schizophrenia occurs is comparatively small, but refuses to commit himself to any definite conclusions owing to an insufficient number of cases, or to enter into statistical comparison of the percentage of marriage at different ages as opposed to the percentage in the total population. Regarding pre-psychotic fertility nothing is said.

Guttmann, Mayer-Gross and Slater (1939) draw attention to the fact that in their discharged cases the post-diagnosis fertility appears to be low. No statistical conclusions are produced. We see, then, that the pre-psychotic sexual history in itself is of little help towards prognosis.

Education and abilities, etc.—The importance of these factors from a prognostic point of view has been considered by Langfeldt (1937), whose observations on his 100 cases are that the prognosis in clever people is not improved thereby, and that indeed, in clever people with a schizoid (or schizothymic) temperament, the outlook is particularly bad. This is probably due to the fact that the lack of external interests is in many the cause of excessive zeal

for and occupation with the study of books. He also disagrees with Mauz that schizokar symptoms (see below) are more common in the more highly educated and intelligent classes than in others. The work of Lewis and Blanchard (1931) and of Bowman and Raymond (1928) also failed to establish any prognostic significance in such factors as education and intelligence. Kahlbaum (1902) could find no significant value in intelligence.

GROUP II.

Disease Manifestations.

Exogenic Factors.

The co-existence of some exogenic factor is to be regarded favourably. Meynert (1928), Bianchi (1928) and Menninger (1928) pointed out the resemblance between reactions in certain confusional states and dementia praecox, and it has already been pointed out that Bleuler would consider these cases as definitely schizophrenic. Menninger (1928) has gone into the question of the onset of schizophrenia following the acute fevers and other diseases very thoroughly, and concludes : " The particular type of psychotic picture revealed by the toxic attack on the encephalon and its conscious fabrications probably depends upon the kind of mental substructure pre-existing, to speak in static terms, or type of habitual conflict solution, to speak in dynamic terms. These pre-existing substructures may be correlated to certain characterological aspects known as temperament, or with certain anatomical aspects known as ' Körperbau '." He adds that if we accept with Bianchi the probable identity of these so-called confusional cases and dementia praecox, their prognosis is more favourable than cases not having such an associated toxic disease. Bresowsky (1928) also stresses the desirability of rating such infective cases as schizophrenias, believing that the specific symptoms are conditioned in these cases by a known type of agent, that were the agent not known no one would hesitate to call them schizophrenias, and that the knowledge of the causative agent should not exclude them from this group.

Schizophrenia following head injuries has been described amongst others by Mapother (1937). The prognosis is not always favourable.

Zilboorg (1938) and others have described schizophrenias following childbirth or during pregnancy, and here again, although many cases do well, the outlook is frequently bad, the attack being often followed by a progressively dementing course. (Cf. Kahlbaum (1902) and Raecke (1910).)

Langfeldt (1937) includes in his description of exogenic precipitating factors alcoholic abuse, " love affairs," unemployment, operations, influenza, gastric ulcer and head injury, and finds that in the cured cases there have been relatively many exogenic traumata immediately prior to the onset of the psychosis. Albrecht (1905) found exogenous factors—imprisonment, influenza, trauma and lactation—present in the histories of only 4·5 per cent. of his 202

cases of dementia praecox, while he quotes Kraepelin as considering acute diseases as responsible for 10 per cent. of all his cases, and imprisonment for 6 per cent. of his males.

Apart from such physical exogenic factors as have been described, various mental factors, such as disappointment in love, financial troubles, unemployment, etc., are mentioned. Strecker and Willey (1927) say that "when the psychosis as a total reaction constitutes an escape and psychological correction of serious circumstances in life which have brought the patient to an impasse, then the prognosis is good." The test they apply in this respect is the appearance in symptomatology of phenomena which correct the hard and uncompromising facts of reality. Henderson and Gillespie (1936) consider that cases associated with obvious exogenic factors tend in general to be more favourable.

The Speed of Onset.

It has been frequently stated that the outlook in cases of sudden onset is better than that in those of insidious onset. Sullivan (1928) and Barrett (1928) and Strecker and Willey (1927) have commented on the comparatively favourable prognosis of acute onset. Bleuler (1936) has commented on the favourable outlook in acute catatonics as opposed to chronic ones. Henderson and Gillespie (1936) state: "Cases which show an acute onset—for instance the katatonic group—have generally been supposed to have a better prognosis than those developing insidiously, but although this may hold true for the majority, it is no absolute criterion. We have seen cases of very acute onset who, far from showing signs of improvement, exhibit a gradual deterioration." Acute onset is also considered favourable by Meyer (E.) (1903).

The Relationship of Group Symptoms to the Subsequent Course.

It has long been the habit to classify schizophrenia according to its acute symptoms into the simple, hebephrenic, catatonic and paranoidal subdivisions, and many efforts have been made to assess the prognostic outlook of each of these divisions.

It may be well to consider for a moment what is meant by these sub-groups. Bleuler (1936) introduces the subject in the following manner: "Although schizophrenia is probably not a homogeneous disease, we are not yet able to divide it into natural subdivisions. Nevertheless, in order to direct oneself in the external forms of the constantly changing morbid picture, four forms have been distinguished according to the presence or absence of definite symptom groups. They are not nosological units and from patient to patient and in the same patient pass over into one another, so that a schizophrenic may be admitted into the asylum for example as a hebephrenic, may remain there for years as a catatonic and may finally be released as paranoid. But most patients remain permanently in their own group."

Simple schizophrenia.—Kraepelin, basing his symptomatology on the original one of Diem (1903), graphically labels its characteristic as " an impoverishment and devastation of the whole psychic life which is accomplished imperceptibly." There is gradual intellectual impairment, so that the early promise of many patients fails to materialize and is replaced by a blight which gradually leads to an increasing inefficiency at work, reducing the sufferer's capabilities to those of simple routine life, sometimes just sufficient to support him in earning his living, but very frequently leading to such a degree of vegetation as to need mental hospital care. As to temperamental changes, Kraepelin says: " Hand in hand with this decline of mental activity there is a change of temperament which often forms the first conspicuous sign of the developing malady. The patients become depressed, timid, lachrymose, or impertinent, irritable, malicious; sometimes a certain obstinate stubbornness is developed. The circle of their interests becomes narrower; their relations to their companions become cold; they show neither attachment nor sympathy; not infrequently a growing estrangement from parents and brothers and sisters becomes noticeable." No delusions or hallucinations or symptoms of catatonia are mentioned by Kraepelin as being present. Bleuler (1936) says: " Where only the *basic symptoms* are visible, we speak of schizophrenia simplex. It is usually a case of a dementia in the sense of schizophrenia that increases gradually in the course of decades." (For details of the basic symptoms the reader is referred to Bleuler's description in his *Text-book of Psychiatry* [1936].)

Kraepelin (1919) refers to its course thus: " The development of this clinical picture invariably takes a series of years. It may stand still for a shorter or longer time, but, on the other hand, it may occasionally experience a more sudden exacerbation. . . . When the disease comes to a standstill it may mean a final though incomplete recovery, but sooner or later the morbid process may again progress . . . . A really profound dementia without fairly acute exacerbations and with continuous, if only slowly progressive, development of the malady does not seem to occur; on the contrary, a dementia simplex which lasts for many years, even for decades, forms often enough the introduction to one of the forms of dementia praecox which goes on to profound dementia." The prognosis in this group may be considered to be normally quite good as regards arrest of the process before profound dementia, but bad as regards recovery.

Hebephrenia was first described in 1871 by Hecker. The characteristics of his syndrome were an onset in early adult life associated with various emotional and affective changes and peculiarities in behaviour, described by Hecker (1871) (quoted by May (1932)) as follows: " The disease begins in the majority of cases apparently as the result of a profound emotional alteration with the various symptoms of melancholia, which soon finds its expression in a vague, indefinite sadness and emotional depression and is then gradually mixed with definite but very changeable delusional ideas. Almost all phases of the

emotional life may, one after another, become involved in the depressive mood, and the melancholia may express itself in contrite self-accusations, sentimental and amorous fancies, or finally in dull brooding ideas of persecution and injury. At the same time, there is soon shown a great superficiality of feeling, and the picture of this melancholia is very different from the pictures of misery shown, for instance, in genuine dysthymia. It often seems as if the patients play or toy voluntarily with their melancholy feelings, and soon a more cheerful mood appears in contrast with the sadness. After an absorption in the awful tragedy, the misfortune which has befallen him, or a lamentation over the sins which he has committed, and the persecution inflicted upon him, the patient often cannot repress a tendency to laugh and make foolish jokes. Then appears an increased tendency to a peculiar activity which may develop into an outspoken expansive mania. As a rule it manifests itself in an aimless, objectless, foolish conduct, in a tendency to tramp life and wandering about, and such individuals may get along in the world for a long while without being recognized as abnormal."

Kraepelin (1919) remarks on the fantastic and bizarre nature of hebephrenic delusions, which involve frequently amazing ideas of bodily change, described thus: "Their morbid sensations sometimes assume the most nonsensical forms. They have no brain any longer. Their back is broken in two; their blood has been taken from them; their body has died; their legs are exchanged. A female patient thought that she had the Kaiser in her stomach, every human being in her body, a telephone, small dolls and a bicycle in her head, that she had a wooden head and that five 'people had been made out of her.'"

Henderson and Gillespie emphasize that this form occurs earlier than the catatonic or paranoid types, and state: "It is characterized by great incoherence of thought, marked emotional disturbance, periods of wild excitement alternating with periods of tearfulness and depression and frequently illusions and hallucinations. . . . The most prominent symptoms are the incoherence in the train of thought, the strange, impulsive senseless conduct and the vivid hallucinations." They say that this type is very difficult to differentiate because often in it there are some symptoms pertaining more to catatonia and others to a paranoid reaction.

Bleuler, on the other hand, states, regarding the typical picture already described by Hecker, "We can also find these symptoms in symptoms of other varieties that break out late," and goes on: "In the present conception of hebephrenia, the age of onset is unimportant, even though most of the cases become sick soon after puberty. It now constitutes the big trough into which are thrown the forms that cannot be classed with the other three forms."

Catatonic group.—Kahlbaum (1874) first described catatonia as a disease having certain definite somatic symptoms in association with psychical changes. Kraepelin, recognizing the tendency of this disease to terminate in dementia, included it to form one of his sub-groups of dementia praecox. Henderson

and Gillespie (1936) say: "Katatonia is usually described as an alternating state characterized by a stage of depression, a stage of excitement and a stage of stupor. . . . We would reserve the name katatonia, as Kraepelin does, for those cases in which are seen the conjunction of peculiar excitement with katatonic stupor."

Bleuler (1936) says: "If catatonic symptoms are permanently in the foreground, the picture is called catatonia. A large part of these forms begins with an acute attack; under certain conditions the psychosis is revealed from one moment to another—other cases begin with a chronic attack with some catatonic peculiarities (e.g. mutism or mannerisms) and remain chronic, while in others chronic and acute conditions alternate. Following acute catatonic attacks a tolerable condition may again recur; the cases that begin furtively all have a bad prognosis without remissions that are worth mentioning."

The catatonic symptoms may be listed as: (1) catalepsy; (2) stupor; (3) hyperkinesis; (4) stereotyped expressions, movements, attitudes, speech (verbigeration), thoughts, wishes or hallucinations; (5) mannerisms; (6) negativism; (7) command automatism and echopraxia; (8) automatism (including compulsive phenomena); (9) impulsiveness.

Henderson and Gillespie (1936) emphasize the emotional side of the picture. There is no doubt that this type of schizophrenic reaction develops much more acutely than other types. Kraepelin himself says that 41 per cent. of such cases tend to develop acutely, 31 per cent. insidiously and others subacutely.

Paranoid group.—Bleuler (1936) says: "Where delusions and hallucinations are in the foreground one speaks of the paranoid type or dementia paranoides. The paranoid type can develop after any melancholic, manic or catatonic acute initial onset, or can begin immediately as such. In the latter case the entire course is, as a rule, chronic throughout." Regarding paraphrenia he says: "Kraepelin attempted to separate from the paranoid forms of schizophrenia, as a special morbid group, those in whom the personality was better retained, and whose feelings, will, and the external behaviour are directly slightly changed; the incorrect actions are determined by delusions. . . . A diagnostic differentiation of the paraphrenias from the other acute or chronic mild paranoid forms was never possible. Moreover our investigations, as well as the course and heredity, show the definite relationship of most, if not all these cases, to the schizophrenias."

Henderson and Gillespie (1936) define the paranoid types as follows: "The paranoid types tend to develop at a later period of life than other forms. The patients affected are usually between 30 and 35 years old. The delusions which are expressed are multiple, unsystematized and changeable, usually of the most fantastic and illogical course and accompanied by hallucinations. These ideas may be of any type: they may be persecutory, depressive or grandiose." They definitely group the paraphrenias with paranoia into a

group which they call "paranoid reactive types"—quite distinct from schizophrenia.

The above short discussion of symptomatology serves to illustrate that there is obvious room for considerable divergencies of opinion regarding the interpretations of the criteria by which a case is labelled as belonging to a definite group. For instance, if one agrees with Bleuler that hebephrenia is a last refuge for all cases not in the other three groups, one will include many cases that might be considered by others as not belonging to this group. In the former case there will appear to be no need for a fifth group, whereas in the latter there seems justification for a fifth "unclassified" group. Again, according to Bleuler's ideas, many cases will be included in the paranoid group which would be excluded as paraphrenias by those supporting the ideas expressed by Henderson and Gillespie.

The matter is certainly rendered no easier when one remembers that Kraepelin's final opinion as revealed in his eighth edition favoured ten subdivisions: (1) Dementia simplex, (2) silly dementia, (3) simple depressive dementia, (4) delusional depressive dementia, (5) circular dementia, (6) agitated dementia, (7) periodic dementia, (8) catatonia, (9) the paranoid dementias (gravis and levis), (10) confusional speech dementia. One finds, moreover, that Bleuler's typical cases are described under such headings as (*a*) catatonic state, (*b*) depressive catatonia, continuous hearing of voices, (*c*) manic catatonia, (*d*) catatonia with religious delusions, (*e*) hebephrenia with manic and depressive attacks, (*f*) depressive hebephrenia, etc.

The actual figures computed to show the percentage of remissions in the various groups are comparatively few and far between. The following may be quoted:

Catatonia.—Kraepelin (1919) reports recovery in 13 per cent. of his catatonic cases, and reports that Mattauschek found "recovery with defect" in 13·8 per cent. of his "catatonic forms." The number of cases dealt with is not stated in either case. Kahlbaum (1902) found in 29 cases, 9 (33 per cent.) completely cured and 7 (25 per cent.) cured with defect. Meyer, E. (1903), claimed that of 26 cases, 14 (30·4 per cent.) were cured, 11 (23 per cent.) cured with defect and 21 (45·6 per cent.) not improved or worse. Of Raecke's (1900) 171 cases, 27 (15·8 per cent.) "were practically cured" and 19 (11·1 per cent.) "improved." Strecker and Willey (1927) found that out of 45 cases of the catatonic type 18 (or 40 per cent.) recovered, but by "recovery" is probably meant "recovery with defect," since elsewhere Strecker says: "I think I would agree that absolute recovery in the sense of restitution does not occur." Bellinger (1932) finds that out of 37 cases of catatonia discharged during a period of ten years (1920 to 1928) inclusive, 9 adjusted themselves to external conditions for a period of over five years, of whom "six seemed to have recovered, while three adjusted themselves to a somewhat sheltered

environment and may be said to have made a social recovery or recovery with defect."

Paranoid forms.—Kraepelin (1919) says that "paranoid forms probably never issue in complete recovery," but quotes Albrecht as finding a few recoveries, and Mattauschek as having 11·1 per cent. of recoveries with defect in his "depressive paranoid form." Strecker and Willey (1927) found recovery (of the quality already discussed with reference to catatonia) in 12 out of 85 cases, or 14·1 per cent. Whitehead (1937) found 8 per cent. of recoveries and 25 per cent. of improved cases. Coles and Fuller (1909) found improvement in 20·8 per cent. of cases.

Hebephrenic type.—Kraepelin's (1919) figures of recovery in this group is 8 per cent. and he quotes the following figures by other authors: Mattauschek, 2·3 per cent. recovery, 9·3 per cent. recovery with defect; Albrecht, no real recovery, 12·5 per cent. recovery with defect; Evensen, 5 per cent. remained independent, 25 per cent. at least still capable of work, and 70 per cent. profoundly demented. Strecker and Willey (1927) found recovery in the sense already described in 8 (16·3 per cent.) out of 49 cases. Whitehead (1937) rates recovery at 14·3 per cent. and improvement at 20·6 per cent. Coles and Fuller (1909) found 20·8 per cent. improved.

The simple form.—The outlook in this type has already been described. I have found no figures which show recovery in this type of the disease, although deterioration tends to be slower in progress and less in degree than in any of the other groups.

The above observations show that although one may speak of general tendencies for cases in each subdivision to progress in a certain way, the variation in opinion regarding the exact criteria differentiating one group from another and one degree of improvement from the next makes exact conclusions impossible.

The continental school of Mauz and Kretschmer, imbued as they are with the importance of "process" symptoms, endeavour to estimate the prognosis of the acute phase by the degree of incidence of these symptoms. Thus Langfeldt (1937) divides symptoms of the acute phase into the following groups: (I) Dementia paranoides, (II) paranoid-katatonic mixed cases, (III) typical katatonia, (IV) cases of a hebephrenic nature, (V) atypical symptomatology of the acute phase of the psychosis; and further complicates matters by dividing the dementia paranoides into three subdivisions.

Mauz (1930) has divided the schizophrenias into two groups, according to the course they take: (*a*) catastrophic, (*b*) episodic. The catastrophic cases pursue a course rapidly deteriorating to dementia. The episodic proceed downwards by a staircase series of acute outbreaks, leaving the patient more deteriorated each time. He describes a new subdivision of cases which he calls the "schizokar" form, and in which there are abundant "process symptoms"

right up to the period of dementia, and in which a catastrophic source is invariably the order of the day.

These new efforts to sift the corn from the chaff do not appear to clarify things from the point of view of British psychiatrists, but, on the contrary, to make them much more difficult, so that a passing allusion is all that one need make here.

The Duration of Psychosis.

The importance of this aspect of the subject has come to the fore with the claim that the new treatments (insulin and cardiazol) produce their most dramatic effects on cases of under six months' duration, and then tail off rapidly until comparatively few cases of over two years' duration show marked benefit. It has been shown, however (as might be expected), by Hunt, Fieldman and Fiero (1938), Taylor and von Salzen (1938), Duncan Whitehead (1938) and others, that a similar state of things exists in cases not treated by these methods, namely, the longer the existence of the psychosis before improvement and cure, the less the chance of these occurring.

Individual Mental Symptoms.

Much has been written regarding the prognostic significance of various individual symptoms, but here again conclusions beyond broad principles have not been reached. The great importance attached to the " process " symptoms by continental psychiatrists has already been explained and stressed, and it would seem well worth while for psychiatrists of other schools to concede at least the very unfavourable nature of such symptoms.

Kraepelin (1919) states, " On the whole the prospects will be more unfavourable the more those peculiarities are developed which we see in the foreground in the multitude of cases finally uncured," and enumerates the following: " Among them there is especially the loss of emotional activity which characterizes the most severe forms of the disease, those that issue in dull dementia ; with it the connecting link falls away which unites rational action to perception and thought. Furthermore the development of fixed mannerisms and stereotyped movements is apparently to be regarded as an unfavourable sign ; they are a sign that the influence of healthy volitional action and inhibition on activity is no longer strong enough to suppress side-impulses and the tendency to repetition. Of specially bad significance is the appearance of simple rhythmical movements ; they seem only to occur when through very deep-reaching destruction of the volitional apparatus lower ancestral motor mechanisms acquire a certain independence. Lastly, the states of excitement and moodiness occurring periodically and abruptly are probably also of evil significance, as they very frequently make their appearance in the incurable

terminal states. These also might indicate that the equilibrating mechanisms were disordered, which otherwise make the psychic life to some extent independent of the fluctuations of bodily conditions.

" We come therefore to the conclusion that the onset of incurable terminal states is announced chiefly by those disorders which signify the loss of mastery over volitional action, be it that the mainsprings of volition are broken, be it that the mechanisms are destroyed which make systematic co-operation of individual volitional actions possible. I would ascribe much less importance to pure disorders of intellect. They appear in general to be further removed from the point of attack of the morbid process, and therefore not so soon to signify incurable phenomena of decay. Not only may hallucinations and nonsensical delusions be again completely lost, but also incoherence of the train of thought, and indeed even marked confusion of speech. Only when with continuance of these disorders emotional activity also gradually disappears is one obliged to consider the hope of equilibrium being restored as very slight."

Meyer, E. (1903), emphasized the unfavourable significance of stereotypy. Raecke (1910) expressed doubt as to the evil significance usually imputed to such symptoms as apathetic personality, uncleanliness, loss of sense of shame, hallucinations of the lower senses—smell, taste and verbigeration—but tentatively agreed that grimacing with inveterate negativism, command automatism and persistent flexibilitas cerea were of bad prognosis.

Hoffmann (1919) wrote a monograph in which he deals with the significance of various individual symptoms and gives a copious bibliography concerning them. Forel (1931), among others, points out the occurrence of delusions to be of little significance from a quantitative point of view, but of considerable consequence from a qualitative one. If the delusions find their source in recent conflicts, or can co-exist with a grip on reality, the outlook is favourable compared with that for the bizarre and non-systematized delusions frequently seen.

The presence of manic-depressive features has been recognized by many writers as prognostically favourable. These writers include Kretschmer, Mauz, Langfeldt, Raecke and Kirby.

Lewis (1935) says that the nature of the symptoms is a very poor guide to the sequel: " . . . It is almost true to say that the only important symptoms in this regard are those which indicate that the illness has already been present a long while and that behaviour and modes and affective response are narrowed and more or less fixed." In the latter respect he instances stereotypies of movement or speech, long-drawn-out stupor with negativism, impulsive violence, muscular tension or vasomotor changes.

Summarizing articles of this aspect of prognosis have been written from various points of view by Muller (1935), Lewis (1935), Forel (1931) and Schaeffer (1938).

SUMMARY.

An eclectic view of our present state of knowledge according to a survey of the literature may be summarized thus :

(1) *Constitutional Factors.*

(a) *Heredity.*

The incidence of schizophrenia in (i) a uniovular twin sibling or (ii) both parents, on the rare occasions when it does occur, must be considered as prognostically very serious. Where it occurs in one parent and in the grandparents on the other side the prognosis must be considered as probably bad, and its presence in a large number of collaterals or siblings renders the outlook dubious (although frequently ominous for the patient).

(b) *Age*

is of greatest importance when considered in relation with the types of schizophrenia, the hebephrenic and simple types coming on earliest, the catatonic type later, and the paranoid later still. Apart from any indications from the type picture, the earlier cases are supposed to have a better prognosis than later ones (except in cases with exaggerated pathogenic symptoms apparently unrelated to exogenic factors (cf. Mauz's schizokar type), which usually have a catastrophic course).

(c) *Sex.*

Conclusions in this respect are dubious, although the prognosis is thought by many to be more favourable in the female than in the male sex.

(d) *Bodily build.*

The pyknic type of build is always to be considered as a favourable factor and the asthenic (leptosomatic) type unfavourable. It must be remembered that many people are of an indeterminate build, and not much significance should be attached to any except the extreme types.

(e) *Temperament.*

An extraverted (or cyclothymic) temperament is favourable, an introverted or schizoid one unfavourable. Again there are many temperaments which must be considered as indeterminate, and only very definite types should be considered as really significant.

(f) *Pre-psychotic personality.*

The previous reactions of the individual to various problems and difficulties of life is of considerable importance. A history of having dealt with these directly and confidently is favourable, whereas one of hedging, dodging the issue, and taking refuge in indulgence in phantasy and dereistic thinking is of sinister significance.

(g) *Sexual history.*

Most schizophrenics have a history of sexual maladjustment of some type, but beyond their effect as producers of conflict, no prognostic significance is really known.

(h) *Education and abilities.*

No prognostic significance can be attached to these. A type which often does badly is the brilliant scholar who has a schizoid temperament.

(2) *Symptoms.*

(a) *Exogenic factors.*

The presence of a definite and obvious exogenic factor is usually favourable.

(b) *Speed of onset.*

The insidious onset is usually prognostically unfavourable compared with the more rapid and acute type.

(c) *Sub-divisions.*

Owing to the tendency for symptoms sometimes to shift from one acute manifestation to another (Bleuler, 1936) prognostic assessment may be difficult in early cases. Of the cases that remain progressively in one group, the catatonics have the best outlook as regards recovery, the hebephrenic next and the paranoidal the worst. As regards intensity the order is the reverse. Variation of individual outlook in diagnosis renders conclusions dubious. Many cases are indeterminate, and it is only the very definite cases in which this prognostic significance is at all valid.

(d) *The presence of process symptoms*

in the sense already described would appear to be prognostically of unfavourable significance, in proportion to the degree of their manifestation.

(e) *The duration of psychosis.*

Speaking generally, the longer the duration of the psychosis, before recovery or improvement, the less the chance of this occurring.

(f) *Individual mental symptoms.*

The presence of manic-depressive symptoms is prognostically favourable in proportion to the quantitative degree in which they present themselves. Delusions are of little significance from a quantitative point of view, but considerably so from the qualitative one. If the delusions find their source in recent conflicts or can co-exist with a grip on reality, the outlook is comparatively favourable. Prolonged existence of stereotypies, grimacing, flexibilitas cerea, negativism and command automatism are to be considered unfavourably.

PART II.

A Katamnesic Follow-up of 120 Male Cases of Schizophrenia Admitted Consecutively to Cane Hill Mental Hospital during the Years 1933–1937 inclusive.

As was pointed out in the introduction to this thesis, this study of prognosis in schizophrenia was undertaken from two different angles: (1) A detailed survey of the literature on the subject; (2) a personal follow-up of cases with the purpose of effecting any correlation possible with the findings in the literature, and of noting any outstanding features that might be of importance to the subject as a whole.

The Material.

It had originally been intended to follow up all male and female cases over a period of ten years. Owing to the lack of adequate social histories in the earlier years (there was no fully-trained hospital social worker as there is now) it was decided to limit the period to the five years 1933 to 1937 inclusive. Such a large proportion of discharged female cases were untraceable that any conclusions regarding this sex were rendered impossible, and it was deemed preferable to omit them altogether. Thus I was finally left with all schizophrenic male patients admitted to Cane Hill Mental Hospital from 1933 to 1937 inclusive. All transfer cases were included in this series, as it was considered unjustifiable not to do so if an accurate history of the whole group were to be obtained. Patients who had a history of having been in a mental hospital previously (in other words, "readmissions" or "relapses") were also all included, as relapses are a constant feature of schizophrenia and their inclusion was desirable to obtain a representative picture of the whole.

Only one other point of selection was used, namely, the exclusion of all cases over 45 years of age on admission. This was done because the comparative rarity of schizophrenia in late age would render its possibilities of any real effect on the figures so remote that the extra work involved in diagnosis did not seem warranted.

The object of this follow-up was to ascertain the histories of all cases

both before and after admission and their final condition on December 31, 1938. With this in view, the following questionnaire was addressed to the nearest relatives of all the patients discharged during the fixed period :

1. Is the patient still alive ? If not, when, and from what causation, did he die ?

2. Has the patient ever been in any other mental hospital or institution since his discharge ? If so, give the names of the hospitals concerned, and the periods of residence in each.

3. Give a history of the patient's mental state since discharge.

4. Give a history of the patient's present mental condition.

5. Give periods of employment and unemployment since discharge, stating what form employment took.

This questionnaire was further substantiated by the visit of the hospital social worker (fully trained and qualified in this specialized work) to the homes of all patients within Greater London about whom satisfactory answers to the questionnaire had not been obtained, and a report was produced by her of all the information obtainable.

The histories of those patients who had been transferred to other hospitals was obtained by requests to the Medical Superintendents of the various hospitals concerned for a report on the patient's progress. When the patients were reported as discharged from the hospital to which they had been transferred, the address of the relative or friend to whom they had gone was obtained, and a special letter was sent, inquiring after their subsequent progress. Where the patients had been in a mental hospital previously, or had attended one of the out-patient clinics, the hospitals or clinics were communicated with, and details obtained of the patient's condition and progress during his connection with the hospital concerned.

Diagnosis.

The question of diagnosis was simple in all cases who had been under observation for a reasonable duration. Any difficulty that did arise was associated with cases of comparatively short stay in hospital. The well-known possibility of mis-diagnosis in early cases was overcome by including in the follow-up all cases of so-called confusional insanity and manic-depressive psychosis. By doing so it was possible to make sure that any cases who in their early stages might be diagnosed as these psychoses, with ultimate maturation into schizophrenia, would not be left out of the series.

The criteria on which the diagnoses were made were those common to most British psychiatrists. The fundamental symptoms and signs were those generally recognized, and the attitude in general was eclectic. Any case in which there was doubt as to the diagnosis was excluded. Paraphrenias or delusional insanities, which are included by Bleuler among the schizophrenias, were not included. The continental division into typical and atypical schizo-

phrenias is not used in this part of the world and was not introduced as an innovation here. Probably my outlook, which, to the best of my knowledge, is representative of the majority of psychiatrists in this country, may be best summed up as a cross between the " reaction formation " ideas of Adolf Meyer and Bleuler's more general conceptions of the psychosis.

Regarding the subdivisions, the commonly recognized criteria of the catatonic, paranoid and simple types were used. Hebephrenia was used in the sense of an entity of its own as described by Hoch and Kraepelin, and not as a backwater for the acceptance of all cases not fitting into the other groups, as conceived by Bleuler. An " indeterminate " group was also included, as I considered that there is always justifiable reason for doing so when considering a large number of cases.

The Scope and Limitations.

I am fully aware of certain deficiencies in this undertaking. (1) First, there are those shortcomings of all questionnaires, namely, inadequate and inaccurate observations of those to whom they are addressed. In this case these deficiencies were probably less marked than is usual, and when they did occur, they tended to do so in the favourable rather than unfavourable direction. Moreover, in a large proportion of such responses matters were cleared up by establishing personal contact with the addressees through the agency of the hospital social worker.

(2) Where patients are to be classified into such groups as " improved " or " much improved," etc., there are always a few borderline cases in which the information obtainable leaves some doubt as to which subdivision the patient should be apportioned to. In all doubtful cases I deliberately tended to the favourable as opposed to the unfavourable side of the question.

(3) Personal examination of all discharged cases was impracticable owing to the large distances from the hospital that most of them had dispersed to.

(4) The criticism might be levelled that the records of diagnosis and progress of the various patients and the reports from outside hospitals were the work of many men and open to excessive discrepancies. Had this been a question of detailed observation the criticism might have held good, but the fact that the investigation dealt with certain salient features only practically obliterated any such possibility, and the information obtained regarding these patients can be said to have almost always been valid.

The Results of the Investigation.

In classifying the condition of patients, those divisions used by Hunt, Fieldman and Fiero (1938) are employed (see p. 403).

This classification is not adopted because I think it necessarily the best in all circumstances, but because I consider it the most suited to the matter in hand. One of the biggest mistakes in psychiatry is over-classification, and

apparent glorification in divisions and subdivisions. This classification has the virtue of comparatively few groups, and the criteria of each group fit in, broadly speaking, with the most important aspects of the question from the social point of view, namely, the number of patients who (1) recover sufficiently to carry on at their old employment; (2) improve sufficiently for discharge to sheltered surroundings, having retained obvious residual symptoms; (3) have to remain permanently in a mental hospital.

The fact that no "recovery" group is included does not mean that I consider that "recovery" (in the sense used by Muller (1937) implying complete disappearance of symptoms, full insight, normal affective activity and ability to return to usual professional work) does not occur; but that in this series, owing to lack of opportunity of personally examining the discharged patients, the occurrence of "recovery" as opposed to "much improved" could never be certain, and I agree with Hunt, Fieldman and Fiero (1938), and Lewis and Blanchard (1931), that differentiation between these two classes is a difficult task at the best.

Most authors of such a follow-up as this content themselves with representing their results in the form of tables, but these all too frequently give a very one-sided impression, the matter being considered from one angle only, or one particular aspect of the subject being emphasized at the expense of the others. For instance, many articles have been written dealing with cases admitted over a large number of years, assessing their condition comparatively soon after the latest admission. The result is that some cases have been followed up for several years longer than others, but notwithstanding this, their conditions are lumped together as equivalents in a table of remission rates, without any mention being made of the period over which each case has been surveyed, and without details being given of the history intervening between admission and the date of the follow-up.

It has been my object in this thesis to produce tables which will view the matter from all angles, leaving no stone unturned to get a thorough and correctly proportioned knowledge of the picture as a whole. The following tables it is to be hoped will give an accurate and unprejudiced idea of the true state of affairs.

Table A represents the fate of the 120 cases as shown by their condition on December 31, 1938.

Table B gives the number of cases admitted each year, the number of these subsequently discharged, their condition on discharge and their condition on December 31, 1938.

Table C shows the condition of the patients at six-monthly intervals following their admission to Cane Hill.

*Graph A** completes the picture by representing the whole history of each patient from the time of admission to any mental hospital. The maximum

* Owing to cost, it was unfortunately not possible to reproduce this.

period is limited to ten years in order to keep the graph within reasonable limits. There are one or two patients whose history extends over a slightly longer period than this, but the extra period has been cut out. The material for this graph includes, as already stated, all readmissions, and in this instance obviously dates from their first admission to any mental hospital, not necessarily Cane Hill. Even now the picture is not complete, as there remains the time before admission to any hospital during which symptoms prevailed. This aspect of the question is tackled under the next section—see Table E.

Table D indicates the present condition of the patients still in mental hospitals.

Symbols used in Tables A, B, C, and D.

Ad. = Admissions.
Disch. = Discharges.
M.I. = Much improved.
I. = Improved.
U.I. = Unimproved.
D. = Dead.
N. = Not employable.

For definitions see text, p. 403.

N.T. = Not traced.
M.H. = In a mental hospital.
W. = Condition worse than on admission.
O. = In an observation ward.
F. = In an open (free) ward.
E. = Employed.

TABLE A.—*Showing the Condition on December 31, 1938, of 120 Consecutive Cases of Schizophrenia Admitted to Cane Hill Mental Hospital during the years 1933 to 1937 inclusive.*

Number of cases admitted 1933–1937.	Condition of cases on December 31, 1938.						
	M.I.	I.	U.I.	D.	N.T.	Discharged.	M.H.
120	8 (6·6%)	11 (9·1%)	83 (69·1%)	6 (5%)	12 (10%)	15 (12·5%)	87 (72·5%)

TABLE B.—*Showing the Conditions of the same 120 Cases (as Table A) at the Time of their Discharge and on December 31, 1938, in Yearly Groupings.*

Year.	Number of cases.		Condition at discharge.			Condition on December 31, 1938.					
	Ad.	Disch.	M.I.	I.	U.I.	M.I.	I.	U.I.	D.	N.T.	M.H.
1933	22	7	2	5	0	1	2	1	0	3	1
1934	30	13	4	5	4	2	2	2	0	7	2
1935	30	9	5	4	0	3	3	2	0	1	2
1936	16	9	2	6	1	2	3	4	0	0	3
1937	22	5	2	1	2	0	1	3	1	0	2
Total	120	43	15	21	7	8	11	12	1	11	10
			43			43					

TABLE C.—*Representing the Mental Conditions of the 120 Patients (as Table A) at Six-monthly Intervals following their First Admission to a Mental Hospital.*

Period after first admission to a mental hospital.	Number of cases traced.	Condition at the end of the period.				
		M.I.	I.	U.I.	D.	N.T.
6 months	111	5 (4·5%)	3 (2·7%)	2	0	1
1 year	107	8 (7·4%)	7 (6·5%)	2	1	5
1½ years	102	9 (8·8%)	9 (8·8%)	3	2	0
2 ,,	93	8 (8·6%)	10 (10·7%)	2	0	3
3 ,,	52	6 (11·5%)	8 (15·3%)	2	2	1
5 ,,	29	2 (7·8%)	3 (10·3%)	0	0	1
7 ,,	10	0 (0%)	1 (10%)	0	0	0

TABLE D.—*Showing the Condition of the 84 Hospitalized Patients still in Cane Hill Hospital on December 31, 1938.*

Number of cases.	M.I.	I.	Unchanged.	W.	O.	F.	E.	N.
84	0	5	28	54	52	35	51	36

Scrutinization of these tables reveals a sad picture indeed. It is seen that the percentage of cases showing much improvement (6·6 per cent.) and improvement (9·1 per cent.) falls far below the average quoted in the literature, and indeed savours more of the fate implied in the name "dementia praecox" than that of schizophrenia. If the matter were to end with a mere publication of these remission rates it might well be said that still more divergence had been added to a field of complete asymmetry. The fact of the discrepancy is obvious, and if it is not to be considered a veritable torpedo of my conclusions from a search into the literature regarding remission rates, it requires adequate explanation. This is to be found in an assessment of the prognosis of each individual case according to the significance of the various specific factors, and acts as a strong vindication of my claim that the publication of figures of remission rates without ample indication of the prognostic outlook in the material considered is practically valueless.

It is not intended here to try and prove or disprove the prognostic significance of various individual signs and symptoms. The limitations of the scope of the katamnesic follow-up already referred to would render this unfeasible. On the contrary, my object at this point is to review each of the 120 cases in the light of conclusions reached in Part I of this thesis and see whether, if such a procedure had been adopted prior to the compilation of the above figures (Tables A, B, C, and D), it would have indicated that such poor results were to be expected. To accomplish this I decided to consider and assess each case with regard to the following points: age, duration of psychosis prior to admission to this hospital, hereditary factors, bodily build, temperament, pre-psychotic reaction, rapidity of onset, symptomatology of the acute phase, course of psychosis, present condition. It seemed to me that there would be little purpose in presenting case histories of all the cases, as has been done by some authors in works of this kind (cf. Langfeldt (1937)). The results of this investigation are therefore represented in tabular form in Table E. This makes possible a rapid comparison of a large number of cases. Many authors of such comparisons as these lose sight of the significant features in a labyrinth of detail. In presenting the accompanying table (Table E) I aimed in my classification at representing salient features at the expense of detail, and used as few gradings as were essential for this purpose. These are given herewith. A blank was left where there was doubt as to assessment.

(1) *Heredity.*

Attention was paid to the existence of mental disease and tuberculosis in relatives. The difficulties of finding out the particular mental disease from which each relative suffered were prodigious, and I decided to content myself with recording the presence of mental illness in known relatives, without details of the type of psychosis entailed. I included besides psychoses the presence of tuberculosis in the family, since the association of these two diseases is so well recognized and is probably of significance in respect to prognosis.

(2) *Bodily build.*

It was only possible to obtain details of bodily build in those patients still resident in this hospital. Assessment was made on an impressionist rather than on an anthropological basis. Four types were used: (i) the asthenic, (ii) the athletic, (iii) the pyknic, (iv) the indeterminate. Only cases with well-marked features establishing their type beyond doubt were included in the first three groups, the rest being placed in Group IV.

(3) *Temperament.*

Schizoid, cycloid, psychopathic, indeterminate and normal temperaments were described. The terms "schizoid" and "cycloid" are used with the usual meanings. Psychopathic is used for the temperament of a psychopathic personality. Indeterminate refers to cases where the facts ascertained do not make it certain which abnormal group should be used. Normal refers to a temperament whose traits occur within the bounds of so-called normality.

(4) *Pre-psychotic reactions.*

The subdivisions of this item were made on purely arbitrary grounds into (1) good, (2) fair and (3) poor reactions, the allotment being made by my personal judgment on having ascertained as much as possible of their past history. It was quite often necessary to leave this column a blank owing to insufficient evidence.

(5) *Rapidity of onset.*

Acute, sudden, gradual and insidious modes of onset are described.

Acute = those cases in which symptoms are severe and appear from the blue within a few days of admission.

Sudden = cases in which relatives had noted moderately severe symptoms for only a few weeks before admission.

Gradual = cases in which relatives had noted symptoms becoming progressively worse for months and years before admission.

Insidious = those cases in whom the symptoms have been of such a pernicious nature as to have escaped notice until the psychosis is fully developed and then been recognized by retrograde inspection.

TAB

1. Serial No.	2. Status.	3. Date of admission.	4. Age on admission.	5. Duration of previous history.	6. Previous hospital treatment.	7. Heredity.	8. Bodily build.
1	T.	13.i.33	33	6 m.	—	Mother died in M.H.	?
2	D.	14.i.33	30	?	—	*Nil*	?
3	C.	20.i.33	23	4 m.	—	,,	Ind.
4	C.	31.i.33	36	4 y.	—	?	Asth.
5	C.	14.iii.33	27	2 y.	M.H. Readm.	*Nil*	,,
6	T.	24.iii.33	31	24 y.	—	,,	?
7	D.	26.iv.33	20	5 w.	M.H.	,,	?
8	C.	1.vi.33	36	3 y.	,,	,,	Ind.
9	V.D.	1.vi.33	26	2 y.	,,	—	?
10	T.	18.vi.33	18	?	—	Mother died of T.B.	?
11	C.	22.vi.33	31	4 y.	M.H.	*Nil*	Asth.
12	C.	23.vi.33	20	?	?	?	,,
13	C.	28.vi.33	31	?	?	?	,,
14	C.	4.vii.33	26	2 y. ?	?	Mother in M.D. hosp.	?
15	C.	10.viii.33	31	7 y.	M.H.	*Nil*	Ind.
16	C.	12.viii.33	23	2 d.	—	?	Asth.
17	C.	19.ix.33	31	4 y.	M.H. (c.)	*Nil*	Ind.
18	T.	30.ix.33	30	9 y.	M.H.	Aunt M.H.	?
19	C.	5.x.33	30	3 y.	—	*Nil*	Ind.
20	C.	14.x.33	32	1 m.	?	?	Asth.
21	T.	28.x.33	20	1 y.	M.H. (V.)	Mother died T.B.; uncle had T.B. at 18	?
22	C.	2.xii.33	20	2 m.	M.H. (c.)	Mother in M.H.	Ind.
23	D.	25.i.34	23	1 m.	—	Father, 2 siblings and self T.B.	?
24	D.	30.i.34	34	3 y.	—	*Nil*	?
25	T.	16.ii.34	27	2 y.	—	Mother died T.B.; twin brother T.B.	?
26	X.	27.ii.34	26	?	—	Case paper lost—patient de	
27	C.	22.iii.34	17	?	—	*Nil*	Asth.
28	C.	5.iv.34	26	1 y.	—	?	Ind.
29	T.	12.iv.34	29	?	—	?	?
30	D.	3.v.34	23	10 d.	—	?	?
31	D.	8.v.34	29	5 y.	—	?	?
32	D.	18.v.34	22	2 y.	—	?	?
33	D.	24.v.34	23	?	—	*Nil*	?
34	C.	30.v.34	21	6 m.	M.H. (c.)	,,	Ind.
35	D.	31.v.34	26	3 y.	—	Mat. aunt insane, —M.H.	?
36	C.	6.vi.34	20	11 m.	O.P.	*Nil*	Asth.
37	C.	28.vi.34	26	14 d.	?	,,	Ind.
38	C.	5.vii.34	34	7 y.	M.H. (c.)	?	Asth.
39	C.	10.vii.34	31	1 y.	M.H.	?	,,
40	D.	21.vii.34	16	18 m.	,,	?	?
41	C.	25.vii.34	35	3 y.	,,	?	Asth.
42	C.	27.ix.34	17	6 m.	?	Grandmother died T.B.	,,
43	C.	18.x.34	29	5 y.	O.P.	*Nil*	Ind.
44	D.	18.x.34	28	10 m.	?	Grandmother died T.B.	?
45	C.	24.x.34	34	7 y.	M.H.	*Nil*	Ind.
46	C.	25.x.34	23	5 m.	?	Mother in M.H.	Asth.
47	C.	27.x.34	29	3 w.	M.H.(R.)	Brother T.B.	,,
48	D.	9.xi.34	26	2 y.	O.P.	Mother died M.H.; uncle in M.H.; aunt suicidal	?

9. Temperament.	10. Pre-psychotic reaction.	11. Onset.	12. Exogenic factors.	13. Acute symptoms.	14. Course.	15. Present condition.
?	?	?	?	Heb.	Decl.	U.O.R.
Norm.	Fair	Grad.	Head trauma	Cat. dep.	Imp.	I.D.E.
Schiz.	,,	,,	Mast.	Ind.	Deter.	W.O.N.
?	?	?	?	Cat.	Unch.	U.O.N.
?	?	?	?	Ind.	Fluct.	W.F.E.
Schiz.	Poor	Insid.	*Nil*	Par.	Unch.	U.O.N.
Ind.	Fair	Sud.	,,	Ind.	Imp.	M.I. N.T.
Schiz.	,,	Grad.	Mast.	,,	Decl.	W.O.E.
M.D.	?	,,	?	Cat. dep.	Unch.	U.D.N.
?	?	?	?	Cat.	Imp.	I.D. N.T.
?	?	?	?	Ind.	Fluct.	I.O.E.
?	?	Grad.	Head trauma	,,	Decl.	W.F.E.
?	?	?	?	Par.	,,	W.F.N.
?	?	?	?	Simple	,,	U.O.N.
Schiz.	Fair	Grad.	Unempl.	Par.	Unch.	U.F.E.
?	?	Ac.	?	Heb.	Det.	W.F.N.
Norm.	Good	Grad.	Head trauma	Ind.	,,	W.O.N.
Ind.	Fair	,,	Father's death	Par.	Decl.	W.O.E.
Schiz.	,,	,,	Unempl.	,,	Unch.	U.F.E.
?	?	?	?	,,	Decl.	W.O.N.
Schiz.	Fair	Insid.	Mother's death	Cat.	Imp.	M.I.(D)
Ind.	,,	Sud.	Def. Unempl.	Proc. par.	Det.	W.O.N.
Cycloid	Good	Grad.	Gastritis.	Cat. dep.	Fluct.	M.I. D.E.
Norm.	,,	,,	*Nil*	Par.	Unch.	U.D.E.
?	?	,,	,,	Heb.	Decl.	W.F.E.
?	?	?	?	Cat. exc.	Det.	W.O.N.
Norm.	Good	Sud.	*Nil*	Heb.	Catast.	,,
Schiz.	Fair	Ac.	Unempl.	,,	Imp.	I.D.N.T.
M.D. Norm.	,,	Sud.	Lack of food	Simp.	M.Imp.	M.I.D.E.
M.D. Psy. P.	Poor	Grad.	Mast.	Ind.	Unch.	U.D.N.T.
Schiz.	Fair	,,	*Nil*	Cat.	Imp.	I.D.N.
Ind.	,,	,,	,,	Heb.	,,	I.D.N.T.
Norm.	,,	,,	,,	Ind.	,,	I.F.E.
Schiz.	Poor	Insid.	,,	,,	Decl.	W.D.N.
?	?	Sud.	?	Cat. dep.	Unch.	U.F.E.
Norm.	?	?	?	Cat.	Imp.	I.O.E.
?	Fair	Grad.	Head trauma	,,	Det.	W.O.N.
Ind.	,,	Ac.	*Nil*	Ind.	Decl.	W.O.E.
Fair	,,	Grad.	Unempl.	Proc. heb.	Imp.	I.D.E.
?	?	,,	Surg. op.	Par.	Decl.	W.F.N.
M.D. ?	Fair	,,	,,	Cat.	Det.	W.O.N.
Schiz.	,,	,,	*Nil*	Heb.	,,	,,
,,	Poor	,,	Psychog.	Proc. heb.	Fluct.	U.D.N.
?	?	,,	Divorce	Ind.	Decl.	W.F.E.
Schiz.	Fair	Insid.	*Nil*	Heb	,,	,,
,,	?	Grad.	?	Par.	Det.	W.F.N.
?	?	,,	*Nil*	Simp.	Unch.	U.D.N.T.

TABLE

1. Serial No.	2. Status.	3. Date of admission.	4. Age on admission.	5. Duration of previous history.	6. Previous hospital treatment.	7. Heredity.	8. Bodily build
49	C.	28.xi.34	21	?	M.H.T.	Mother in M.H.; brother died M.H.	Ind.
50	C.	8.xi.34	34	2 m.	?	?	Asth.
51	C.	20.xii.34	24	3 y.	O.P.	*Nil*	,,
52	V.	31.xii.34	19	2 y.	M.H. (c.)	,,	,,
53	C.	8.i.35	21	9 m.	—	,,	,,
54	C.	9.i.35	33	4 y.	M.H. (R.)	,,	Ind.
55	C.	10.i.35	20	1 m.	—	,,	,,
56	X.	10.i.35	30	1 y.	—	,,	?
57	C.	5.ii.35	32	5 y.	—	,,	Asth.
58	C.	5.ii.35	28	6 y.	M.H.	,,	,,
59	C.	4.iii.35	37	4 y.	—	,,	Ind.
60	C.	24.iv.35	34	2 y.	—	,,	Asth.
61	C.	25.iv.35	29	4 m.	M.H.	Grandfather, aunt and sister in M.H.	?
62	D.	29.iv.35	22	1 d.	—	*Nil*	?
63	D.	1.v.35	21	4 d.	—	,,	?
64	C.	4.vi.35	30	11 m.	—	,,	Asth.
65	D.	25.vi.35	22	3 w.	—	,,	?
66	D.	26.vi.35	19	2 y.	—	Grandfather in M.H.	?
67	C.	9.vii.35	29	3 m.	—	*Nil*	Pyk.
68	C.	9.vii.35	28	?	—	,,	?
69	D.V.	11.vii.35	32	3 m.	—	,,	?
70	D.	16.vii.35	38	8 y.	—	,,	?
71	C.	30.vii.35	26	2 y.	—	,,	Ind.
72	X.	7.viii.35	20	?	—	,,	?
73	C.	18.viii.35	24	?	—	Sister in M.H.	?
74	D.	29.viii.35	29	6 m.	—	*Nil*	?
75	C.	13.ix.35	38	1 y.	M.H. (c.)	,,	?
76	X.	21.viii.35	24	?	,,	,,	?
77	X.	24.ix.35	35	?	?	?	?
78	T.	30.ix.35	22	3 y.	?	1 sibling schiz.; mat. aunt mania	?
79	C.	10.x.35	28	?	?	?	?
80	C.	25.x.35	19	?	?	*Nil*	Ind.
81	C.	4.xii.35	25	3 m.	M.H. (c.)	,,	,,
82	C.	23.xii.35	35	5 y.	?	,,	Pyk.
83	C.	13.i.36	35	1 y.	M.H. (c.) O.P.	1 sibling died schiz.; Father died at 40 T.B.	Asth.
84	D.	21.i.36	34	2 m.	?	?	?
85	D.	29.i.36	36	14 d.	?	*Nil*	?
86	D.	22.ii.36	21	3 y.	?	Grandmother died T.B.	?
87	D.	30.ii.36	20	9 w.	?	*Nil*	?
88	D.	25.iii.36	20	1 w.	?	,,	?
89	C.	5.vi.36	20	2 y.	O.P. (c.)	Sister T.B.	Asth.
90	C.	19.vi.36	25	14 m.	M.H. (c.)	*Nil*	,,
91	C.	9.ix.36	20	10 m.	,,	Father died M.H.	Ind.
92	C.	18.ix.36	27	9 m.	?	Mother died T.B.	Asth.
93	C.	22.ix.36	30	10 y.	?	*Nil*	,,
94	D.	15.x.36	28	3 y.	M.H.	Aunt suicidal	?
95	C.	20.x.36	38	1 y.	M.H. (V.)	*Nil*	Asth.
96	D.	11.xi.36	34	1 y.	?	Grandmother suicidal	?
97	C.	12.xi.36	33	?	?	?	Asth.
98	D.	30.xi.36	26	1 w.	?	?	?

E.—*Contd.*

9. Temperament.	10. Pre-psychotic reaction.	11. Onset.	12. Exogenic factors.	13. Acute symptoms.	14. Course.	15. Present condition.
?	?	Insid.	Infl.	Cat.	Unch.	U.O.E.
?	?	?	?	,,	Decl.	W.F.N.
Ind.	Poor	Insid.	*Nil*	Heb.	,,	W.O.E.
Norm.	Good	Grad.	,,	Cat.	Unch.	U.F.E.
?	?	,,	,,	,,	Det.	W.O.N.
?	?	,,	,,	Ind.	,,	,,
Schiz.	Poor	Insid.	,,	,,	,,	,,
,,	,,	Grad.	,,	Proc. ind.	Unch.	Dead.
,,	,,	,,	,,	Heb.	Det.	W.O.N.
M.D. Schiz.	,,	Insid.	,,	Simp.	Decl.	W.O.E.
Ind.	Fair	,,	,,	,,	Unch.	U.E.E.
Schiz.	Poor	,,	,,	Ind.	Decl.	W.O.N.
?	?	?	?	Par.	Det.	,,
Norm.	Fair	Ac.	*Nil*	Cat. exc.	M.Imp.	M.I.D.E.
Schiz.	Poor	Sud.	Unempl.	Ind.	Imp.	I.D.E.
Ind.	Fair	Grad.	Tooth extr.	Cat.	Det.	W.F.N.
Norm.	,,	Sud.	Excessive work	Par.	M.Imp.	M.I.D.E.
,,	,,	,,	*Nil*	Cat.	,,	,,
Schiz.	Poor	Insid.	*Nil*	Ind.	Unch.	U.F.E.
Ind.	,,	,,	Head trauma	Par.	,,	U.D.N.T.
Schiz.	Fair	,,	*Nil*	Cat.	Imp.	I.D.N.T.
Norm.	Good	,,	,,	Par.	M.Imp.	M.I.D.N.T.
Schiz.	?	Grad.	,,	,,	Unch.	U.F.E.
,,	?	,,	,,	Cat.	Det.	Dead.
?	?	?	Kitchen work	Heb.	Imp.	I.O.E.
Schiz.	Fair	Grad.	Business failure	Ind.	,,	I.D.N.T.
Ind.	,,	,,	*Nil*	Cat. dep.	Det.	W.O.N.
,,	,,	,,	,,	Cat.	Fluct.	Dead.
Schiz.	Poor	Insid.	Blindness; Starvation	Ind.	Unch.	,,
,,	,,	Grad.	Psychog.	Heb.	Imp.	I.O.E.
?	?	?	?	Par.	Unch.	U.F.E.
Schiz.	Poor	Insid.	*Nil*	Heb.	,,	U.O.E.
?	?	Ac.	,,	Cat.	Decl.	W.O.E.
?	?	Grad.	,,	Par.	Fluct.	,,
Norm.	Fair	Sud.	Overwork	Cat. dep.	Catast.	W.O.N.
?	?	?	?	,,	Det.	Dead.
Schiz.	Fair	Ac.	Financ. worry	Par.	Fluct.	W.D.N.
,,	Foor	Insid.	?	,,	Imp.	I.D.E.
Ind.	?	Grad.	*Nil*	Ind.	Fluct.	W.O.N.
Schiz.	Poor	,,	,,	Cat. dep.	Unch.	U.D.N.
,,	,,	Insid.	,,	Heb.	Catast.	W.O.N.
,,	Fair	Ac.	Head trauma	Cat. dep.	Decl.	W.O.E.
,,	Poor	Sud.	*Nil*	Heb.	Fluct.	U.F.N.
?	?	,,	?	Par.	Det.	W.O.N.
Schiz.	Poor	Insid.	*Nil*	Simp.	Decl.	U.O.N.
,,	Fair	Grad.	Ac. append.	Cat. exc.	Imp.	M.I.D.E.
Ind.	,,	Insid.	*Nil*	Par.	Det.	W.F.N.
Schiz.	Good	Grad.	Mast.	Cat. dep.	Imp.	M.I.D.E.
?	?	?	?	Ind.	Decl.	W.O.E.
?	?	?	?	,,	Fluct.	U.D.N.

TABLE

1. Serial No.	2. Status.	3. Date of admission.	4. Age on admission.	5. Duration of previous history.	6. Previous hospital treatment.	7. Heredity.	8. Bodily build
99	T.	6.i.37	23	9 y.	?	*Nil*	?
100	C.	29.ii.37	..	?	?	,,	Asth.
101	C.	11.iii.37	39	?	?	,,	Ind.
102	C.	20.iv.37	33	10 y.	?	Uncle died M.H.	Asth.
103	C.	26.iv.37	34	10 y.	M.H.	*Nil*	Ath.
104	C.	25.v.37	39	6 y.	,,	,,	Ind.
105	T.	26.v.37	32	5 m.	—	Father died M.H.	?
106	C.	5.vi.37	29	5 y.	O.P.	?	Ind.
107	D.	18.vi.37	26	3 y.	M.H.	*Nil*	?
108	C.	7.vii.37	28	2 m.	M.H. (M.D.)	F.H.; Insanity mother's side	Ind.
109	T.	23.vii.37	41	3 y.	T.	Mother died M.H.	?
110	C.	11.viii.37	24	7 y.	C.	Sister in M.H., 1936	Asth.
111	C.	13.viii.37	23	6 y.	M.H.	*Nil*	?
112	T.	20.viii.37	23	4 y.	,,	Mother died M.H.	?
113	C.	21.viii.37	31	8 m.	—	Father d. del. insan.; mother d. mania	Asth.
114	C.	3.ix.37	26	1 y.	?	Brother died T.B.	Ath.
115	T.	28.ix.37	26	18 m.	Obs.	*Nil*	?
116	D.	29.ix.37	30	18 m.	O.P.	Grandmother M.H.	Ind.
117	C.	15.x.37	21	18 m.	M.H.	*Nil*	Asth.
118	C.	18.x.37	32	6 m.	?	2 siblings T.B.	,,
119	C.	10.xi.37	29	3 y.	?	Brother in M.H.	Ind.
120	C.	25.xi.37	38	?	M.H. (V.)	?	Asth.

C. = Certified case still in Cane Hill Mental Hospital.
V. = Voluntary patient still in Cane Hill Mental Hospital.
T. = Transferred to another mental hospital.
D. = Discharged.
d. = Days.
w. = Weeks.
m. = Months.
y. = Years.
M.H. (R.) = Readmitted to a mental hospital but now relapsed.
M.H. = Previously resident in a mental hospital.
M.H. (c.) = Clinic (cf. Maudsley Hospital).
M.H. (V.) = Previously resident in a mental hospital as a voluntary patient.
O.P. = Out-patient Department treatment.
M.H. = Mental hospital.
T.B. = Tuberculosis.

E.—*Contd.*

9. Temperament.	10. Pre-psychotic reaction.	11. Onset.	12. Exogenic factors.	13. Acute symptoms.	14. Course.	15. Present condition.
Schiz.	Poor	Insid.	*Nil*	Ind.	Unch.	U.O.E.
,,	,,	,,	,,	Cat.	,,	,,
M.D. Ind.	Fair	Grad.	,,	Par.	Det.	W.O.N.
Norm.	Good	Insid.	Mental stress	,,	Decl.	W.F.E.
?	?	,,	*Nil*	,,	,,	,,
Schiz.	Poor	,,	,,	Cat.	,,	W.O.E.
,,	Fair	Sud.	Surg. op.	Par.	,,	,,
?	?	Insid.	?	Ind.	Unch.	U.F.E.
?	Fair	Grad.	*Nil*	,,	Imp.	I.D.N.T.
M.D. Psychopath.	Poor	,,	,,	Proc. heb.	Unch.	U.O.N.
Norm.	Good	,,	,,	Par.	,,	U.O.E.
Schiz.	Poor	,,	Head trauma	Proc. heb.	Det.	W.O.N.
M.D. Schiz.	,,	Insid.	*Nil*	Ind.	Unch.	U.F.E.
Schiz.	,,	Grad.	,,	Simp.	Fluct.	,,
—	?	?	?	Ind.	Decl.	W.O.E.
Schiz.	Poor	Insid.	*Nil*	Cat.	,,	W.O.N.
Ind.	Fair	Grad.	,,	Par.	Imp.	I.D.E.
Schiz.	,,	,,	,,	,,	Unch.	U.D.N.
Ind.	,,	Insid.	,,	Simp.	Det.	W.O.N.
,,	,,	Sud.	,,	Cat. dep.	,,	W.O.E.
?	?	Grad.	?	Cat.	Unch.	U.O.N.
Norm.	Fair	?	?	Par.	,,	U.F.E.

d. = Died.
Pyk. = Pyknic.
Ind. = Indeterminate.
Norm. = Normal.
Cycl. = Cycloid.
Schiz. = Schizoid.
Ac. = Acute.
Sud. = Sudden.
Cat. = Catatonia.
Cat. exc. = Catatonic excitement.
Cat. dep. = Catatonic depression.
M.I., M.Imp., I. Imp., see text.
U. or Unch. = Unchanging or Unchanged.
Decl. = Declining.

Ath. = Athletic.
Asth. = Asthenic.
Grad. = Gradual.
Insid. = Insidious.
Mast. = Masturbation.
Unempl. = Unemployment.
Surg. op. = Surgical operation.
Psychog. = Psychogenesis.
Heb. = Hebephrenic.
Par. = Paranoid.
Proc. = Process symptoms present.
Fluct. = Fluctuating.
Det. = Deteriorating.
Catast. = Catastrophic.

For explanation see text.

(6) *Exogenic factors.*

Such mental and physical factors of this nature as might be of significance were noted specifically for each case.

(7) *Symptoms of the acute stage.*

The usual subdivision into the simple, hebephrenic, catatonic and paranoidal groups is maintained, but added to these is the indeterminate group into which many cases fall.

(8) *Course of disease.*

The course of the disease was labelled according to its progress from the time of admission onwards and graded into the following categories: much improved, improved, unchanged, declining, deteriorating, catastrophic, and fluctuating.

Much improved
Improved } Used in the sense already defined in the text (p. 403).

Unchanged = mental condition neither improves nor declines; remains materially unchanged since admission.

Declining = a gradual insidious downhill course to dementia.

Deteriorating = a steady and rapid degeneration.

Catastrophic = an abruptly rapid downhill course to degeneration and vegetation.

Fluctuating = showing alternating improvement and relapse.

(9) *Present condition.*

Three columns of symbolic capital letters are used. The first letter of each trio tells the mental condition of the patient relative to that at the time of admission (M.I. = much improved, I. = improved, U. = unchanged or unimproved, W. = worse). The second letter indicates what type of abode the patient now occupies (D. = discharged home, O. = observation ward, F. = non-observation ward). The third states whether the patient is employed or not, no grading to indicate efficiency at employment being used (E. = employed and N. = unemployed).

It is to be noted that several of the group graded "improved" (five, to be precise) are still in the hospital. These patients are doing useful work here, and would be fit to go home were it not for the fact that their homes do not provide the shelter and care required.

Table E reveals the position regarding the above factors, for each individual case and for the material as a whole. To establish what I have previously contested the following questions must be answered:

(i) Are there any general features which might lead one to anticipate the very poor collective results?

(ii) Are there any individual cases whose course, bearing the picture of their traits as a whole in mind, is the opposite to what one might expect it to have been, and if so, why ?

Collectively we have the following distributions :

TABLE F.

Age on Admission (all periods inclusive).

20 and under.	21–25.	26–30.	31–35.	36–40.	41–45.
17	31	35	27	9	1

Duration of Psychosis Prior to Admission.

Under 7 days.	Under 1 month.	2–6 months.	7–12 months.	1–2 years.	3–5 years.	6–10 years.	Above 10 years.	Not known.
3	10	15	12	24	23	14	2	19

Previous Mental Treatment.

In a mental hospital.	In a clinic.	At out-patients.
29	9	8

Heredity.

35 cases had a positive hereditary history of psychosis.
13 ,, ,, ,, ,, ,, tuberculosis.

Bodily build.

Asthenic.	Athletic.	Pyknic.	Indeterminate.
30	9	2	25

Temperament.

Schizoid.	Cycloid.	Indeterminate.	Normal.	Psychopathic.
45	1	16	16	2

Pre-psychotic Reaction.

Poor.	Fair.	Good.
29	41	9

Mode of Onset.

Insidious.	Gradual.	Sudden.	Acute.
21	51	12	7

Exogenic Factors.

Of some sort were present in 36 cases.

Type of Acute Manifestation.

Paranoid.	Catatonic.	Hebephrenic.	Simple.	Indeterminate.
28	35	19	7	28

A survey of these figures alone would convince one of the bad prognosis of the material being treated. The comparatively large proportion of cases with an age of over 30, a pre-psychotic history of over two years' duration, an asthenic build, a schizoid temperament, a poor pre-psychotic reaction, a slow onset, hebephrenic, paranoid and simple group symptoms, a definite hereditary factor, and a previous history of mental treatment, and the comparatively low proportion of cases with a young age, a pyknic build, a cycloid temperament, a good pre-psychotic reaction and a rapid or acute onset, all point to this conclusion. But these symptoms could not in themselves indicate the serious nature of things, and it is only when the picture of the individual cases is before one (as in Table E, p. 438) that this is fully realized.

An inspection of this table reveals that the final outcome in the individual cases is usually what one would expect from the broader prognostic factors available. There are certain cases of discrepancy, however, and these will now each be reviewed in greater detail, in a search for an explanation of the unexpected outcome of each case.

Cases in which Prognostic Indications were Somewhat Indefinite.

(*a*) Cases in which Progress was Favourable.

Case 7.—The features shown in Table E indicate possibilities of a favourable outcome. Further details enhance these chances; his young age, the short duration and complete recovery of his only previous sojourn in a mental hospital; his average intelligence and reasonable acquittal at his employment (especially during his re-employment following his previous mental attack when his ability indicated a return of ambition and interest), and the sudden and almost acute onset of his present attack, all point to a favourable outcome, as also do the absence of any hereditary factor, or a schizoid temperament. The outcome, therefore, is not surprising.

Case 9.—This was rather a low-grade imbecile. He had been in an institution for the mentally defective for the 18 months prior to admission here when he had a gradual onset of catatonia, exhibiting flexibilitas cerea, echolalia, echopraxia, delusions and hallucinations. These cleared up soon after admission, but he remained in a semi-stuporose state with grinning and grimacing and outbursts of mischievous impulsiveness. By April, 1934 (nine months after admission), he was in a semi-stuporose condition, and he was granted discharge under Section 79 in the care of his father one year after his admission. From the meagre past history obtainable, the outcome of discharge without improvement was not unexpected.

Case 10.—Details of this patient were very deficient. His mother died from tuberculosis. It was also known that he was an illegitimate child. As far as could be ascertained the onset was acute, but this was not certain. At the time of admission he was confused, and soon after went into a catatonic stupor. In view of these all too insufficient data improvement was not unlooked for.

Case 11.—Again only a very imperfect history was available, and very little can be gauged from it. The fact that he had previously been in a mental hospital in Australia and apparently effected a recovery was a favourable indication. His asthenic build was an unfavourable factor. His changeable course was not surprising, and the fact that he was graded as in a state of improvement on 31.xii.38 does not blind one to his almost certain early relapse.

Case 21.—This was the case of a young man of 20 years, the son of a doctor, and a medical student himself. He seems to have ailed considerably from various

illnesses during childhood, and always to have been difficult to manage. There was a hereditary factor and he had a schizoid temperament, an apparently asthenic build (judging from a photograph) and an insidious onset—all unfavourable omens. On the other hand, he was young; the duration of his psychosis had been only one year; he had worked quite well at medicine, and had a fairly good pre-psychotic reaction, and although the onset had been insidious, it had ended in a sudden acute flare-up into a state of catatonic excitement. His symptoms were very typically catatonic, and cleared up in that rare and abrupt manner described in the literature from time to time. We see then that the outcome was not surprising, although a persistence of catatonia might have been equally well expected.

CASE 30.—It is obvious from an examination of Table E that apart from the presence of a hereditary factor of doubtful significance, the characteristics point to a favourable outcome. A young patient with a short history, a normal temperament, a fair pre-psychotic reaction and lack of food as a precipitatory cause. It is worthy of remark that this patient was a mental defective, but this did not prevent his being recorded as much improved, which implied that his illness regressed to such an extent as to leave his personality, even if a poor one, functioning in its normal manner.

CASE 32.—Although still at home in an improved state, this case has only attained a poor grade of improvement, having been able to do no more than casual work since discharge (he was in employment on 31.xii.38; apart from this he sits about the house). This outcome is not contrary to prognostic indications.

CASE 40.—The young age of this patient, his rapid recovery from a previous attack, normal temperament, fair pre-psychotic reaction and acute onset of the present attack would lead one to expect a good prognosis, although the hebephrenic nature of the acute phase was, of course, a pointer in the other direction. The strong battery of favourable factors have so far prevailed. It would be interesting to see the final picture.

CASE 69.—Despite the ill omen of the patient's schizoid temperament, his age at onset (32 years old), and the insidious incidence of the psychosis, his fair pre-psychotic abilities to face the world, short duration of symptoms and catatonic acute manifestation were of a sufficiently favourable significance to render the patient's improvement a distinct prognostic likelihood. It is unfortunate that he is now untraced, as the ultimate prognosis is not so good as the immediate one, and it would be interesting to know what has happened to him.

CASE 70.—This case might on the surface of things have been thought to do badly because of his age, the long duration of his psychosis, and the paranoid nature of his symptoms. It is found on further investigation, however, that the patient was a physician of a normal temperament and quite good pre-psychotic reaction history; that he had some sexual difficulties with his wife which may have helped on the present trouble; that although the psychosis began eight years previously it had been episodic as opposed to continuous, despite its originally having crept on in an insidious manner; accordingly, a favourable outcome was far from contra-indicated.

CASE 78.—The outlook in this case was from a prognostic point of view unfavourable in every way: long history of psychotic symptoms before admission, marked hereditary factor, schizoid temperament, poor pre-psychotic reaction, gradual onset and hebephrenic symptomatology render the prognostic outlook very dull. His grading as improved is indeed an extremely generous one on my part, since although he is well behaved, clean, tidy and regularly employed at the occupational therapy centre in simple work, he was still very dull and largely self-absorbed, not always accurate in his reply to questions, and subject to neologisms. His ability to survive in the outside world in an employed capacity, even if the surroundings were very favourable, is, to say the least of it, questionable. It is to be noted that he was still in an observation ward on 31.xii.38. There are one or two other cases of improvement in a somewhat similar category, but all showing a more substantial improvement than the present case.

CASE 85.—This patient had a schizoid temperament and a poor personality at its best. He was probably of a homosexual disposition, and this and financial worries proved exogenic factors in his history. His prepsychotic reactions were fair and the onset of the illness was acute. It is not surprising really then that a verdict of " improved " was returned, since this was, of course, reached bearing in mind the patient's usual personality and comparing his condition with that.

CASE 86.—This was of the same type as Case 85. The patient was a mental defective with a poor type of personality who has attained a poor grade of improvement, symptoms still being present. The result is not altogether surprising, although a failure to have improved was more to have been expected.

CASE 94.—This patient had a schizoid temperament and had always been sensitive to the difficulties and setbacks in life. He had done well at school reaching Standard VII at the age of 13. After that he had been an iron moulder first and a general labourer subsequently. His first breakdown had occurred at the age of 22, when he had suffered from what was said to be loss of memory, necessitating his stay in a general hospital for 18 weeks. In actual fact this may have been an attack of catatonic stupor. This was rendered even more probable by the fact that at the end of this time he became extremely excitable and had to go to a mental hospital. He was there for seven weeks, staging thereafter what appeared to be a complete recovery. Despite unemployment on his discharge he remained apparently well and eventually got a good job as a barman. Unfortunately, six weeks later he got acute appendicitis, necessitating an operation, and during convalescence had the present attack of schizophrenia, again of a catatonic type. That such a catatonic case, with a previous history of an attack from which a recovery was made and an acute recurrence following acute appendicitis on the present occasion, should once more improve sufficiently for discharge was to be anticipated. Since discharge he is reported to have been his usual self once more and to be at a Bristol training centre acquiring a training for a new trade.

CASE 96.—Although this patient had a schizoid temperament, his pre-psychotic reactions were apparently quite good and he had been for as long as seven years in one job as an engineer's fitter. The onset was gradual, having commenced twelve months before admission, with a falling-off of general interest and initiative. It launched into a stage of catatonic excitement quite suddenly at the end of this period. He soon veered over to catatonic depression. The strong affective portion of his catatonic symptoms combined with the fact that he did not develop stereotypies was also significant. All these facts suggested the possibility of a favourable outcome, which was more than justified by his subsequent history.

CASE 107.—The information obtained in this case was not very satisfactory. However, his prepsychotic history seemed quite good, as he worked from the age of 14 to that of 23, when he had his first breakdown in the General Post Office, having obtained the position of sorting-out clerk. The onset of his first attack in August, 1934, was reported to have been acute and of only one week's duration before admission. The symptoms were of an indefinite nature (as they were on the present occasion), and after rapid improvement followed by a relapse he improved again to be discharged finally in May, 1935. After that he appears to have remained " recovered " until the onset of this attack, which occurred quite acutely ten days prior to admission. From what was known, then, improvement was really more probable than not.

CASE 115.—The patient had a temperament of an indeterminate type which, although it had suspicious traits, could not be definitely labelled as schizoid. His pre-psychotic history seemed fairly good. He was a good boxer, made friends quite easily and appeared cheerful and lively to his family. They had never noticed anything abnormal in him until two years prior to admission when, following the death of his father, he became worried and more moody. His history following this is one which would fit in well with increasing paranoid ideas. He changed his employment frequently, was in Fulham observation ward twelve months prior to admission following arrest by the police for loitering: nine months prior to admission was arrested for knocking someone down in the street. On the present occasion

he was taken by the police for breaking telephones in kiosks. On admission he had delusions and hallucinations of persecution, but comparatively little emotional dissociation was noted, and there was little deterioration or degradation of the personality as a whole. The absence of schizoid temperament, the presence of a fairly good prepsychotic reaction and the relatively good preservation of the affective side of his personality were favourable points which put the possibility of improvement definitely in the forefront.

PROGRESS WAS UNFAVOURABLE.

(*b*) CASES WHOSE COURSE BELIED PROGNOSTICALLY FAVOURABLE INDICATIONS.

CASE 17.—The patient was a merchant ship's officer who had had a brilliant school record, having obtained a scholarship at the age of 11 and the London Matriculation at 16. His temperament seems to have been normal and his pre-psychotic reactions good. His bodily build was indeterminate, approaching the asthenic type more than the pyknic. There was a family history of one aunt having died in a mental hospital after being there for many years. While at sea he had had malaria and dengue fever, but these had not seemed to affect him. In February, 1929, he had influenza, after which he was reported to have been never the same. During his voyage from February to June, 1929, he is said to have had a head injury which affected him detrimentally. After his return home on this occasion he never returned to sea. From that time on his schizophrenia gradually developed. He was a voluntary in-patient in the Maudsley Hospital for 13 months in 1929–30; he discharged himself, but his condition had not improved. In 1932–33 he was a certified patient in this hospital for two months, diagnosed as manic-depressive psychosis and discharged, primarily on trial and subsequently as "recovered." His normal behaviour did not last for long, however, and he developed typical schizophrenic traits and was readmitted six months after his discharge.

It might have been thought from the patient's age at onset, his temperament, intelligence and prepsychotic reaction and the fact that influenza was a precipitating cause that the outlook was favourable, but the hereditary taint and the history of serious head trauma pointed in the other direction. Weighing things up, one would probably have given a quite good, if guarded, prognosis at the onset of the trouble; but by the time he came here with a four years' more or less progressive history, the prospects of improvement were poor and his present condition was the most likely outcome. The importance of head trauma as a detrimental factor in such cases is to be noted (see Mapother, 1937).

CASE 24.—The patient would seem from his normal temperament and good prepsychotic reactions to be a candidate for improvement. He was a cheerful and hopeful person who had been employed at one time as a plumber, another as a pawnbroker's assistant and a third as a wireless operator. In the last capacity he had travelled all over the world. He married at the age of 23 and had had two children. Prior to the onset of his illness he had been a good father and husband. So far the omens appear favourable, but his age on admission (34), the long previous duration of his psychosis (3½ years) and the paranoid type of its manifestation prove a sufficiently adequate counterbalance to warrant a very guarded prognosis. Thus his discharge in a fundamentally unchanged state on 28.i.37 was to be considered as quite a likely outcome. Since then he has remained at home, still deluded and hallucinated and sometimes noisy and shouting. He manages to do all the housework, but has not been able to accept any other employment.

CASE 28.—This was a very interesting case. He was the youngest of ten children, two by his father's first wife, and eight by his own mother. One of the two by the first wife had died from tuberculosis when a boy. There was no family history of insanity. The patient had done very well at school and had won a trade scholarship to the Arts and Crafts school. He became a compositor by trade, and

was in one post for four years prior to the present illness. He married three years before admission and had two children. He was very kind and good to his wife and was very sociable and had many friends. On the other hand, he was reported to have always been wasteful with money and very self-willed. Eighteen months before admission he lost his job owing to slackness and inability to concentrate. These were the first symptoms of his illness, but from then onwards his character gradually seemed to change completely. He became cruel to his wife and knocked her about. At the time of the birth of his second child (eight months old at the time of his admission) he did not get anyone to look after his wife or cook for her, but, on the contrary, made her get up and cook for herself and him as well. Despite this he celebrated the birth of the child lavishly. He was noticed to sit about all day and laugh to himself, no adequate external cause being present. He stated that he was not going to work, since he got his food and lodging without doing so. He also became a heavy drinker. On 4.iii.34 he attempted to kiss a girl against her will and was arrested by the police; he was sent by them to the observation ward and thence on here.

The patient was admitted in a state of typical hebephrenic schizophrenia; emotionally he was dissociated and full of the most fantastic and bizarre delusions and hallucinations. He deteriorated with catastrophic rapidity and on 31.xii.38 was completely inaccessible, keeping up a flow of absolutely unintelligible and disconnected language. His habits were faulty and his behaviour infantile. He was completely out of touch with reality.

The importance of this history lies in the fact that had the patient been seen in the early days of his psychosis (or even, possibly, at admission), from the factors already mentioned, a good prognosis would have had to have been given. What a precisely opposite course the symptoms took to what one would have expected is obvious. On 31.xii.38 no explanation could be given for this prognostic contrariness, but since then the patient has died and a feature discovered at post-mortem examination which is probably the explanation of the unforeseen outcome in his case, namely, the very small size of the patient's heart. The ominous significance of small-sized hearts was recorded by Lewis (1923), and it is well to bear in mind in cases such as the present one, when prognostic indications are falsified, that such an unexpected influence may be at work.

CASE 52.—On the surface the prognosis in this case looked good. He was the third child of a family of four, in which there was no hereditary factor. He did very well at elementary school and won a scholarship to a polytechnic, where he continued to excel. He was bright, friendly and sociable; even tempered, diligent and ambitious; fond of games and a good athlete. He had been friendly with a girl at one time, but for a considerable period prior to admission had taken no interest in her or any other girl. His pre-psychotic reactions had ostensibly been good until at 17½ years he left school. Owing to the industrial slump then prevailing he was unable to get work, and this disappointed his ambitions to get a good job and help his parents financially. This produced a reaction in him, and he started talking about having obtained a job and boasting to friends about it. Although he attended the Maudsley Hospital his condition progressed, and on 31.xii.34 the patient was admitted to Cane Hill in a state of catatonia, and from then onwards has not shown any signs of a recession of the disease process. A portent of misfavour is the patient's bodily build, which is the tall, thin, short trunk, long limbed, asthenic type. Despite this, one must admit that this was a case in which there seemed grounds to pronounce a good prognosis, and this has to be rated as one of those cases in which prognostic assessment was falsified by the subsequent course of the disease for reasons as yet unknown.

CASE 75.—The onset of schizophrenia in a man of 38 is always to be considered serious, so that the deteriorating subsequent course was to be looked for.

CASE 83.—The outlook in this case appears quite good in many respects. He was a married man with three children who had been a good husband and father. He had done normally well at school and at work he always had a good record. He had

been an errand-boy from 14 to 15 years old, worked in the Woolwich Arsenal from 15 to 18, and then joined the R.A.F. and became a first-class mechanic. Following the war he had been a lorry driver, and for the five years prior to this illness had been employed by one firm, earning £3 17s. a week. His personality was described by the social worker thus: "A well-liked, pleasant fellow; not a leader but quiet and reserved. Is unselfish, a good husband and father and takes a pride in his home and family. Steady and even-tempered and never appeared to worry over things. Very neat and tidy in habits and careful of his appearance. Rather 'fussy' with food. Went to the 'pub' very occasionally but was usually at home in his spare time." His wife attributed his breakdown to the adequate cause of overwork. He was particularly hard worked immediately before the onset of the psychosis, frequently working from 6 or 7 a.m. to 12 midnight. Over and above this, the acute symptoms were those of catatonia, so that so far the picture as a whole looks good.

Looking in the other direction, however, we find two unfavourable factors: the age of the patient at the time of onset and the hereditary factor. The patient was the fourth of five children, all boys. The youngest brother from all accounts had a schizoid temperament. He died in a mental hospital at the age of 23 (almost certainly from dementia praecox). The patient's father had died at the age of 40 from tuberculosis said to be brought on by excessive drinking.

Thus considering the case as a whole, we may say that prognostically the outlook was indeterminate. The catastrophic deterioration of the patient was not definitely indicated, but the strong hereditary factor may be said to have prepared in the patient what the biological school would call a "milieu" particularly susceptible to the schizophrenic disease process, and from their point of view at least the downhill progress was not surprising.

CASE 109.—This is another case of schizophrenia of the paranoid type developing late and with a poor prognosis despite the previous normal temperament and quite good prepsychotic reaction. The fact that the patient's mother died in a mental hospital was another adverse factor. Therefore the typical gradually increasing deterioration which occurred was more to be expected than not.

CONCLUSION.

In concluding this katamnesic follow-up of 120 cases I shall summarize my findings thus:

(1) It was found that the outlook for the 120 patients followed up for periods varying from one to six years after admission to the hospital was very gloomy. Only eight cases (6 per cent.) were "much improved," and 11 (9·1 per cent.) "improved."

(2) Examination of the details of certain prognostic factors from a general point of view pointed to the above possibility, and this was confirmed beyond doubt by a study of individual cases.

(3) The outcome in the individual cases was as would have been expected from the prognostic facts except for one or two cases, and in only two instances was it absolutely contrary to expectations. In one of these the solution was found at post-mortem to be a small heart.

(4) The above facts support my contention that certain factors are of value in assessing prognosis in the individual case, and that in attempting to estimate the potentialities of various treatments of schizophrenia, adequate details regarding the prognosis of the various cases treated are essential. The

production of so-called statistical figures of remission rates obtained by such treatments without such prognostic qualifications is misleading and comparatively useless.

PART III.

Prognosis in Cardiazol Treatment.

It is not the purpose of this thesis to enter into a disquisition on the therapeutic potentialities of cardiazol and insulin in the treatment of schizophrenia. The virtues of each were well vaunted by their original sponsors, and from that time onwards a continuous glut of articles supporting or controverting these claims has flooded medical and psychiatric literature. It is not intended here to conduct a detailed survey of all that has been written on this subject; suffice it to say that the matter is still under dispute with regard to both treatments, and to examine the present state of opinion concerning them.

There has been a tendency for each of these treatments to follow the course common to many previously-claimed remedies for schizophrenia, such as continuous narcosis, sulfosin, pyrifer, thyroid, etc. Each of these in turn has been hailed with a great initial enthusiasm, which has gradually dwindled with time until it has finally been abandoned and relegated to the waste-heap of disappointments. Both cardiazol and insulin have gone through the initial stages of this process, having already received almost fanatical support by some and prejudiced scepticism by others. The final verdict has not yet been reached, but what may be said is that the original claims are now considered by general opinion as excessive.

One of the main reasons for the inability to reach a verdict has been the differing criteria of recovery and improvement adopted by different authorities, but the factor of greatest importance has been the failure to compare the results of treatment with prognostically comparable groups of cases treated by the usual hospital methods of rest, occupation, etc. As already mentioned, it is because of the variance of opinion regarding the remission rates of cases treated in the latter manner that there has been no real yard-staff against which to measure the effects of these treatments. Apart from the average remission rates, there is also the question of the prognostic features of the individual case, and here again there is lack of agreement on the importance of the various features concerned. Nevertheless, as already shown, there seems good ground to believe that taken as a whole the prospects of one case may be considerably better than another, and consequently the necessity for comparing comparatively favourable cases is obvious. As Hinsie (1928) remarked: "To be in a position to judge the efficacy of any mode of treatment at least the following requirements should be met—a tolerable uniformity in the general personality constitution, but this should not be construed too rigidly."

Cardiazol Treatment.

The production of artificial convulsions by the intravenous injection of cardiazol was first introduced by Meduna (1935). He claimed as many as 90 per cent. of remissions in cases of under one year's duration of symptoms.

Fig. 34*c* represents the results obtained by a few authors who treated over 40 cases in the earlier days of the use of this drug.

Fig. 34.—*Cardiazol.*

Author.	Total number of cases.	Duration of psychosis.	Results. Number of remissions.	Number of non-remissions.
Meduna, L. (1937)	110	Under 1 year	39 (90%)	4
		1 to 2 years	9 (50%)	9
		2 to 5 years	6 (35%)	17
		Over 5 years	..	26
			54 (50%)	56
Cook, L. C. (1938)	45	Under 1 year	7 (77·7%)	2
		1 to 2 years	6 (60%)	4
		Over 2 years	11 (42·3%)	15
			24 (53·3%)	21
Angyal and Gyarfas (1936)	45	Under 1 year	12 (44·4%)	15
		Over 1 year	5 (27%)	13
			17 (36·7%)	28
Low *et al.* (1938)	43	Under 1 year	5 (38·4%)	8
		1 to 2 years	1 (10%)	9
		Over 2 years	2 (10%)	18
			8 (18·6%)	35
Briner (1937)	112	Under 1 year	20 (58%)	14
		Over 1 year	8 (10·2%)	70
			28 (33%)	84
Kuppers (1937)	262	Under 1 year	59%	Number of cases not stated.
		Over 2 years	2% (full remissions)	

Recently various articles have appeared summarizing the results in large numbers of cases. Von Meduna and Friedman (1939) reviewed the results obtained by various psychiatrists in both the United States and in Europe. The total number of cases dealt with was 2,937, of whom 1,465 came from the U.S.A. and 1,472 from Europe. Their results are represented in Fig. 35.

Reitmann (1939) in a recent article points out the difficulties met with in trying to correlate the results of various authors. He says: "The various authors classify their results so differently that it is very difficult to use them as a homogeneous group in which the results can be tabulated. . . . Some of the authors for example report the number of acute, subacute and chronic cases, but do not say what their therapeutic results in the separate groups (acute, subacute and chronic) have been. Other authors again represent only percentages. . . . The classification of the remissions is rather loose—e.g. the very relative notion of social remission or very good improvement is used." As seen in Fig. 36, he confines himself to the percentage remissions in acute and subacute cases (i.e. under 18 months' illness), and finds a 50 per cent. full remission rate.

Pollock (1939) has very recently compared statistically the results of cardiazol and insulin with cases treated by the routine methods in what he says are strictly comparable groups of 1,140 patients, and finds the results of cardiazol treatment much inferior to those of insulin, and very little better than cases not treated with either.

FIG. 35.—*Table summarizing the Collective Findings of von Meduna and Friedman* (1939).

Total number of cases	2,937
,, ,, of full remissions	737 (25·0)

U.S.A.—1,465 *cases.*

	Number of cases.	Remissions.	Improvements.
Under 6 months	201	128 (60·55%)	42 (20%)
6 to 12 months	210	74 (36·8%)	47 (23·13%)
Over 1 year	1054	88 (8·36%)	398 (37·7%)

Europe—1,472 *cases:*

Full remissions	30·37%
Acute and subacute (i.e. less than 18 months' duration)	584
Of these there were 290 remissions	49·66%

FIG. 36.—*Taken from Reitmann's Article on Collective Cardiazol Results* (1939).

Nation.	Number of cases. Total.	Less than 18 months (acute and subacute).	Full remissions.
Austria	130	64	32 (50%)
England	71	31	13 (41%)
Germany	310	129	51 (39%)
Hungary	433	178	94 (53%)
Italy	120	53	42 (79%)
Switzerland	162	51	22 (43%)
U.S.A.	785	334	183 (54%)
Total	2,011	840	437 (51%)

In the absence of any definite criterion against which to measure the claims of cardiazol and insulin, various methods of obtaining valid comparisons have been suggested. It is interesting to note the recommendations of Isabel Wilson (1937). In an article headed, "Some Control Observations should be made," she says:

"The question bristles with difficulty . . . , but I believe something of the sort should be tried. (1) The method of giving insulin only to every alternate schizophrenic admitted suggests itself, but useful comparison is only possible over large numbers, so that this plan would be very tedious. (2) Treatment of female patients only would be interesting in view of opinions expressed upon this, but even if they improved significantly in comparison with male untreated cases we would be left, after long work, with a sex-weighted result. (3) The least objectionable plan might be for as many patients to be treated as possible in the treatment hospital, while an equal number of cases diagnosed by the same doctors were given conditions and treatment, except that they were not given insulin, as like that given to the insulin-treated group as possible. Care should be taken that the number of 'early' cases in both groups should be approximately equal. Such investigations would admittedly bring us no exact result, but might help us to form ideas on the real efficacy of insulin therapy."

All three of these methods have one paramount objection which, since none of them was applied in the earlier days, has rendered then inapplicable later. This is the fact that the treatments have received such general recognition as therapeutic agents that psychiatrists have been loth to withhold one or the other to cases who did not rapidly show progress under routine hospital treatment; and even if *they* had no scruples on this point, the public have

received such information on the subject as more often than not to demand one of them for their relatives. We are left, therefore, with the only alternative of comparing results with those of previously hospitalized cases. In this respect Freudenberg (1938) has argued that each hospital should compare its results with previous results of its own ; but the labour and difficulty of this plan are frequently great and, it is hoped, may be avoided by resort to the figures and conclusions already reached in this thesis. The comparison of cardiazol and insulin results with those of the cases treated by the usual hospitalization, and which I have reviewed earlier, will now be discussed.

It will be seen from the above figures that the best results are obtained in the earliest cases, and that the fall in effect with increased duration of psychosis is phenomenal. A comparison according to duration of psychosis between cardiazol, insulin and hospitalized cases is very interesting. The latter are represented by the works of Briner, O. (1937), Guttmann *et al.* (1939), Hunt, Fieldman and Fiero (1938), Pollock (1925) and Whitehead (1937).

It is seen that the cardiazol figures are definitely superior to those of hospitalized cases, but on close inspection are not so much so as at first seems to be the case. This is due partly to the fact that the cases treated by cardiazol cannot possibly have been followed up for so long as those of the other series, and partly to the possible discrepancies in duration of illness, and proportions of the various sub-types of cases, etc., in each of the groups of different authors. As an example of the second contingency, it is obvious that in groups of, say, 50 cases of under six months' duration of history, the scatter may vary tremendously, some groups having the largest proportion with a history of under two months, others with that of over four months. These facts have not been dealt with in sufficient detail in the various articles concerned. Apart from the duration of history, the usual absence of details of other prognostic factors influencing expectation of recovery renders the matter even more inconclusive. (To appreciate the importance of the former factor, reference should be made to Figs. 23, 27, 30, and to Table V.)

Even if the effect of such factors is disregarded, it is seen that there is a large divergence of results. For instance, Guttmann *et al.*'s figure of 34·7 per cent. complete and social remissions over a period of two to five years in 188 cases of one year's duration compares favourably with Low *et al.*'s (1938) figure of 38·4 per cent., and not unfavourably with Angyal and Gyarfas's figure of 44·4 per cent., and von Meduna and Friedman's figure of 36·8 per cent. for American cases of six months' to one year's duration. Briner, O.'s, figure compares even more favourably with the majority of cardiazol figures, including von Meduna's and Friedman's American cases of under six months' duration. Klaesi's (1937) claim of 60 per cent. of social remissions in cases treated without cardiazol or insulin is also noteworthy.

Pollock (1939) sounds a note of complete disharmony, as revealed by Fig. 37, and reaches the conclusion that cardiazol treatment results do not warrant its

use in the U.S.A. state hospitals. Others voice of scepticism have recently been added, amongst whom the following may be quoted: Gillman and Parfitt (1938) produce evidence to show that the antagonism of schizophrenia and epilepsy is far from proved, and that fits produced in insulin treatment and by cardiazol "do not affect the ultimate prognosis in schizophrenia and at the most only accelerate expected recoveries." Stalker, Millar and Jacobs (1938), after a comparative study of 218 cases, of whom 48 were treated with insulin and 41 with cardiazol, state: "There is no significant difference in the numerical results obtained in schizophrenia by ordinary hospital treatment, hypoglycaemic treatment and convulsant treatment." The latter opinion is further confirmed from Hungary, where Lehoczky, Horanyi *et al.* (1939) examined cases of schizophrenia from one to four years after treatment. In 132 untreated cases they found a remission rate (full and good remissions) of 35 per cent., whereas in 85 treated with insulin they found only a 30·6 per cent. rate, and in 50 cases treated with cardiazol one of only 22·8 per cent. They therefore conclude that cases treated by these methods have an outlook no better than those not so treated.

FIG. 37.—*Results of Cardiazol and Insulin Treatments compared with a Control Group of* 1,140 *Cases (after Pollock)*

	Rec.	M.I.	Imp.	Unimp.	Dead.
Control group . .	11·2	7·4	7·5	65·8	4·6
Insulin . . .	12·9	27·1	25·3	33·4	1·3
Metrazol (= cardiazol)	1·6	9·9	24·5	63·5	0·5

Apart from these reports the question of complications has come increasingly to the fore. Tooth and Blackburn (1939) have shown that intellectual impairment as evidenced especially by memory defects may be produced by convulsion therapy. In early works complications of any consequence were considered to be very rare. Thus such works as those of Meduna (1935), Cook, L. C. (1938), Kennedy (1937) and Harris (1938), and Rees Thomas and Wilson (1938) make only cursory mention of the subject and all concluded that serious complications are rare. A survey of recent literature does not bear this out, however, but on the contrary shows that serious complications may be considered quite frequent. The most important of these is fracture of the vertebrae, which was previously unsuspected, but has now been revealed by X-ray of the spine (Fig. 39). I have had five such fractures in X-rays of 20 cases treated with cardiazol. I have also seen two cases of double fracture of the femur and two of single fracture in the course of treatment of 120 cases. One of these cases died following an operation. Fig. 38 represents a table of such fractures recorded in the literature. Fig. 40 represents fractures of

other bones noted in the literature. Apart from fractures, these other serious types of complication occur: (1) lung abscess, (2) pneumonia, (3) a lighting up of latent tuberculosis, (4) various cardiac arrythmias. I myself have seen one case of (3) who died within the course of six weeks.

FIG. 38.—*Representing the Frequency of Fractures of the Femur in Schizophrenics Treated by Cardiazol or Triazol Convulsions.*

Author.	Number of cases.	Unilateral.	Bilateral.	Fatal.
Kerstens (1938)	Not mentioned	0	1	..
Pameijer, J. H. (1938)	1,200	2	3	..
Nightingale, G. (1938)	44	1	0	..
Goldstein *et al.* (1938)	102	1	0	..
Walk, A., and Mayer Gross (1938)	61	1	1	1
Beckenstein, N. (1939)	695	2	0	1
Pollock, H. M. (1939)	1,140	5	0	..
Bellinger, C. H. (1939)	538	1	0	1
Hamsa, W. R., and Bennett (1939)	..	4	..	..
Carp, Louis (1939)	687	5	..	..
Somers and Richardson (1939)	1	0	1	..
Myself	95	1	1	..
	4,563	23	7	3

= ·66%.

FIG. 39.—*Representing the Frequency of Fractures of the Vertebrae Produced by Cardiazol or Triazol Convulsions.*

Author.	Number of cases.	Number X-rayed.	Number of fractures.
Carp, Louis (1939)	687	?	2
Bennett and Fitzpatrick (1939)	17	8	8
Polatin, Friedman *et al.* (1939)	58	51	22
Wespi, H. (1938)	?	?	1
Palmer, H. A. (1939)	20	20	5
Stalker, H. (1938)	?	?	1
Myself	120	20	6
	902	99	45

FIG. 40.—*Representing Frequency of Fractures other than those of the Femurs or Vertebrae in Cardiazol and Triazol Convulsions.*

Author.	Number of cases.	Number of fractures.		
		Humerus.	Mandible.	Scapula.
Pameijer, J. H. (1938)	1200	3	1	3
Goldstein *et al.* (1938)	102	3	0	0
Pollock, H. M. (1939)	1140	2	1	0
Carp, Louis (1939)	687	5	1	0
Kraus, G. (1938)	?	1	0	0
Briner, O. (1938)	111	0	0	1
Good, Rankin (1939)	?	1	0	0
	3240	15 (2·1%)	3 (·1%)	4 (·13%)

It has been said that the former are largely the result of septic teeth, and may be almost eliminated by careful dental attention prior to treatment. To eliminate the latter complication, routine X-ray examination of the chest is recommended. Even if these steps are undertaken in every case, as seems desirable, it is questionable whether they would eliminate all such cases, although it is certain that many such tragedies would be averted.

Not all cases are benefited or unchanged regarding their symptoms: some are definitely made worse. Kronfield and Sternberg (1937), Küppers (1937), and Humbert and Friedman (1937) are quoted by Rees Thomas and Wilson (1938) as reporting such cases, and I have seen several among the cases I have treated.

In view of what has been said above, it might be thought that there was no further desire for the use of cardiazol, but I consider that it cannot be lightly discarded. Briner (1937) (quoted by Rees Thomas and Wilson (1938)) emphasizes the importance of clinical experience as opposed to statistics, and my experience of its effects has convinced me that until further evidence is forthcoming its use is still warranted.

During my stay at Cane Hill Hospital there have come under my care many schizophrenics after convulsion therapy. Below are the findings of its effect on 120 consecutively treated cases: Table H represents the effect of cardiazol proportionate to the duration of the illness, results being assessed according to the already defined terms. Unfortunately, as may be seen, the majority of cases were very chronic. The figures of early cases are too small in themselves to produce any definite conclusions. Nevertheless the improvement in early cases is stressed. It is to be noted that of the five much improved and two improved cases of under six months' duration, two of the

TABLE

Table Indicating the Prognostic Outlook in 35 Cases of Under Three Years' Duration

Serial No.	Status.	Date of commencement of treatment.	Age.	Duration of psychosis prior to treatment.		Previous hospitalization.	Hereditary factors.
				In hosp.	Total.		
1	C.	10.i.38	28	3 m.	4 m.	M.H. 1931	4 ?
2	C.	18.i.38	21	6 m.	7 m.	M.H. 1936	Father died in M.H.
3	C.	19.ii.38	31	7 m.	1 2/12 y.	*Nil*	Mother was in M.H.; father in N.H. now
4	C.	21.ii.38	37	1 y.	3 y.	M.H.	1 sibling died schiz.; father died T.B.
5	C.	9.iii.38	26	1 2/12 y.	2 1/12 y.	M.H. twice	*Nil*
6	C.	16.iii.38	21	15 m.	2 1/12 y.	*Nil*	,,
7	C.	10.iii.38	31	2 1/2 y.	2 1/2 y.	,,	,,
8	C.	16.iii.38	26	3 m.	2 1/2 y.	M.H. (V.)	,,
9	C.	27.iii.38	30	3 y.	3 y.	M.D. colony 8 years	,,
10	C.	27.iii.38	36	3 w.	8 m.	*Nil*	,,
11	C.	13.iv.38	23	1 w.	10 m.	Transfer from M.H.	,,
12	C.	19.iv.38	31	2 w.	1 1/2 y.	O.P.	Grandmother in M.H.
13	C.	25.iv.38	34	3 w.	7 w.	*Nil*	*Nil*
14	C.	26.v.48	26	10 d.	10 d.	M.H.	,,
15	C.	6.vi.38	33	3 w.	1 3/8 y.	*Nil*	Pat. aunt in M.H.
16	C.	2.vii.38	23	3 w.	8 w.	,,	Pat. uncle in M.H.
17	C.	15.vii.38	35	18 m.	18 m.	,,	*Nil*
18	C.	22.vii.38	35	5 m.	6 m.	,,	Mat. aunt—suicide
19	C.	28.vii.38	30	1 m.	7 m.	,,	*Nil*
20	C.	30.vii.38	17	1 10/12 y.	2 7/12 y.	,,	Mother died T.B.
21	C.	12.viii.38	32	10 m.	1 5/12 y.	,,	2 siblings T.B.
22	C.	12.viii.38	33	1 7/12 y.	1 7/12 y. ?	?	?
23	C.	17.ix.38	29	2 w.	6 w.	*Nil*	*Nil*
24	V.	19.x.38	24	2 w.	9 w.	,,	,,
25	C.	7.xi.38	26	3 m.	3 y.	,,	,,
26	C.	27.xi.38	20	3 w.	4 w.	,,	Mother died T.B.
27	C.	17.xii.38	28	2 w.	1 y. 2 w.	,,	*Nil*
28	C.	5.i.39	28	6 w.	3 m.	,,	,,
29	C.	17.i.39	20	10 d.	1 1/2 y.	,,	Mother in M.H.
30	C.	20.ii.39	24	1 m.	7 m.	,,	*Nil*
31	C.	15.iv.39	33	1 m.	2 m.	,,	,,
32	C.	4.v.39	28	3 m.	4 m.	,,	?
33	C.	13.v.39	23	1 m.	2 m.	M.H. 1935	Uncle suicide; aunt in M.H.
34	C.	17.v.39	42	6 m.	1 1/2 y.	*Nil*	*Nil*
35	C.	23.v.39	29	1 y.	1 2/12 y.	T.B. in gen. hosp.	Brother died T.B.

G.

Prior to Treatment, together with the Effect of Treatment on the Cases Concerned.

Bodily build.	Tempera-ment.	Pre-psychotic reaction.	Onset.	Exogenic factors.	Acute symptoms.	Number of fits.	Immediate result of treatment.	Present condition.
Norm.	Schiz.	Fair.	Grad.	*Nil*	Cat.	29	M.I.	M.I.D.E.
,,	,,	Poor	Sud.	,,	Heb.	25	U.	U.F.N.
Asth.	,,	,,	Grad.	,,	,,	17	U.	W.O.E.
Norm.	Norm.	Fair	Sud.	Overwork	Cat. dep.	20	U.	W.O.N.
Asth.	Schiz.	Poor	Insid.	Head trauma	,, ,,	20	U.	W.O.E.
?	,,	,,	Sud.	*Nil*	Par.	18	M.I.	U.D.N.
Asth.	?	?	?	?	Cat.	20	U.	U.O.N.
Norm.	?	?	Acute	*Nil*	,,	7	U.	W.O.E.
Asth.	M.D.	Poor	Grad.	,,	Ind.	25	W.	W.O.N.
,,	Schiz.	,,	,,	,,	Cat.	..	I.	,,
Norm.	Norm.	Good	Sud.	Malaria	,,	18	I. (12)	M.I.D.E.
,,	Schiz.	Fair	Grad.	*Nil*	Par.	20	I. (R.)	U.O.N.
?	Ind.	Good	Sud.	Unempl.	Ind.	4–5	M.I.	M.I.D.E.
Norm.	Schiz.	Fair	Grad.	*Nil*	Cat.	11	M.I.	,,
,,	,, M.D.	,,	,,	,,	Par.	28	U.	U.O.E.
,,	Norm.	,,	? Ac.	?	,,	25	U.	M.I.D.E.
?	Schiz.	Poor	Insid.	*Nil*	Ind.	10	U.	U.O.N.
Asth.	,,	,,	Grad.	,,	Cat.	13	I.	,,
Norm.	Ind.	Fair	?	Malaria	Par.	9	U.	U.F.L.
Ath.	?	?	Sud.	?	,,	5	U.	W.O.N.
Asth.	M.D. Ind.	Fair	,,	*Nil*	Cat.	19	U.	U.O.E.
,,	?	?	?	?	Ind.	27	U.	W.O.E.
?	Schiz.	Good	Acute	Unempl	,,	25	M.I.	M.I.D.E.
?	Norm.	Fair	Grad.	Mental shock	,,	9	U.	U.N.T.
Ath.	Ind.	,,	Grad.	*Nil*	Cat.	..	I.	U.O.N.
?	Norm.	,,	Acute	Unempl.	,,	15	M.I.	M.P.D.E.
Ath.	Ind.	,,	Grad.	*Nil*	Heb.	17	U.	U.O.N.
Norm.	Norm.	,,	Sud.	Unempl.	Cat. dep.	17	I.	M.I.D.E.
Ind.	Schiz.	Poor	Insid.	*Nil*	Heb.	21	U.	W.O.N.
Norm.	Ind.	,,	Grad.	Sex	Ind.	2	U.	I.N.T.
,,	,,	Fair	Sud.	*Nil*	Par.	4	U.	M.I.D.E.
Ind.	Schiz.	,,	?	?	Ind.	12	M.I.	M.I.D.N.
Asth.	,,	Poor	Insid.	*Nil*	Heb.	7	U.	W.O.N.
,,	,,	Fair	,,	Onset war	Par.	9	U.	U.O.N.
,,	M.D. schiz.	Poor	,,	*Nil*	Par.	6	U.	Dead.

former and the two latter occurred in catatonic cases and rapidly relapsed following the cessation of cardiazol.

Table G shows the prognostic factors of all cases under three years' duration, according to the criteria and standards already discussed and described in relation to Table E. Of the unchanged cases a few were made slightly better and some slightly worse, but the extent of these was so minor as not to be considered worthy of special mention. The phenomenon of convulsive therapy enabling many chronic patients previously silent, immobile and inaccessible, etc., to behave and work well where they had not previously done so (as described by Cook, 1938, and others) was conspicuous by its absence. Detailed histories of each of the cases who were benefited to the degree of much improvement or improvement is shown below and must be read in conjunction with Table G.

TABLE H.—*Showing the Effect of Convulsion Therapy on* 120 *Consecutively Treated Cases of Schizophrenia at Cane Hill Hospital.*

Period of duration of symptoms prior to treatment.	Number of cases.	Immediate effect of treatment.			Condition of cases on 31.xii.39.				
		M.I.	I.	U.	M.I.	I.	U.	N.T.	D.
0 to 6 months	10	5 (50%)	2 (30%)	3 (30%)	4	1	5	0	0
7 to 12 „	6	0	0	6	0	0	5	1	0
1 to 2 years	10	0	0	10	0	0	9	0	1
2 to 3 „	8	1	1	6	0	0	8	0	0
3 to 5 „	22	1	1	20	0	1	21	0	0
5 to 10 „	35	0	0	35	0	1	33	0	1
Over 10 years	29	0	0	29	0	0	29	0	0
Total	120	7	4	109	4	3	110	1	2

CASE HISTORIES.

CASE 36.—L. G—(i.e. over four years' history), male patient, aged 28. No insanity in the family. Subject to all the usual childish complaints, including bronchitis every winter. He was backward at school and only reached Standard IV, but he was quite happy there, although he never played games and made few friends. After leaving school he was employed as a butcher's assistant in his father's shop and did quite well.

Personality.—He was always of a reserved and retiring temperament and tended to be timid and hypochondriacal, making much of such injuries as scratches, etc. Although he did not make many friends, he was affectionate, good-tempered to his family and easily managed by them. He had only one brother, who was as brilliant as he was dull, and this made him very envious, and played no small part in his mental upset.

Psychosis.—The first symptoms were only recognized a year before admission, when he started such mannerisms as repeatedly looking at himself in the glass, scratching his fingers, chewing his food and not swallowing it. The mother now realized that he was becoming more apathetic and had lost power of concentration in the previous three years. In recent months he became more dreamy and would laugh and talk to himself and finally gave obvious signs of hallucinations, waking up his mother in the night and asking whether the detectives were coming, and being terrified that a man was tracking him down to kill him. He suffered from insomnia and his appetite was poor.

On 15.xi.38 he was admitted to Cane Hill Hospital as a certified patient, having previously been in Bexley hospital as a voluntary patient for three months. On admission he was deluded and hallucinated and grimacing, manneristic, irrational and irrelevant in his answers to questions and unable to give a good account of himself. He exhibited considerable anxiety associated with his delusions and emotionally was frequently depressed. From this time until the time of treatment his condition did not change.

On 20.i.39 cardiazol treatment was commenced. Improvement was noticed from the beginning, and by the time he had seven injections his emotional control was much improved and he was quieter in manner and behaviour. He had lost his mannerisms and could discuss his position with some insight.

After the twelfth injection his schizophrenic symptoms had apparently disappeared; he was quiet, well-behaved and a good worker. His mental defective background, of course, remained.

20.iv.39.—Discharged on trial.

18.v.39.—Discharged recovered.

Unfortunately the remission did not last for long, and by 7.vii.39 he was readmitted suffering from symptoms similar to those on the previous occasion. This time cardiazol had no beneficial effect and he is still in the hospital materially unchanged.

Comment.—This was a case of schizophrenia in a mental defective. There was a strong element of anxiety state present also. The cardiazol was entirely effective, despite the four years' history, on its first application, and attained its effect primarily on the emotional state. Perhaps the length of history and unfavourable prognostic significance of paranoid schizophrenia in a man of 28 were responsible for its failure in the second application.

CASE 25.—R. E. W—, male patient, aged 26. The sixth of nine children, and parents and siblings all of an excitable nature. Brother had a severe breakdown (probably psychotic) during the war. One sibling was M.D. and died of Tb. The patient was a strong child and did well at school. When he left school he was employed successively as a chauffeur, apprentice in an engineering shop, as a stock-broker's clerk and then as an assistant in an armament firm.

Personality.—He was reported to be sociable and popular and to get on well with his family, but he was always excitable, argumentative, headstrong and egotistical. Prior to his marriage he had never been regularly with any girl, and had declared he would marry the first girl he touched. This was true, and when he married his wife three years before admission she was already pregnant. Prior to the outbreak of the present illness his wife was thinking of leaving him owing to his excessive sexual demands on her and his bad temper. Quarrels ensued from this, which became more and more frequent.

Psychosis.—For the two years prior to admission he was more irritable and excitable than ever. Quarrels with his wife were more frequent and his relations with his fellow workers became strained. He claimed to have invented a new speeding-up technique and wrote to the Government describing flaws in the shells that his firm were producing. He started looking for burglars in the house and became jealous and suspicious of his wife. At home he talked incessantly and would never rest for two or three minutes on end.

In November, 1936, he became very excited by the Crystal Palace fire. His doctor stopped him from work and sent him to bed. He became even more garrulous and even during the night talked of politics and religion. One day soon after Christmas, 1936, he left the house, saying that he was going to meet a friend, and was next heard of at Maidstone in Kent, where he had been found wandering and taken into custody. He was certified insane and admitted to Kent County Mental Hospital on 15.i.37.

He was restless, over-active and excitable; negativistic, aggressive and violent; deluded and hallucinated; given to mannerisms and fixed attitudes; slovenly and untidy, faulty in habits, and indulging very frequently in masturbation; inaccessible

and lost to the world of reality. Occasionally he had more rational and quieter times.

On 3.ix.37 he was admitted to Cane Hill hospital materially unchanged from the above. He was given a course of continuous narcosis, during which he became less restless and excitable, but otherwise unchanged.

On 7.xi.37 cardiazol treatment commenced. He soon began to improve, and by the time he had had five injections he was reasonably quiet, talked rationally about his discharge, wrote excellent letters to his wife, engaged himself efficiently in rug-making and showed intelligent interest in public affairs. The injections were continued. By the time he had had the thirteenth injection he had relapsed considerably (being confused and retarded), and he never got so well again. Nevertheless while he was having injections he was more or less in touch with reality. The first course was ended after 30 injections, by which time although he was euphoric, excitable, truculent and devoid of insight, he was still in touch with reality. After cessation of treatment he soon became an inaccessible catatonic again. Since then he has had three further courses of convulsion therapy with cardiazol. Each course has improved his emotional stability to a reasonable level. He has become reasonably alert and amiable, able to do a little work and take some interest in dancing and reading a newspaper, and to a certain extent is in touch with his surroundings; but still he is devoid of insight, irrational and dissociated in speech and deluded and hallucinated and he always relapses into an inaccessible catatonia when injections are suspended.

Comment.—The initial effect of the cardiazol treatment was truly dramatic. One wonders whether the continuance of treatment was not responsible for the subsequent regression. Its subsequent infallible beneficial effect on the affective side of his personality is to be noted. The degree of improvement has become less on each occasion.

CASE 12.—A. W. E—. This patient's wife had left him and only deficient details were obtainable from a neighbour.

Male patient, aged 36. A strong hereditary taint, his mother being in a mental hospital and his father having committed suicide when he was ten years old. The patient says he did fairly well at school but afterwards led an irregular life, and was employed successively as page boy, waiter, packer and at odd jobs. He married at 20, but his wife drank and he separated. From the age of 29 he had lived with another woman by whom he had one child. He got on well with her until the onset of the present trouble.

Psychosis.—The patient had to give up his job as a packer owing to its being too heavy for him. Since then he has only had odd jobs. He started behaving peculiarly a few weeks before admission, after losing a job. He wandered round in a depressed way, saying repeatedly that he could not pay the rent and had no money. He refused his food, saying that he could not eat; became untidy and refused to wash or shave. One day he suddenly started cleaning the floor himself becaused he was "going to be good in future." Following an attempt at suicide he was taken to a general hospital and was admitted into Cane Hill Hospital as a voluntary patient on 10.viii.37.

He was sullen, restless and mute, and soon lapsed into a catatonic stupor. From then onwards he fluctuated from a state of stupor or pseudo-stupor to more alert and lucid intervals, but even in these he remained sullen, aloof, negativistic and eccentric; difficult with his food; given to grinning and laughing to himself for no apparent reason but really due to hallucinations; and dull and indifferent to his condition and his surroundings.

On 19.iv.38 cardiazol treatment commenced. He soon started to improve, and by the time he had had his eighth fit he had improved to such an extent that his sullen and resentful attitude had disappeared, his dull and gloomy outlook given way to an alert and cheerful one; his insight and ability to discuss things rationally returned and his behaviour became exemplary.

On 16.vi.38 the patient took his discharge as a voluntary patient completely

recovered. He soon relapsed, however, and on 31.viii.38 was readmitted as a certified patient. On this occasion his symptoms were much the same as on the first occasion, but coloured to a greater extent with hallucinations. Cardiazol was tried again, and after five fits he was much brighter and able to converse rationally and had regained insight and his hallucinations had disappeared. The course was stopped after seven fits. He soon relapsed, however. Two further courses were given, with the same beneficial result on both occasions and the same subsequent relapse. The patient states that despite his apparent improvement he has never been completely free from hallucinations since their onset.

Comment.—The prognosis in this case was not good from the beginning. The marked effect of cardiazol on the affective side is obvious. The repeated subsequent relapse is interesting.

CASE 6.—C. A—, male patient, aged 20. Family history nil. Reached top standard at school. Left school at 14. Was an errand boy until 16 years old and since then has had several odd jobs, the longest being eight months.

Personality.—He had always been quiet and reserved; was usually popular with his mates but never made real friends. He had few interests and was inclined to live a solitary and vegetative existence.

Psychosis.—Four months prior to admission the patient first expressed ideas of reference and delusions of persecution. He became unemployed; sat about all day laughing and talking to himself; exhibited sexual delusions and his speech became inconsequent and irrational. He was quite willing to go to a mental hospital. At the time of admission he was a typical grinning, grimacing schizophrenic, full of bizarre delusions and hallucinations. He became dull, indolent and indifferent and the hallucinations continued.

On 14.ii.38 cardiazol treatment commenced. He had a course of twelve fits, by which time he was "much improved." His outward behaviour was normal and his mannerisms gone. He had only a hazy recollection of his delusions and hallucinations. His schizoid personality, however, remained obvious.

On 3.xi.38 he was discharged recovered. His behaviour since then has been in keeping with his schizoid tendency and his condition has regressed. He got odd jobs occasionally, but always failed to keep them; he now remains at home and makes no friends, and although dull and apathetic, is inclined to a generally paranoid outlook.

Comment.—A schizoid personality in whom the prognostic outlook was poor. That cardiazol removed the patient's dull and indifferent indolence and with it the hallucinations is remarkable. The subsequent regression was only to be expected in view of his previous history.

CASE 23.—T. H—. male patient, aged 29. Family history nil. Patient was always strong physically. He did well at school, where we reached the top standard. After school he was an errand boy for two years, porter of a block of flats for eleven years and since then had only had odd jobs. He has been very sensitive about his inability to find a job recently.

Personality.—Always of a quiet, shy and retiring nature and a poor mixer. He seemed to have a sense of inferiority and ideas of reference.

Psychosis.—Seven weeks before admission the patient started a new job as a painter, and was always very nervous of climbing the ladder. About four days before admission was depressed and rather silent. Next day he complained that people were making fun of his eyes. Next night he woke his mother and slowly pushed her to the window, with homicidal intentions. On 31.viii.38 he was admitted to Cane Hill hospital. He was sullen, depressed and resistive and under the influence of auditory hallucinations. He was subject to bizarre delusions and hallucinations. He heard a voice telling him to rape his mother. He thought that she gave him one of the leaders of her eye. He was irrational in speech, but there was a certain degree of insight left.

On 17.ix.38 cardiazol treatment was commenced. By the time he had had four fits his condition had started improving. After this he improved gradually.

Altogether 25 injections were given. He was quiet, well-behaved and a good worker; no longer hallucinated and having insight into his condition. He remained eccentric and his speech frequently contained verbal mannerisms.

He was discharged to the care of his mother on 18.i.39 and since then has remained much the same.

Comment.—The prognosis in this case was comparatively good despite the schizoid temperament—no family history, acute onset, unemployment as an exogenic precipitating cause, good record of employment, and prepsychotic reaction. The cardiazol probably only accelerated a process that would have taken place in the ordinary course of events.

CASE 13.—J. M—, male, aged 34. No family taint. He did quite well at school, and afterwards was a trumpeter in the Army, a waiter, a batman, an employee in Siemen's works, and finally for the twelve years previous to this trouble (i.e. psychosis) worked in the building trade. The last few months he has had to work in the T.N.T. department of an arsenal. This was very heavy work and got him run down.

Personality.—He was good-tempered and not prone to worry unnecessarily. He was not very sociable, but fond of his own family and home and a good father and husband. He smoked continuously, but drank very little. He was inclined to be introverted and keep his thoughts and troubles to himself.

Psychosis.—The patient had found his work in the armament factory very heavy, and a few days before admission started to get confused on names and dates and to talk incessantly of going to see a relative abroad. When seen by the doctor he was sent to the Maudsley Hospital, from there to an observation ward, and then to Cane Hill.

On admission on 29.iii.38 he was euphoric in mood, mildly confused in thought and dissociated and irrational in speech. He frequently grinned and grimaced to himself and soon constructed ideas of reference, and became very suspicious of the nursing staff.

On 25.iv.38 triazol commenced. Improvement was rapid. After five fits the patient had become emotionally stable, and had lost his delusions and suspicions and had no recollection of them. He maintained his progress, soon regained insight and could be said to have recovered completely. His whereabouts cannot now be ascertained.

Comment.—The prognosis in this case was good. Despite the patient's rather introverted temperament, his prepsychotic reaction and adjustment was good. The exogenic factor of severe physical strain at his work and the rapidity of the onset all pointed towards a favourable outcome, as did the comparative paucity of paranoid symptoms. Nevertheless, the rapid beneficial effect of the treatment was remarkable, and undoubtedly saved the patient a considerable period of hospitalization and very likely produced a more thorough recovery.

CASE 26.—D. W. J—, male patient, aged 20. There was no family history of insanity, but the mother died of tuberculosis eight months after the patient's birth. He reached the top standard at school and afterwards attended evening classes. After leaving school he was employed in the electrical trade.

Personality.—He was always rather solitary and unsociable although he got on well with his relatives and neighbours. He is said to have been of a worrying disposition. He was studious and a heavy reader. His chief interest was his garden. He had made himself a really efficient and skilled gardener and was very proud of his work.

Psychosis.—Twelve weeks prior to admission the patient seemed "off colour" and complained of pains in the stomach, etc. He was kept off work. For ten weeks he showed no overt symptoms. He got no better, began rambling in his conversation, was certified and admitted to Cane Hill on 6.xii.38. He was incoherent and inaccessible. Emotionally he was unstable—shouting, screaming and crying. He was very deluded and hallucinated, picking rats off the floor and the Holy Ghost off the wall. He was restless, destructive and faulty in habits.

Before cardiazol treatment had started the patient had begun to improve, being less restless and emotionally more co-ordinated.

27.x.38 cardiazol commenced. By the time he had had two fits he had made excellent progress. Emotionally he was stabilized. His apathy had given place to a general interest, and he applied himself to occupational therapy with real zeal and enthusiasm. His delusions and hallucinations had disappeared and he had quite good insight into his condition. He was given 15 fits in all, but did not improve much further. He was discharged " much improved " on 26.v.39. Since then he has remained his usual self, obtained work and returned to his hobby of gardening.

Comment.—The prognosis in this case was obviously good (a young age, absence of family history, acute onset, and precipitating factor of inability to obtain a permanent job; also the indefinite nature of the symptoms of the acute phase), and such improvement was to be expected. The remarkable manner in which this was rapidly produced by two injections of cardiazol was interesting.

CASE 28.—J. D—, male patient, aged 28. single. No family history of insanity. Patient had a brilliant school career and won a scholarship for £200 at Darjeeling College. He came to England and trained as an engineer at Trinity College, eventually taking a degree in engineering. He worked for Callendar Cables, then went to New Zealand on a ship as a refrigerating engineer. When he was discharged from the ship he had no work or prospects of any, and became depressed.

Personality.—Details of this were not obtainable, as his parents were in India, but he gave the impression (after his recovery) of being a cheerful, intelligent person, sociable and a good mixer, but with a rather childish irresponsibility and lack of objective.

Psychosis.—Following failure to get employment he became dull and depressed, and one day when he saw an advertisement in the newspaper for recruits for the R.A.F. he felt that this was a special message for him—" everything in the paper was woven about my life and there was even a drawing of me in it." He applied and was rejected, and thereafter developed auditory hallucinations. The voice of an old man told him that he would be sent to Devil's Island for neglecting to re-apply for admission to the R.A.F. He became terrified and threw himself under a taxi in an effort to commit suicide. He was admitted to Cane Hill on 5.i.39.

He was almost perpetually occupied with hallucinations and was dull, retarded, depressed and lachrymose. He required washing and hand-feeding; was incapable of spontaneous activity.

On 30.ii.39 cardiazol was commenced. After three injections he showed some signs of improvement, being more alert, less deluded and hallucinated. After a few more fits his affective condition had changed further. He was now in a state of euphoria and fatuously pleased with himself and the world in general. He was still deluded and hallucinated. By the time the course of 15 fits was terminated he had not changed very much further. He was still euphoric, and clung to the idea of being asked by God's voice to join the R.A.F. He continued to improve to such an extent that he was discharged " much improved " on 5.vi.39. Since then he has remained in good health and recently joined the Army, at which he has been an adept soldier. Three features of interest are noteworthy: (1) the persistent gain in weight during and following cardiazol treatment; (2) the change of the patient's facial expression during improvement; (3) the limited success of cardiazol, leading on to ultimate success after it had been suspended.

Comment.—The prognosis in this case was very good—normal build, normal temperament, good prepsychotic reaction, acute onset and exogenic factor of unemployment: so that the limited effect of cardiazol treatment during its 15 fits is hardly flattering. What improvement was produced was caused by the early injections.

CASE 37 (over four years' history).—D. J. S—, male patient, aged 36. It was impossible to get a satisfactory history in this case, but according to his brother he did fairly well at school and afterwards became employed as a clerk.

Personality.—From the time of adolescence onwards he had shown certain schizophrenic traits. He never kept a job for long, was facile and fickle in his opinions, kept much to himself and indulged in phantasy. He asserted that he was going to make his name by setting up a firm to sell luncheon baskets to motorists. His brother stated that he has been a continuous source of trouble and worry to the family for the past 17 years, having never retained a job more than a few weeks, and frequently plagued them for financial assistance. His symptoms developed into acute paranoid schizophrenia, and he was admitted to Cane Hill Hospital on 26.viii.39.

On admission he was resistive, aggressive, violent, and frequently made impulsive attacks on anyone near him. Usually he would not answer when spoken to, but sometimes accused others of persecuting him. He was confused and disorientated, and his mood was one of depression. He soon improved and became quieter in behaviour and discussed his case and stated that his hallucinations were less, but he relapsed a few days later into a state of catatonic stupor and remained in it for 14 days, until cardiazol treatment was commenced on 24.x.39.

He improved at once, and by the time he had had three injections he had recovered completely from his stupor. His delusions and hallucinations soon disappeared and he took a normal interest in life and worked fairly well in the clerks' office, although his schizoid personality was still obvious. On 22.xi.39 he was discharged to the care of his brother, but he relapsed the same day and became silent, sullen, deluded, hallucinated and depressed, and has remained so.

Comment.—The prognosis in this case was poor, and although the cardiazol dispelled the stupor momentarily, relapse was rapid when the patient was subjected to the strain of the outside world.

CASE 32.—W. G. S—, male patient, aged 28. Very little of this patient's past history was obtainable. He was of a fair educational level; after leaving school he had been a bandsman in the Army for seven years, being discharged two years before coming to the hospital. During this time he had been unable to get employment as a musician, and was only able to get odd jobs.

Personality.—A quiet, reserved and introverted person, shy, sensitive and artistic.

Psychosis.—Admitted to Cane Hill Hospital on 13.iv.39. He was correctly orientated and realized to a certain extent that he had gone to pieces. He was very hallucinated aurally and visually; dull and retarded in his outlook and depressed emotionally; laughed inexplicably to himself. His condition remained much the same until on 4.v.39 cardiazol treatment was commenced. After only two fits he felt better, and by the time he had had ten he had improved to the extent of being able to discuss his position with insight, his hallucinations had disappeared, and he was taking an alert interest in the ward and playing in the hospital band. He was given only twelve fits in all.

He maintained his improvement and was discharged on 5.x.39 much improved, although his schizoid personality traits were still obvious. Since then he has remained much the same.

Comment.—The prognosis in this case was again quite good (as far as could be ascertained): his previous good record in the Army band; sudden onset precipitated by the exogenic factor of unemployment worries, all pointed to a favourable conclusion. Cardiazol accelerated this, but the patient would probably have got better more gradually without its effects.

CASE 24.—E. S. W—, male patient, aged 24, single. Family history nil. He did quite well at school, but never wanted to do homework and preferred to make model aeroplanes and chemical experiments. He worked for 2½ years in a wholesale firm, gave it up spontaneously for no particular reason and after that tried for many jobs. He wanted to go into the Air Force, but was failed owing to his eyesight. He worried considerably about this.

Personality.—Had always had a nervous disposition and been inclined to overdo things. He never gave his brain a rest and switched too rapidly from one subject

to another. Very sociable and made friends easily, and has many hobbies. Had always been shy of girls—confided in his mother. A heavy smoker, but a teetotaller.

Psychosis.—Nine months before admission certain circumstances associated with his uncle's death worried the patient very much. After that he became very hypochondriacal. He was also unemployed at this time, and failure to get work, although he tried hard, worried him further. He became quieter and more disinterested; gave up his hobbies. Three days before admission he felt very ill and sent for a doctor and asked to be sent to a mental hospital.

On 29.ix.38 he was admitted to Cane Hill Hospital as a voluntary patient. On admission he said that he was psychic; aurally and visually he was very hallucinated; he had feelings of bodily change relieved by turning somersaults; he was restless and overactive, incontinent in habits, and in need of constant care and supervision.

On 19.x.38 cardiazol was commenced. Nine fits were given. The patient soon improved and became emotionally more stable, less restless and overactive, and his hallucinations disappeared. He took his discharge against advice on 15.xi.38.

Comment.—Despite the patient's rather defective personality traits the prognosis in this case was good: quite good pre-psychotic reaction, exogenic factor of worry over unemployment, acute onset, etc. Cardiazol may be said to have only accelerated a process which would have taken place in any event.

CASE 39 (over four years' history).—W. S. O'F—, male patient, aged 23, single. No family history. Patient did fairly well at school, and afterwards was employed as an engineer's fitter and a labourer.

Personality.—A difficult person; shy and seclusive; introverted and rather apathetic and indifferent to the world at large. He was always religiously inclined and was an ardent Roman Catholic.

Psychosis.—On 4.xii.34 the patient was admitted to Banstead Mental Hospital in what was thought to be an attack of mania. He soon recovered and was discharged on 15.vii.35. After this he got on very well until he suddenly became mute, negativistic, impulsive and violent. This was in February, 1936, two weeks before his admission to Cane Hill Hospital which took place on 17.ii.36.

On admission he was found to be in a typical catatonic stupor. He was dull, apathetic, indifferent and inaccessible; slovenly, untidy and faulty in habits.

By 15.vii.36 the patient had recovered spontaneously. His conversation was rational and his behaviour good, and he was discharged on 8.x.36. He behaved well following this, until another attack occurred and he was readmitted on 7.vi.37 to Cane Hill. He soon recovered and was discharged. His fourth attack of catatonia necessitated readmission to Cane Hill on 13.v.38.

On 30.v.38 triazol was commenced. By the time he had had four fits he had recovered in a manner similar to that noted on previous occasions, but lapsed into stupor a fortnight later. This process was repeated several times. On one occasion he recovered after only one injection, but no matter how many he had, he always relapsed.

Comment.—In this case of recurrent catatonia there was an obvious inherent tendency to recovery. The manner in which convulsion treatment invariably stimulated this tendency reveals its very definite effect on cases of catatonic stupor, although the case would probably have staged recovery phases without such treatment.

CASE 18.—J. L. K—, male patient, aged 35, single. A maternal aunt committed suicide. He was always "mother's boy" and very spoilt in his childhood. Did moderately well at school. Took up engraving on leaving school, but did not like it and soon gave it up. Then found work in his father's office and was not a success. Since then he has made no serious effort to get employment, living on a private income of £150 to £200 a year and doing the housework; for the last six years, since his sister got married, he has lived alone.

Personality.—He has always been a very strange, solitary, self-sufficient person, not wanting society and completely ignoring other people's convenience or feelings. He was prone to be slovenly and untidy and neglectful of his personal appearance. He never read books and his only interest seems to have been making model trains. Despite his peculiarities, his neighbours liked him well enough to invite him to various outings.

Psychosis.—This appeared to come on quite suddenly, following the termination of his one and only friendship with a girl, which was nothing more than platonic. He felt ill and went by himself in the night to a general hospital. He was admitted to Cane Hill Hospital on 16.ii.38. He was confused and retarded in his responses to questions; he had ideas of reference and delusions of persecution, and was impulsive, aggressive, resistive and violent. He remained dull and apathetic in spite of bizarre delusions of persecution.

On 22.vii.38 triazol treatment commenced. After the first course of 12 fits the patient was not improved. Soon after he lapsed into a genuine stupor. Five further fits brought him out of the stupor and a total course of 13 was given, by which time he had improved very considerably and was able to converse freely and showed some insight. He soon lapsed into stupor after treatment was finished, however. A further course was given with a similar result, another lapse following its cessation.

Comment.—The prognosis in this case was very gloomy. The repeated ability of cardiazol to dispel a catatonic stupor is again well illustrated. The bizarre and rather fantastic delusions also disappeared, but it is to be noted that these were of a more superficial and effervescent nature than those of a well-established paranoid schizophrenic.

CASE 1.—R. S—, male patient, aged 28, single. No family taint. Did quite well at a convent school. He afterwards joined the Army and when he left there took up mental nursing.

Personality.—Appeared to be schizoid, musical type.

Psychosis.—While in the Army he was found wandering about depressed and lachrymose. He was confused and emotionally unstable and was subject to ideas of reference. Also he had numerous bizarre unfixed delusions. His condition improved rapidly, and he was soon discharged to the care of his father. He soon recovered, and was employed in two different mental hospitals and dismissed from each for what was described as his paranoidal attitude to other members of the staff. He then took up private nursing. One month before admission the patient began to feel ill. He soon developed acute symptoms, and was admitted to Cane Hill Hospital on 26.viii.38.

On admission he thought that he was to be eaten by rats and that his eyes were shrinking up. He was very deluded and depressed, exhibited fantastic persecutory delusions and had no insight. One of his main symptoms was anxiety.

On 3.xi.38 convulsion treatment commenced. By the time of his seventh fit he had improved considerably; he said that he had never felt better in his life and that his mind was "afloat." He was still hallucinated and still had ideas of reference. He was given 25 fits in all, and at the end of the course had not regained insight, and delusions and hallucinations still persisted. Improvement continued, and on 23.iii.39 he was discharged. Since then he has remained his usual self, showing a schizoid temperament.

Comment.—The outlook in this case did not appear particularly good, as far as the details would allow any prognosis to be made, but the acute onset, previous recovery and fair pre-psychotic reaction, etc., made an improvement quite probable. Cardiazol accelerated this, and attained its effect in the first few injections.

CASE 38.—J. R. R—. The patient's mother was very difficult and only a sparse history was obtainable.

Male patient, aged 20, single. No family insanity. He did well at school, reaching the top standard two years before leaving. Following this, he was an errand boy in an off-licence shop, then a packer. He is said to have had a nervous

breakdown nine months prior to admission. He soon got over this and then joined the Army.

Personality.—No details obtainable, but in hospital he gave the impression of the "strong, silent man." He was quiet and introverted and self-contained. He was quite sociable and fond of games.

Psychosis.—After six months' service in the Army a change in personality was noted. He lost interest in his work, at which he was previously quite efficient, and there was a general loss of emotional reaction. On admission to the Military Hospital he was deluded, hallucinated and impulsive and affectively depressed. On admission to Cane Hill Hospital on 6.vi.34 his condition was as above, but he was also noted to laugh inanely to himself. He made a very rapid improvement and was discharged recovered on 11.x.34.

On 11.x.35 he was readmitted. He was incoherent and rambling in speech and displayed confusion, restlessness, mannerisms and bizarre attitudes; he was wandering in attention and deficient in concentration. He gave evidence of being hallucinated. He improved under routine hospitalization, and became more alert and stable and worked quite well in the occupational centre, but he remained dull and unsociable and devoid of insight into his condition.

On 16.iii.38 cardiazol commenced. He soon began to improve and became more alert and emotionally stable, but was still devoid of real insight and retarded in thought. After twelve injections treatment was stopped. He never got much further, remaining rather shy, diffident, indifferent and lacking in initiative until the outbreak of war spurred him on to ask for a period of trial to "do his bit," and on 30.xi.39 he was discharged. Since his discharge he has remained well.

Comment.—So far as was known the outlook in this case was fair. The fact that this patient had recovered once before made the outlook better. Cardiazol did produce improvement, especially on the emotional level, but it is probable that this would have eventually occurred spontaneously.

Apart from these cases the following points are of interest: One case had a very good prognostic outlook. Eighteen fits were given; after the first few fits the patient had improved considerably, only to relapse as fits were continued. Ultimate recovery took place a considerable time after cardiazol had been stopped. The patient improved so much that he is now out and doing well in the Army.

Case 15 did not benefit from cardiazol treatment. A few months later the patient improved considerably and was later discharged "much improved."

The complications that occurred in the 120 treated cases were:

Deaths: 2, one from tuberculosis and the other following bilateral fracture of the neck of the femur.

Fractures of the neck of the femur: 2 double and 2 single. One case died following operation (see above). In the other cases the results of extension and pegging by orthopaedic surgeons were so successful that the two single fracture cases are now walking as well as they did before the fracture, and the one bilateral walks with only a slight limp (Gissane, Blair and Rank).

Fractures of the vertebrae: 20 cases have been X-rayed and six cases discovered so far. No untoward symptoms have manifested in any of these four so far (Blair, 1940).

Dislocation of the jaw: several cases occurred sporadically, and in one so invariably as to necessitate cessation of treatment.

Conclusions.

These observations point to certain definite conclusions which I have substantiated in observation of many other treated cases :

(*a*) Cardiazol and triazol convulsions have a beneficial effect on many schizophrenics. The cases they affect are those which from a prognostic point of view have in any case the most favourable outlook. This emphasizes emphatically my contention that the publication of remission rates in treated cases without mention of the prognostic outlook in the various cases is dangerously misleading and comparatively valueless.

(*b*) Convulsion therapy may reduce the duration of hospitalization and improve the quality of remission in such cases, and in a few may even tip the scales sufficiently to produce a recovery which would not otherwise have occurred.

(*c*) Convulsion therapy acts through its effect on the emotional and affective side of the individual. Delusions of a superficial and bizarre nature attached to or resulting from changes of mood may disappear on treatment. The firmly rooted delusions of a typical paranoid schizophrenic are extremely rarely affected.

(*d*) Convulsion therapy, if it is to prove beneficial, will give definite signs and symptoms of improvement before ten injections are given. It is seldom that more than a few injections are needed to produce improvement to a point where contact can be established with the patient. A further injection or two may be allowed, but not more. Persistence in injection frequently leads to a reverse effect.

(*e*) Convulsion therapy has very little effect on patients with a history of over three years' duration. In a few suitable cases its trial is warranted.

The complications of convulsion therapy are serious and not to be viewed light-heartedly. For the following reasons they are not yet to be considered absolute contra-indications to the treatment :

(1) It has yet to be proven that the type of fracture which occurs in the vertebral bodies has any markedly debilitating effect. (2) Fracture of the femur, provided that it is treated promptly by recognized orthopaedic methods, offers excellent prognosis. (3) Other fractures and dislocations have a similar good prognosis if properly treated. (4) X-ray examination of all cases of asthenic build or with a family history of tuberculosis should almost rule out the flaring up of old tuberculosis. (5) Attention to teeth and other septic foci such as tonsils and antra should minimize the possibility of lung abscess. (6) My personal experience of over 100 cases treated with cardiazol is that it has a very markedly beneficial effect in cases of emotional upset.

I may therefore summarize the matter by saying that although cardiazol therapy has not fulfilled its initial promise, it still has a definite place in the

treatment of very carefully selected and prepared cases of schizophrenia, but that its indiscriminate use is dangerous and deeply to be deplored. A selection of cases should be made, and in my opinion treatment should never be persisted in for more than ten injections if definite improvement is not produced, and in any case when much improvement has been obtained, the treatment should not be persisted in for more than another two injections. Such a procedure would minimize the chances of complications, especially the evil effects of further convulsions on a fracture of a vertebra (which may occur without any clinical indication whatsoever—see Donald Blair, *Lancet*, 1940, in course of publication), while the chances of benefit from the treatment would be reduced very little, if at all.

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ADAPTIVENESS AND EQUILIBRIUM.

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The behaviour of animals and man may be approached from many points of view, but there is one feature of their behaviour which is outstanding in its importance and in its difficulty. I refer to the peculiar "adaptiveness" of animals' behaviour. The concept is vague, but everyone knows, roughly at least, what is meant by it. It is certainly one of the most remarkable features of animal behaviour. In psychiatry its importance is central, for it is precisely the loss of this " adaptiveness " which is the reason for certification.

We may demonstrate the phenomenon very clearly by writing, not " the burnt child dreads the fire," but " the burnt child seeks the fire." In this latter statement we see at once that the adaptiveness has disappeared.

But the concept of " adaptiveness," though important, has several marked disadvantages. Firstly it is vague. It is very difficult to define exactly what we mean by the word. Secondly it is not quantitative ; and although one can recognize, roughly, degrees of adaptation yet there is, at present, no means of expressing this quantitatively. Its third disadvantage is that it is apt to involve subjective elements from the mind of the observer. Instead of the question of " adaptiveness " being decided purely by an objective examination of the animal and its circumstances, it is apt to be a judgment on the part of the observer, and there is no guarantee that different observers will all come to the same conclusion.

It would clearly be better if this concept could be changed for another which would be equivalent to it as far as its essential features are concerned but which would be free from these objections.

It is suggested in this paper that the concept of " stable equilibrium " may perhaps be equivalent to it.

In order to discuss the question adequately, however, we must first study the question of " equilibrium " in more detail, for there is more in the subject than meets the eye.

THE NATURE OF "EQUILIBRIUM."

We may start with the classic example of physics. We have three objects on the table before us: one is a cube resting on one face, the second is a sphere, and the third is an inverted cone exactly balanced on its point. They correspond to the usual "stable," "neutral" and "unstable" equilibria respectively. The criterion used to distinguish the types of equilibria is that we apply a small disturbance to the object and see what happens. We find that the cube tilts and then returns to its original position; that the sphere starts rolling slowly; while the cone topples over. But we can make our test much more general and more precise. We apply a force to the body to be tested, tending to make it move a little. This movement changes the distribution of forces acting on the body, and we then notice how the resultant force compares with the original disturbing force. We find that in the case of the sphere there is no resultant force (ignoring simple inertia). In the case of the cube, or any body in stable equilibrium, we find that the resultant force always acts *against* the original disturbing force, while in the case of the cone the resultant force acts *with* the disturbing force. Consequently, by comparing the resultant force with the original disturbing force we may decide the question of the type of equilibrium in a purely objective and quantitative manner. (The word "equilibrium" is used to include unstable as well as stable equilibrium.)

We must notice some minor points at this stage. Firstly, we notice that "stable equilibrium" does *not* mean immobility. A body, e.g. a pendulum swinging, may vary considerably and yet be in stable equilibrium the whole time. Secondly, we note that the concept of "equilibrium" is essentially a dynamic one. If we just look at the three bodies on our table and do nothing with them the concept of equilibrium can hardly be said to have any particular meaning. It is only when we disturb the bodies and observe their subsequent reactions that the concept develops its full meaning.

But our definition so far is not quite precise. Equilibrium belongs properly to a single variable and not to an entire physical body. This may be demonstrated most clearly by an example. Consider a square card exactly balanced on one edge. For displacements at right angles to the plane of the card it is in unstable equilibrium, while for displacements parallel with the plane of the card it is, theoretically at least, in stable equilibrium. The point is that there are two separate variables to be considered (two angles of deviation), and either may be stable or unstable independently of the other.

We may now define stable equilibrium more precisely: a variable is in stable equilibrium if, when it is disturbed, reactive forces are set up which act back on the variable so as to *oppose* the initial disturbance. If they go with it then the variable is in unstable equilibrium.

Since the reactive forces are set up by the change in the variable and then

come back to the variable to affect it, we are clearly dealing with a functional circuit. A straightforward example is given by an incubator with gas-flame and capsule as regulator. We will trace the functional circuit. We may start with the temperature of the air in the incubator. (It is to be noted that every variable mentioned is capable of direct measurement.) We have:

Temperature of incubator	controls	temperature of capsule.
,, of capsule	,,	diameter of capsule.
Diameter of capsule	,,	volume of gas flowing per minute.
Volume of gas flowing	,,	output of heat per minute.
Output of heat	,,	temperature of incubator.

So we have arrived back at the beginning and have demonstrated the real physical existence of the circuit.

We see therefore that the concept of "equilibrium" necessarily involves the existence of a functional circuit. We may symbolize this by writing $x_1 \rightleftarrows x_2$, where x_1 and x_2 are variables and the arrow $(x_1 \rightarrow x_2)$ means that the value of x_1 determines the value of x_2.

Next we have the inverse problem: Does the existence of a circuit necessarily involve an equilibrium? The answer is certainly "Yes," for if we have $a_1 \rightleftarrows a_2$, then by the upper arrow, a disturbance of a_1 will necessarily disturb a_2 and, by the lower arrow, this will disturb a_1. This latter disturbance, being a change of the variable a_1, will be comparable (or dimensionally similar) to the initial disturbance of a_1 and must therefore compound with it. This means that it will reinforce it or counteract it, thus giving the conditions of equilibrium (unstable or stable respectively). (The precise after-effect will depend on the particular hypothesis we may make about the compounding of the first and the second disturbance.)

The next point is that all systems in equilibrium have a "neutral point." In general, if we have variables $x_1, x_2, \ldots x_n$, the change of a particular variable x_i will be given by equations of the type.

$$\Delta x_i = f_i(x_1, x_2, \ldots x_n) \qquad (i = 1, 2, \ldots n).$$

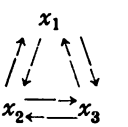
If we put all $f_i = 0$ we have n equations involving n variables and the equations may, in general, be solved for the variables. We thus obtain a particular set of values of the variables, $X_1, X_2, \ldots X_n$. If all $x_i = X_i$ then all Δx_i are 0, and the system will tend to undergo no change. This multi-dimensional point $X_1, X_2, \ldots X_n$ may properly be called the "neutral point" of the equilibrium. If the system is stable it will tend to come to rest at this point, while if it is unstable the system, if at this point, will undergo no immediate change (e.g. a cone exactly balanced on its point). The importance of this is that in talking of a stable system we are implicitly assuming that we are dealing with deviations from this neutral point. Thus in the case of a stable thermostat

the neutral point is the temperature about which the thermostat is continually oscillating and to which it is continually tending.

This leads to the next concept of a "range" of stability. If we consider stable systems we find that they are stable for small deviations from the neutral point but that, if pushed too far from their neutral point, they ultimately become unstable. Thus a cube resting on one face is stable for tilts up to 45°. If it passes this deviation, however, it becomes unstable and falls over. Similarly a thermostat is stable for fairly large deviations of temperature from its neutral point, but if the temperature becomes too high the metal, etc., will eventually melt and the system will lose its stability. The maximal deviation from the neutral point which still allows the system to remain stable may be called the "range of stability."

An interesting example of "range of stability" is given by explosives. Commercial explosives must be stable substances. Were they in unstable equilibrium the minutest disturbance would cause them to break down. For this reason a useful explosive must have a fairly large range of stability in order that it may stand up to the processes of manufacturing and subsequent handling. It is only when it is driven outside this range of stability that it should demonstrate its marked instability.

So far the discussion of equilibrium has been simple, and it may be objected that so simple a concept is quite incapable of dealing with the enormous complexity of function of known living organisms. This objection, however, does not appear to be valid, for the subject of equilibrium soon leads into much greater complexities. Thus instead of a single circuit we may have two circuits joined by a common variable: $x_1 \rightleftarrows x_2 \rightleftarrows x_3$. We may have three variables influencing one another to form a compound circuit:



and so on. In such cases the properties of the system from the point of view of equilibrium soon become much more complicated. We will give an example of the curious and interesting properties of such compound systems. If we take our incubator again and consider the variable "temperature in the incubator" to be the main variable (x_1), and regard the variable "diameter of the capsule" as a stabilizing variable (x_2) acting on x_1, and if we join x_2 on to a new circuit with a variable x_3 which has the effect of stabilizing x_2, then the effect of "stabilizing the stabilizer" is to render x_1 *less* stable. It will be seen, therefore, that there is no lack of complexity when we come to deal with compound systems of circuits.

Another point to be noticed in compound systems is that the behaviour of a given variable is now a function of the whole system, and this, again, leads to an endlessly increasing complexity.

Finally, there is one point of fundamental importance which must be grasped. It is that stable equilibrium is necessary for *existence*, and that systems in unstable equilibrium inevitably destroy themselves. Consequently, if we find that a system *persists*, in spite of the usual small disturbances which affect every physical body, then we may draw the conclusion with absolute certainty that the system must be in stable equilibrium. This may sound dogmatic, but I can see no escape from this deduction.

To give an example, it is well known that there are stable and unstable chemical substances. And it is a fact that if we look round any laboratory's stock of chemicals we shall find only stable chemicals on the shelves. Not only is this a fact: it is a logical necessity. Again, while it is common to find bricks resting on one face, it is rare to find bricks exactly balanced on one edge. And it is clear that this must be so.

Having given this preliminary survey of the nature of "equilibrium" we may now proceed to the discussion.

It is clear that the adaptiveness of animal behaviour is not its only feature. There are other aspects and problems such as that of memory, etc. With such we are not concerned.

There are certainly many examples, in animal organization, of variables which are known definitely to be in stable equilibrium. Thus the *p*H of the blood is stabilized by the circuit: *p*H of blood → activity of the medulla → rate and depth of breathing → rate of removal of CO_2 → concentration of CO_2 in the blood → *p*H of the blood. It should be noted that this is not quite as simple as it looks, for were any one of the linkages reversed in its effect the system would then be in *unstable* equilibrium, and this would quickly result in the death of the animal.

Pupil diameter is similarly in stable equilibrium through its optical effect on the intensity of the light on the retina and the subsequent changes through the nervous system. This is a slightly more complex circuit, since the neutral point is no longer absolutely fixed but depends on the intensity of the illumination outside the eye.

The blood sugar of an animal is also usually in stable equilibrium, for it is well known that if the blood sugar drops, through lack of food, complex behaviour is set up which results eventually in the blood sugar *rising*.

There is no necessity to give many examples. Reflection soon shows that vast numbers of variables associated with the animal are all in stable equilibrium. Not only is this so as an observed fact, but it is clear that it *must* be so because any variable or system in unstable equilibrium inevitably destroys itself.

The question of whether adaptiveness is *always* equivalent to "stable equilibrium" is difficult. First we must study the nature of "adaptiveness" a little closer.

We note that in all cases adaptiveness is shown only in relation to some

specific situation: an animal in a void can show neither good nor bad adaptation. Further, it is clear that this situation or environment must affect the animal in some manner, i.e. must disturb it, for if it has no effect on the animal it does not exist as far as the animal is concerned. Further, for adaptive behaviour, the animal must affect the environment in some manner, i.e. must change it, since otherwise the animal is just receiving the stimulus without responding to it. This means that we are dealing with a circuit, for we have, first: environment has an effect on the animal, and then: the animal has some effect on the environment. The concept of adaptive behaviour deals with the relationship between the two effects. It becomes meaningless if we try to remove one of the effects. Uexküll (1926) recognized this clearly and insisted that the animal and its environment must be thought of as a series of "function circles." He did not, however, reach the next deduction, which is that every reacting circuit must involve some state of equilibrium, either stable, neutral or unstable. The moment we see that "adaptiveness" implies a circuit and that a circuit implies an equilibrium, we can see at once that this equilibrium must be of the stable type, for any unstable variable destroys itself. And it is precisely the main feature of adaptive behaviour that it enables the animal to continue to exist.

Whether "adaptiveness" is always interchangeable with "stable equilibrium" must remain an open question, for the subject is a large one. It is clear, however, that there is a striking similarity between the two concepts as far as their objective features are concerned, and it seems reasonable, as a working hypothesis, to explore the possibilities that they may prove to be identical.

Summary.

Animal and human behaviour shows many features. Among them is the peculiar phenomenon of "adaptiveness." Although this fact is easily recognized in any given case, yet it is difficult to define with precision.

It is suggested here that adaptive behaviour may be identical with the behaviour of a system in stable equilibrium, and that this latter concept may, with advantage, be substituted for the former.

The advantages of this latter concept are that (1) it is purely objective, (2) it avoids all metaphysical complications of "purpose," (3) it is precise in its definition, and (4) it lends itself immediately to quantitative studies.

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HAS FEAR ANY THERAPEUTIC SIGNIFICANCE IN CONVULSION THERAPY?

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It is not uncommonly believed that convulsion treatment produces its successes mainly or entirely through the fear which it engenders. This opinion, more often implied than definitely stated, has been crystallized by McCowan (1), who boldly wrote :

" No reasonable explanation of the action of hypoglycæmic shock or of epileptic fits in the cure of schizophrenia is forthcoming, and I would suggest as a possibility that as with the surprise bath and the swinging bed, the ' modus operandi ' may be the bringing of the patient into touch with reality through the strong stimulation of the emotion of fear," and " that the intense apprehension felt by the patient after an injection of cardiazol, and so feared by the patient, may be akin to the apprehension of the patient threatened with the swinging bed. The exponents of the latter pointed out that fear of repetition was an important element in success."

The little experimental and statistical work on the subject that I can trace does not support the role of fear as a therapeutic agent.

Blaurock *et al.* (2) divided a number of cases into three groups. To the first group they administered convulsive doses of cardiazol ; to the second similar doses, but too slowly for convulsions to occur ; for the third group they substituted normal saline, of course without the patients' knowledge. All their subjects had previously experienced induced convulsions and were therefore apprehension-sensitive. The authors found that marked effects on the vital signs (blood-pressure, pulse, respiration) and on the blood pH and CO_2 were not secured unless a convulsion occurred.

They conclude that the influence of the treatment is produced through the fit rather than by fear or by the pharmacological action of the drug.

Cohen (3) induced definite and often prolonged states of fear in 19 patients by means of ten successive daily injections of cardiazol, administered too slowly to produce fits. A month after this course the 16 patients of the group whose mental state was unaffected were given ten successive daily cardiazol fits. The clinical results showed that " the procedure with ' induced fear ' was of less therapeutic value than that characterized by convulsions."

Low *et al.* (4) studied the fear reaction of 66 cardiazol treated cases. They report : " 30 were labelled as ' always fearful,' of these 10 recovered and 20

failed to recover. Of 26 patients who were 'usually fearful,' 11 recovered. Of 10 patients who either were 'indifferent' or 'spontaneously asked for treatment,' 9 recovered. Patients who subsequently recovered exhibited less fear of the treatment than those who did not recover." Cohen (3) confirms this view from his experience of 146 schizophrenic patients.

This paper attempts no more than to record the degree of fear engendered by convulsion therapy in 275 cases treated at Bexley Hospital, and to discover whether there is any obvious correlation between the emotional reaction and the success of the treatment.

Method of Assessment.

In compiling this record two assessments incurring an observer's judgment have been necessary—that of the amount of fear experienced by each patient, and that of the result of the treatment. Such judgments are apt to be vitiated by the predilection of the observer, and statistics compiled from them are valueless unless the strictest precautions are taken to eliminate any possible bias. Bearing this in mind, the assessments of the degree of fear of the treatment were assigned to the sisters and nurses, who not only had charge of the patients during their course of treatment, but were present during the convulsion-episodes. They were thus in a position to observe the patients' reactions between the fits as well as immediately prior to each injection. They were asked merely to categorize the amount of fear displayed by each patient in + or — terms according to Table I. The staff concerned were not aware of the object of the inquiry, and the patients' subsequent fate was not considered at the time.

The assessment of the result of treatment has been mainly in my hands; consequently it may err on the side of optimism, although I have tried to conform honestly with Muller's criteria of recovery, remission, etc. (Muller (5), Cook (6)). Whether or not I have altogether succeeded has little bearing on the present research, as the assessments were made, except in a few very recent cases, before this investigation was thought of, and therefore before any subjectively desired correlation could exert its influence.

Table I.—*Symbols Expressing Degrees of Fear.*

+++	Extreme dread with manifest terror even at the mention of the injection.
++	Considerable apprehension and agitation.
+	Definite but not excessive fear of the injections.
±	Normal reaction elicited by a course of mildly painful injections, i.e. a certain amount of dislike, but little or no actual fear.
—	Indifference.

TABLE II.—*Relation of Fear to Results of Treatment (Males).*

Degree of fear.	Recovered.		Remitted.		Temporary remission.		Improved.		Temporary improvement.		Not improved.		Total.	
+++	1		0		1		0		1		3		6	
++	5	12	0	3	1	3	3	8	8	15	9	17	26	58
+	6		3		1		5		6		5		26	
±	7	16	3	6	1	2	2	5	3	9	6	19	22	57
—	9		3		1		3		6		13		35	
Total	28		9		5		13		24		36		115	

TABLE III.—*Relation of Fear to Results of Treatment (Females).*

Degree of fear.	Recovered.		Remitted.		Temporary remission.		Improved.		Temporary improvement.		Not improved.		Total.	
+++	0		0		0		1		1		3		5	
++	10	21	3	4	0	2	2	3	3	10	12	30	30	70
+	11		1		2		0		6		15		35	
±	14	47	0	2	0	3	0	3	6	7	10	28	30	90
—	33		2		3		3		1		18		60	
Total	68		6		5		6		17		58		160	

TABLE IV.—*Relation of Fear to Results of Treatment (Males and Females).*

Degree of fear.	Recovered.		Remitted.		Temporary remission.		Improved.		Temporary improvement.		Not improved.		Total.	
+++	1		0		1		1		2		6		11	
++	15	33	3	7	1	5	5	11	11	25	21	47	56	128
+	17		4		3		5		12		20		61	
±	21	63	3	8	1	5	2	8	9	16	16	47	52	147
—	42		5		4		6		7		31		95	
Total	96		15		10		19		41		94		275	

TABLE V.—*Relation of Fear to Results of Treatment in Recovered or Remitted and in Not Improved Cases.*

Degree of fear.	Recovered or remitted.			Not improved.		
	Males.	Females.	Total.	Males.	Females.	Total.
+++	1	0	1	3	3	6
++	5 } 15	13 } 25	18 } 40	9 } 17	12 } 30	21 } 47
+	9	12	21	5	15	20
±	10 } 22	14 } 49	24 } 71	6 } 19	10 } 28	16 } 47
—	12	35	47	13	18	31
Total	37	74	111	36	58	94

DISCUSSION OF RESULTS (Tables II, III, IV, V).

It will be seen at once that, while no definite correlation between emotional reaction and result of treatment can be established, there is a general tendency for greater success to attend the treatment of patients who showed little or no fear.

If doubtful results of treatment are omitted (Table V), we find that out of 111 patients who recovered or remitted, 40 (36 per cent.) showed definite fear, and 71 (64 per cent.) did not, while for the 94 patients who did not improve, the respective figures were 47 (50 per cent.) and 47 (50 per cent.). Extreme terror (+++) was noted only in 11 (4 per cent.) out of all cases, and of these 1 alone recovered.

Indifference was shown by 95 (34·5 per cent.) out of all cases, and of these 42 (44·2 per cent.) recovered.

Despite the direction towards which these findings point, it would be folly to argue from them that fear tends to inhibit recovery or that its presence contra-indicates convulsion treatment. Too many recoveries occur in the most agitated of cases for this to be seriously considered. It would appear more probable that some of the factors contributing to a bad prognosis are also conducive to the formation of morbid apprehensiveness. The word "morbid" is used advisedly, because in my experience states of grave fear are of the rarest occurrence, when insight is returning and remission on the way to completion.

FACTORS CONCERNED IN PRODUCING EXCESSIVE FEAR.

The degree of emotional reaction to convulsion treatment appears to depend mainly on four factors: (1) the general temperament of the patient, (2) the influence of the prevalent psychotic phase, (3) the degree of accessibility, (4) the amount of memory for the convulsion-episode. Of these, the second is probably the most important.

1. *General Temperament.*

The timid, suspicious individual, particularly if he is also obtuse and obstinate, might be expected to show and in fact does show an apprehension which is above the average. Again, a number of people, many of them highly intelligent, are temperamentally unable to overcome their horror of general anæsthesia, quite disproportionate to the dictates of reason. Such subjects naturally experience a similar dread of convulsion therapy, with its even more rapid lapse into unconsciousness.

2. *Prevalent Psychotic Phase.*

Many patients appear to incorporate the unpleasantness of the convulsion-episode with imaginary horrors symptomatic of their psychosis. Such cases, whose interpretations may be inconceivably terrifying, are amongst the most apprehensive and least accessible to explanation. On the other hand some are so preoccupied with bizarre ideas of a fearful nature that they scarcely notice any external unpleasantness.

The influence of the particular phase of the illness upon the patient's emotional reaction to treatment is well shown in some cases who have undergone more than one series of fits.

CASE 1.—A girl, aged 18, admitted in February, 1937, started a course of cardiazol convulsions in July, 1937, when she was highly excited and hallucinated. After six fits treatment was stopped owing partly to the violence of her agitation and apprehension, but mainly to the occurrence of regular post-convulsion maniacal states amounting almost to furore. Fits were restarted in March, 1938, when she had sunk into a semi-stuporose condition, in which she sat staring dully before her, was faulty in habits, and required hand-feeding and all other attentions. In this state she displayed no emotional reaction either before or after the fits, but her mental condition improved steadily and an uneventful recovery took place. She has now earned her living as a shop-assistant since her discharge in September, 1938, and remains very bright and alert.

CASE 2.—A married woman, aged 29, admitted in July, 1937, suffering from a schizophrenic paranoid reaction state, recovered after 13 fits, which she experienced without any signs of apprehension. In March, 1939, she was readmitted with a similar attack, except that she was considerably more suspicious and hostile. Twenty-five convulsions were induced with subsequent recovery, but this time she displayed a very definite fear of the treatment. This case demonstrates nicely that the result of treatment is not necessarily determined by the patient's emotional reaction.

3. *Accessibility.*

Except in cases of stupor or gross emotional apathy, the degree of fear tends to vary inversely with that of accessibility. Most of the very agitated (+++) patients were totally inaccessible, exhibiting a blind terror, which could not be influenced in any way. The effect of accessibility and insight was shown by a number of patients, who at first manifested every sign of dread, but as improvement set in began to realize that the injections were a form of treatment—not very pleasant, but apparently successful—and accordingly lost their agitation and the sharp edge of their fear. This observation, the truth of which is confirmed by my colleagues and by the nursing staff, does not coincide with Giorgi's statement (7) that as patients improve the aversion to treatment becomes increasingly greater. Such cases do occur, but in our experience the reverse is far more usual.

4. *Memory of Convulsion-episode.*

Patients differ considerably in their memory for the convulsion-episodes. Many can relate the whole course of events up to their loss of consciousness; a few on recovering consciousness ask when they are going to have the injection. The amnesia is variable, even in the same patient, but there are few who have not at least some vague idea of unpleasantness associated with the episode. In this connection my colleagues and I have failed to confirm the observation of Walk and Mayer-Gross (8) that triazol fits produce a more effective amnesia than cardiazol fits.

Even partial amnesia helps to allay subsequent apprehension, and a state of complete amnesia, sufficiently retrograde to include the preparatory phases, should go far to remove one of the greatest drawbacks to convulsion therapy.

Conclusions.

Quite apart from the indications of the statistics presented here, close personal observation of more than half of these 275 cases leads me to believe that fear of treatment plays no serious part in producing or accelerating remission. On the other hand, there is no valid reason for supposing that it inhibits recovery.

The question of the role of fear assumes a particular importance in connection with the recent introduction of electrically induced fits. By this method unconsciousness is nearly instantaneous and complete amnesia for the episode is claimed. If fear were in truth the basis of recovery and if it is abolished (except in those who have a temperamental dread of artificial unconsciousness, however produced) by electrical induction of fits, this method is foredoomed to failure. As it is, the results already claimed by workers in this field as well

as the findings of this paper tend to discredit the alleged curative role of fear in convulsion therapy.

SUMMARY.

1. The degree of fear presented in 275 cases of cardiazol and triazol convulsion treatment is recorded and correlated with the result of treatment. The findings supply no evidence for assuming that fear exerts any curative influence.

2. Factors influencing the production of emotional reaction to the convulsion episode are discussed.

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found. Only those tests were applied that have already proved reliable. We used the following methods:

1. Bilirubin test in blood (van den Bergh), qualitative and quantitative.
2. Takata reaction.
3. Sedimentation of blood corpuscles.
4. Urobilin test in urine (Schlesinger).
5. Proof of histidine in the urine (Adler-Kapeller).
6. Conversion of sodium benzoate into hippuric acid (Quick).

The significance of the single tests may be shortly stated:

1. Bilirubin is an isomer of hematoporphyrin, the iron-free derivative obtained from haematin by the action of strong acids. The van den Bergh reaction for bilirubin in blood-serum involves the development of a pink to red colour by the interaction of diazobenzene-sulphanilic acid with bilirubin. According to Schellong, the relation of albumin to globulin is essential for the direct diazo-coupling. Therefore this reaction is concerned with the tests for examining protein-metabolism. Büchler found increased bilirubin-content in 90 per cent. of depressions. Jahn and Greving found low bilirubin in 21 of 27 catatonic stupors, and postulated an increased erythropoiesis and diminished decomposition. These authors were able to prove the characteristic thickening of blood, which is founded on an increased erythropoiesis with diminished decomposition. In five fatal cases of catatonia the authors also found a thickening of blood, and as a cause of the increased erythropiesis a red metaplasia of the long bones was mentioned.

2. Takata: This reaction is especially positive in cases of liver cirrhosis and liver atrophy. For this reaction the albumin-globulin quotient is of outstanding importance. Dirr and Meyer report about 4,500 reactions, in which they nearly always found a relative increase of globulin. The effecting cause is to be seen in damage to the protein-forming organs, especially the liver. The reaction was not influenced in their experiments by the decomposition-products of sugar and fats, whereas after adding di-amino-acids or amines the Takata reaction became positive. These results lead to the unequivocal conclusion that only a qualitative and perhaps also a quantitative change of the composition of the serum proteins is responsible for the result of the Takata reaction. The degree of the precipitation corresponds to the parenchymatous degeneration of the liver. A negative reaction consists of the absence or only slight presence of cloudiness. Two or three times as much cloudiness, but no precipitation, means a doubtful result. Precipitation in one tube is a positive reaction, but in the present investigation no reaction was considered positive unless precipitation occurred in at least two tubes.

3. Sedimentation rate: An unduly rapid sedimentation has been claimed to be due to an accumulation of albuminous decomposition products in plasma which upset the balance of plasma proteins. The presence of fibrinogen formed in the liver is an essential factor in the maintenance of the sedimentation rate. Dirr and Meyer mostly found a rapid sedimentation rate when the Takata reaction was positive. Schrijver describes a tendency to increased sedimentation-rate in cases showing an atypical course of schizophrenia (remission or absence of progress to dementia). Freeman has frequently observed a rapid fall of cells in excited or catatonic cases.

4. Urobilin: Urobilin is found in small quantities in normal urine. When there is liver damage the liver allows more urobilinogen, the precursor of urobilin, to get through. The test was only regarded as positive when a distinct green fluorescence was obvious.

5. Histidine: Histidine belongs to the basic amino-acids, and is found in globin, the albuminous factor of the haemoglobin. Its decomposition in the liver through histidase has been thoroughly examined, and it is found to be completely decom-

posed by liver-pulp in the experiment. Pulps of other organs do not have the same effect (Edlbacher). Schimmelpfeng believes the presence of histidine in urine to be pathognomonic of almost all states of depression. The test was originated by Adler-Kapeller.

6. Hippuric acid: One of the most important functions of the liver is the detoxication of noxious substances which have been absorbed by the gut. The best known example of this action is the formation of benzoyl glycine or hippuric acid which is synthetized from benzoic acid and glycine in the liver. The synthesis of hippuric acid depends partly on the speed with which glycine is utilized by the liver, which is also mainly responsible for its production. It is a fact for instance that, after benzoic acid has been given, the concentration of the secreted hippuric acid per hour is constant within certain limits and independent of the quantity of the benzoic acid. Therefore the presumption of a diminished formation of glycine in cases of degeneration of the liver was justified. With the diminished formation of glycine there is also a diminished detoxication of the benzoic acid in consequence of the disturbed synthesis of hippuric acid. Bearing this in mind, Quick worked out a test which takes into account the share of the liver in the synthesis of hippuric acid. The average excretion of hippuric acid amounts to 3·43 gm. after a dose of 6 gm. sodium benzoate. The upper limit in normal cases is 3·55 gm., the lower limit 3·0 gm. Quick found a diminished excretion in cases where liver damage was beyond question. There are good reasons for presuming that the diminished formation of hippuric acid takes places before clinical symptoms of liver damage are obvious. Quastel has examined secretion of hippuric acid in cases of mental disease. He found that in catatonia there is regularly a diminished secretion of hippuric acid in contradistinction to the other groups of schizophrenia and the non-schizophrenic psychoses. A further classification of non-schizophrenic psychoses is not marked by the author. The average of the secretion of hippuric acid in non-catatonic schizophrenias is 3·4 gm. and in the catatonic group 2·2 gm. Quastel assumes that the abnormal secretion of hippuric acid is partly responsible for the development of the psychoses. The objection that there might be a delay of absorption of benzoic acid from the gut has been proved not to be valid by the same worker.

In 17 cases of our schizophrenic and depressive groups the illness had passed the acute phase. The patients had entered a steadier state of their illness after a duration of at least three years. In other cases there were symptoms which made it unlikely that a change of the condition of the illness would still occur. In the majority of cases, therefore, we were in a position to reckon with a fairly steady state of the primary symptoms. The tests were repeated if there was a change in the condition, as, for example, a sudden change from a depressive to a manic phase. The tests were also repeated if it was doubtful whether excretions were corresponding to the intake of fluid. This often happened with catatonic and stuporous patients. Tests were not repeated with patients when mere accidental emotions occurred, for investigations which were made with normal controls first in balanced temper and then immediately after emotional fluctuation (resentment, reactive depressive mood) showed that these influences did not affect the result of the Takata reaction, the bilirubin content of blood or the sedimentation rate. Secretion of histidine remained uninfluenced by temporary emotions in these controls, in contrast to the lack of influence of the emotions on the tests concerning the protein metabolism corresponding to emotional changes. The wide investigations of

Diethelm confirm these findings: the more acute an emotion, the more marked are the changes in the sugar-tolerance curves.

Kraepelin's classification of the psychoses was used as a clinical basis in these investigations, but we made a further separation on the basis of heredity between depressions with anxiety (forming the greater part of involutional depressions) and manic-depressive psychoses. Among 18 depressions were eleven manic-depressives, five involutional depressions, two reactive depressions. Among the schizophrenias were eight catatonias and four hebephrenias. Seven cases of the depressions displayed catatonic features; three of them belonged to the manic-depressive group, four to the involutional depressions.

The conception of catatonia as set forth by Kahlbaum, and which still prevails, is not pathognomonic of any particular form of disease. Depressive states resembling catatonia occur in cases of schizophrenia, in cases of depression, especially in cases of middle-aged persons, and in cases of senile dementia. Kahlbaum's idea of catatonia embraces a number of disturbances which in many respects resemble extrapyramidal symptoms. Among our cases were vegetative symptoms, such as disturbances of sleep and skin secretion, and of motor symptoms, such as akinesia, hyperkinesia and flexibilitas cerea. In all depressions showing a positive result with Quick's reaction we found psychomotor disturbances. In Cases 9, 10, 11, 14 and 15, lack of movement, rigidity of muscles and loss of swinging of the arms when walking were obvious. Parkinsonism could be excluded. In contrast to the extra-pyramidal disturbances in which the automatic mechanism of movement does not continue in a normal way, and new efforts of will are frequently necessary, cases of catatonia show a tendency for movement not to start at all, but when once fully initiated the automatic movement runs steadily on.

The results of Quick's reaction was positive in all catatonias (schizophrenias). Thus we were able to confirm the results of Quastel. Moreover, we discovered that in those cases of depressions which showed catatonic features, a reduction of secretion of hippuric acid was found also. In two cases the secretion was just below the limit of normal. The content of bilirubin was normal in 22 cases. In the catatonic (schizophrenic) group we found a diminution in six cases, and the same result in three cases of depressions with catatonic symptoms. The diminution may be pathognomonic of catatonia (Jahn and Greving).

In 12 cases histidine was found in the urine. We could not confirm the excretion of histidine in each case of depression, as has been asserted by Schimmelpfeng. Among the catatonias (schizophrenia) histidine was found five times; among the depressions with catatonic features were five positive tests; two pure manic-depressive cases had the same result. It is striking that none of the cases of non-catatonic schizophrenia excreted histidine.

Among 16 cases which showed urobilin in the urine, there were no results showing any relation to a particular group of psychoses.

The Takata reaction was positive in 12 cases. Among them were two

alcoholic psychoses. The reaction was positive in more cases of catatonic schizophrenia (six out of eight) than in all other groups. Four depressions with catatonic symptoms showed a positive Takata reaction. In non-catatonic schizophrenias and depressions the Takata reaction was negative.

Rapid sedimentation was found in five cases of catatonia (schizophrenia). The result coincides approximately with the result of the Takata reaction. Five catatonic depressions and one alcoholic psychosis also had rapid sedimentation.

Shortly summarized, the Quick reaction was positive in the majority of psychoses with catatonic symptoms (two at the border of the normal secretion). The other reactions, except urobilin, showed prevailing positive results in the catatonic psychoses (schizophrenias and depressions). Though the number of the cases is comparatively small, in the catatonic cases the tests are so frequently positive that this cannot be due to mere chance. In those cases where the tests had to be repeated, the result was the same or almost the same. The discrepancy, shown by different results from the various tests in the same cases, suggests that each test estimates only a partial function of the liver. Therefore it is necessary to apply several tests in each case.

These results show first only whether the liver is involved in any way in the course of disease. They do not show whether the liver damage is secondary to brain disturbance or primary, where the brain disturbance would be the result and not the cause of liver impairment. The liver disturbance, when secondary, may be apt to produce in its turn psychic symptoms or to aggravate those already present. Lingjaerde, who divides his schizophrenias into active and passive phases, without further classification, has found liver insufficiency in 80% of the first group. Lingjaerde assumes that undernutrition may be partly responsible for the pathogenesis of the disturbances of liver function. An inspection of the tables of weight of our patients from the beginning of their period in hospital shows the following result: It may be anticipated that in cases of refusal of food the artificial feeding exceeds abundantly the minimum of necessary calories. Large losses in weight did not generally occur, even in cases of depression. We may mention in this connection the result of Roggenbau, who saw permanent increase of weight in depressions and schizophrenias when he added to the general diet nutritive material such as glucose and cod-liver oil. As soon as the patients were left to attend to their own feeding on a diet free from extras the curve changed to the opposite. From an empirical point of view it is not likely that in our cases undernutrition has had any important share in the liver damage. It is much more likely that the liver damage was caused by split products of proteins and toxins absorbed from the gut. As mentioned in the beginning, Jahn and Greving have found important changes in the blood in connection with diminished bilirubin in serum. The same authors were able to produce by means of histamine injections the same symptoms in the blood, including red change of the white marrow of the long

bones, as in catatonias. They also think it possible that toxic substances similar to histamine play a part in the causation of the bodily disturbances in catatonic cases. This assumption finds support also in investigations and results recently obtained by Dirr and Strehle. During their research on the albuminous bodies of serum and their changes under pathological conditions, these workers found that with the analysis of constituent parts quantitative differences appeared in those sera which showed a positive Takata-reaction. They believe they have proved that many diseases are accompanied by changes of the albuminous bodies of serum and interfere profoundly with the structure of the molecule. They think that it is precisely these changes of the molecule which are finally responsible for the increase of globulins and for the lack of capacity for binding toxins and other substances. The damage to the cell is obviously responsible for the change in the composition of the amino-acids of serum-proteins. The authors have pursued the fate of amino-acids under physiological conditions. They succeeded one hour after intravenous injection of arginine in recovering a serum protein which exceeded considerably the normal content of arginine. This result may open new therapeutic prospects as to the physiology of the albuminous bodies in serum and the utilization of amino-acids : the accumulation of protein in the liver cells is dependent on the state of nutrition and occurs only after the ingestion of protein, and not in any way after fats and carbohydrates. The power of deaminating foreign amino-acids is a function of the sound liver cell. A diminution in the intake of protein may contribute to a return to normal conditions in the liver, where arginine protein is formed, and thus the progressive accumulation of proteins in the liver would be prevented.

How far entero-hepatic disturbances and toxic factors have a pathogenic importance for psychoses cannot be generally decided. But if in a certain group of psychoses certain liver-function tests have a positive result again and again, one may be allowed to assume that the liver has a share in the aetiology of these groups. The experiments of Claude, Baruk and Olivier support this view. These authors have injected the bile of patients suffering from catarrhal jaundice into pigeons. One and a half to two hours after the injection the animals showed cataleptic states. These states were not produced with the bile from patients suffering from other diseases. De Jong and Baruk come to the conclusion that in principle there is an entire conformity of experimental and clinical catatonia, as exemplified by symptoms such as catalepsy, negativism, hyperkinesia, mannerism, stereotypy, and vegetative disturbances. The writer is of the opinion that interesting information might be obtained from experiments utilizing the bile of catatonic patients withdrawn by duodenal tube.

The question arises why many serious liver diseases do not cause psychic symptoms. It can be answered at present only by introducing the general idea of individual disposition. Darusch and Cremer report distinct cataleptic symptoms in children with icterus catarrhalis. It is hypothetical whether the

juvenile brain possesses a special affinity for the toxins circulating in the blood in consequence of liver disturbance. Just as the juvenile brain reacts in a different way from the adult brain to the noxa of encephalitis lethargica, a similar difference in the modes of reaction at different ages may also call for consideration under the present heading. In cases of catatonia a feebleness of the brain-stem may be in question, but this is only a reflective suggestion which arises in this connection.

As already mentioned, the conception of catatonia includes symptoms very similar to extrapyramidal symptoms, the exact knowledge of which has been gained by analysis of extrapyramidal motor disturbances. Leonhardt especially has occupied himself in elucidating the relations between catatonic and extrapyramidal states. He divides the schizophrenic states of dementia into the "rigid defect-catatonia" and the "buffoon-like defect-catatonia." They show close relation to the extrapyramidal illnesses, parkinsonism and chorea. Attitude, mimics, akinesia and states of tension of muscles display indeed a striking resemblance to the amyostatic syndrome, and the choreic catatonia with motor unrest in St. Vitus' dance. But there is still a difference, the extrapyramidal symptoms being of a more organic and peripheral nature, while the catatonia has its field at a higher level, more central and nearer to the cortex.

The analysis of extrapyramidal and catatonic symptoms and the considerations of those features common to both has stimulated investigations into the relations between brain and liver. In a large number of liver diseases Staedler has found histological changes in the brain entirely comparable to the histological changes of Wilson's disease. He had no doubt that all these changes which he believed to be characteristic of hepato-lenticular degeneration may arise also in liver diseases without clinical symptoms of this syndrome. As to Wilson's disease, one of its most typical features is that the hepatic lesion develops at an earlier period than the cerebral one. This may mean that the substances injurious to the organism are absorbed and neutralized by the liver, which is injured itself in this defensive work, and only when the insufficiency of the hepatic function increases does the injurious effect on the sensitive areas of the brain make itself felt.

In the same way as there is a relation between extrapyramidal and catatonic symptoms as reported above, we may assume that the same consideration is valid for the biochemistry of both illnesses, so far as liver damage is concerned.

In the large number of investigations we mentioned at the beginning, many bodily symptoms have been found in schizophrenias and depressions: the function of the thyroid gland, metabolism (especially of carbohydrates and fats), cholesterol, and the endocrine glands have been the subject of investigations. The significant fact about all these disturbances was the considerable fluctuation of the results (except the cholesterol), which was found not only with different patients under equal conditions and psychic states, but also with the

Histidine.

		Number of cases.	Negative.	Positive.
Non-catatonic	manic-depressive	8	6	2
	involutional-depressive	1	1	0
	reactive-depressive	2	2	0
	schizophrenia	4	4	0
	chronic alcoholism	2	2	0
Catatonic	manic-depressive	3	0	3
	involutional-depressive	4	2	2
	schizophrenia	8	3	5

Urobilin.

		Number of cases.	Negative.	Positive.
Non-catatonic	manic-depressive	8	7	1
	involutional-depressive	1	1	0
	reactive-depressive	2	2	0
	schizophrenia	4	2	2
	chronic alcoholism	2	0	2
Catatonic	manic-depressive	3	1	2
	involutional-depressive	4	0	4
	schizophrenia	8	3	5

Bilirubin.

		Number of cases.	Normal.	Diminished.
Non-catatonic	manic-depressive	8	8	0
	involutional-depressive	1	1	0
	reactive-depressive	2	2	0
	schizophrenia	4	4	0
	chronic alcoholism	2	2	0
Catatonic	manic-depressive	3	1	2
	involutional-depressive	4	3	1
	schizophrenia	7	1	6

Sedimentation Rate.

		Number of cases.	Normal.	Increased.
Non-catatonic	manic-depressive	8	8	0
	involutional-depressive	1	1	0
	reactive-depressive	2	2	0
	schizophrenia	4	4	0
	chronic alcoholism	2	1	1
Catatonic	manic-depressive	3	0	3
	involutional-depressive	4	2	2
	schizophrenia	7	2	5

Takata Reaction.

		Number of cases.	Negative.	Positive.
Non-catatonic	manic-depressive	8	8	0
	involutional-depressive	1	1	0
	reactive-depressive	2	2	0
	schizophrenia	4	4	0
	chronic alcoholism	2	0	2
Catatonic	manic-depressive	3	1	2
	involutional-depressive	4	2	2
	schizophrenia	7	1	6

Hippuric Acid in Terms of Benzoic Acid.

		Number of cases.	Average.
Non-catatonic	manic-depressive	8	3·42
	involutional-depressive	1	3·84
	reactive-depressive	2	3·55
	schizophrenia	4	3·34
	chronic alcoholism	2	3·62
Catatonic	manic-depressive	3	2·27
	involutional-depressive	4	2·53
	schizophrenia	8	2·31

	Manic-depressive.	Involutional-depressive.	Reactive-depressive.	Manic-depressive with catatonic symptoms.	Involutional-depressive with catatonic symptoms.	Catatonia (schizophrenia).	Non-catatonic schizophrenia.	Chronic alcoholism.
Number of cases	8	1	2	3	4	8	4	2
Takata	+ −	+ −	+ −	+ −	+ −	+ −	+ −	+ −
	.. 8	.. 1	.. 2	2 1	2 2	6 1	.. 4	2 ..
	n. inc.	n. inc.	n. inc.	n. inc.	n. inc.	n. inc.	n. inc.	n. inc.
Sedimentation rate	8 ..	1 ..	2 ..	.. 3	2 2	2 5	4 ..	1 1
	n. d.	n. d.	n. d.	n. d.	n. d.	n. d.	n. d.	n. d.
Bilirubin	8 ..	1 ..	2 ..	1 2	3 1	1 6	4 ..	2 ..
	+ −	+ −	+ −	+ −	+ −	+ −	+ −	+ −
Urobilin	1 7	.. 1	.. 2	2 1	4 ..	5 3	2 2	2 ..
	+ −	+ −	+ −	+ −	+ −	+ −	+ −	+ −
Histidine	2 6	.. 1	.. 2	3 ..	2 2	5 3	.. 4	.. 2
Hippuric acid in terms of benzoic acid—average	3·42	3·84	3·55	2·27	2·53	2·31	3·34	3·62

n. = normal ; inc. = increased ; d. = diminished.

	Male or female.	Diagnosis.	Beginning of illness.	Duration of present state.	Takata-reaction.	Sedimentation rate.	Bilirubin.	Urobilin.	Histidine.	Hippuric acid in terms of benzoic acid.
1	F.	Catatonia (schizophrenia)	1926	5 years	+	1/10	Diminished	+	+	1·87
2	F.	,, (,,)	1934	5 ,,	+	1/28	,,	+	+	2·23
3	M.	,, (,,)	1932	7 ,,	+	1/25	,,	—	—	2·35
4	F.	,, (,,)	1931	8 ,,	+	1/25	Normal	+	—	1·86
5	F.	,, (,,)	1917	?	+	1/20	Diminished	—	+	2·54
6	F.	,, (,,)	1924	10 years	..	..	..	+	+	2·52
7	F.	,, (,,)	Aug., 1931	8 ,,	+	1/25	Diminished	+	—	2·69
8	M.	,, (,,)	Feb., 1935	4 ,,	—	1/1	,,	—	+	2·40
9	F.	Manic-depressive catatonic symptoms	1926	8 ,,	+	1/20	,,	+	+	2·66
10	M.	Ditto	1901	1 year	—	1/21	Normal	+	+	1·97
11	M.	,,	1907	5 years	+	1/28	Diminished	—	+	2·20
12	M.	Involutional depression, catatonic symptoms.	1938	1 year	+	1/5	,,	+	—	2·85
13	F.	Ditto	Oct., 1935	3½ years	—	1/15	Normal	+	+	2·90
14	F.	Involutional depression, catatonic symptoms, stupor	1934	5 years	+	1/27	,,	+	—	2·52
15	M.	Involutional depression, catatonic symptoms	1935	4 ,,	—	1/19	,,	+	+	1·87
16	M.	Hebephrenia	1938	About ½ year	—	1/2	,,	—	—	3·43
17	M.	,,	Feb., 1937	2 years	—	1/5	,,	—	—	3·29
18	M.	Schizophrenia (paranoid)	Oct., 1937	2 ,,	—	1/5	,,	+	—	3·47
19	M.	Hebephrenia	1935	4 ,,	—	1/5	,,	+	—	3·16
20	M.	Manic-depressive (depression)	1936	1 year	—	1/12	,,	—	+	3·62
21	M.	Endogenous depression	?	About ½ year	—	1/11	,,	+	—	3·52
22	F.	Manic-depressive	Previous attacks	1 year	—	1/5	,,	—	+	3·05
23	F.	,,	1925	2 years	—	1/8	,,	—	—	3·50
24	F.	,,	2 previous attacks	4 months	—	1/6	,,	—	—	3·76
25	M.	Manic-depressive (depression)	1930	5 years	—	1/5	,,	—	—	3·27
26	M.	Ditto	1916	3 months	—	1/12	,,	—	—	3·22
27	F.	,,	Previous attacks	,,	—	1/4	,,	—	—	..
28	F.	Involutional depression	1936	3 years	—	1/3	,,	—	—	3·84
29	M.	Reactive depression	May, 1939	Several months	—	1/5	,,	—	—	3·45
30	F.	,, ,,	About 1 year		—	1/4	,,	—	—	3·65
31	F.	Chronic alcoholism	?	?	+	1/57	,,	+	—	..
32	M.	,, ,,	?	?	+	1/2	,,	+	—	3·62

same patients within short periods. In contrast to these results, the characteristic of our investigations was the constancy of our tests, made several times in many cases over longer periods but under the same conditions of nutrition. From the regularity of our results, we assume a definite connection between the catatonic symptoms (which remained unchanged during our observation), and the disturbances in protein metabolism and insufficient detoxicating power of the liver. Our hypothesis of the outstanding role of the liver in this process leads to the consideration of the possibility of influencing the detoxicating capacity of the liver. An alteration in this function of the liver would influence the composition of the amino-acids in the serum; and thus, in turn, would influence the constituents that are believed to play the main role in the function of protein.

A first attempt to reach this aim is seen in the use of decholin, containing dehydrocholic acid, which is considered to be a powerful stimulant for the formation of bile (which contains a large scale of substances being secreted as final products out of the body). Decholin has been introduced by de Crinis in the therapy of depressions. We saw in one case a surprising, but only temporary, improvement. The patient (depression with catatonic features), who had not shown the least change for several months, displayed, two hours after the decholin injection, a striking improvement lasting ten hours. At the same time food poor in albumin was given. The attempt to influence depressions by restrictions of albumin in food may be justified from another point of view. A shift of the acid-base equilibrium towards the acid side may cause depressive temper. Production of alkalosis by avoiding blood and milk in the food and by giving corresponding remedies is said to have improved single cases.

Summary.

The results obtained from liver tests in cases of schizophrenia, depressions and symptomatic psychoses have been made available to the nosologic demarcation of psychoses.

The following tests have been applied: Takata reaction, bilirubin tests in blood, sedimentation rate, urobilin test in urine, proof of histidine in the urine, and conversion of sodium benzoate into hippuric acid. Their relations to the protein metabolism and to the detoxicating capacity of the liver have been discussed.

Catatonia and depression with catatonic features have shown positive results much more frequently than the other groups of psychoses.

The conception of catatonia in the sense of Kahlbaum is not pathognomonic of any particular form of mental disease. It includes symptoms very similar to extrapyramidal disturbances.

The assumption that undernutrition may be partly responsible for the pathogenesis of disturbance of liver function is not generally valid. It is much

more likely that split products of proteins and toxins, absorbed by the gut, cause the liver damage. This view finds its support in investigations which have recently been made in the field of albuminous bodies in serum and in investigations concerning the fate of amino-acids under physiological conditions.

It is assumed that there is a close relationship between the psychoses with catatonic features and liver function.

The results of our investigations and of experiments with animals by other authors support this view. The relations between extrapyramidal motor and catatonic disturbances have been considered.

It is assumed that a similar comparison is valid for the biochemistry of both diseases, as far as liver damage is concerned.

In contrast to the results of investigations into the metabolism of carbohydrates and into the function of the endocrine glands, the constancy of the results of the liver function tests, applied to our cases over longer periods, is noteworthy. The possibility of influencing the detoxicating capacity of the liver and consequently of influencing the composition of the amino-acids in the serum has been suggested.

I am greatly indebted to the Committee of the Warneford Hospital for having granted the means to do this work.

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PROLONGED NARCOSIS WITH PARALDEHYDE AND DIAL.

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In the course of routine clinical work with excited patients I found that a dose of 3 drm. of paraldehyde with 3 gr. of dial (2 tablets) often produced a long and sound sleep where other powerful narcotics were relatively ineffective. It therefore seemed worth while to try the combination for prolonged narcosis. At the outset it was attractive in that it was cheap, was given by mouth, and that both drugs had a good reputation for efficiency and safety. Paraldehyde has also the special advantage of not being a cardiac depressant (Edmonds and Gunn, 1936; Sollman, 1937). Both drugs have been used before for prolonged narcosis, but not in this combination, and usually in much higher doses. [For references, see reviews of Palmer (1937) and Gillespie (1939).]

Technique.

The paraldehyde is prepared as a suspension in the strength of 1½ drm. of paraldehyde and 1 minim of liquor atropinae to the ounce. Dial is given in 1½ gr. tablets which may be crushed into the draught. The normal dose is 1 oz. of the paraldehyde mixture and one tablet of dial. The draught is further diluted with water for each dose. Even so, it is very unpleasant, and many patients like to suck a slice of lemon with it.

The preparation and nursing of the patient, daily urine testing, recording of temperature, pulse, respiration and amount of sleep are carried out as with somnifaine narcosis. The first dose of the day is given about ¾ hour after breakfast, and nearly always needs to be repeated in the evening. Many patients sleep quite satisfactorily on these two daily doses, but others need a further dose during either the afternoon or the night. This extra dose should be of the paraldehyde mixture only, without dial, so that dial is not given more than twice in 24 hours. Sometimes the dosage has to be increased after a few days. If so, double doses of paraldehyde mixture and 2 tablets of dial are given as required. Not more than 3 double doses of paraldehyde mixture (= 9 drm. of paraldehyde) and 4 tablets of dial (= 6 gr. of dial) should be given in 24 hours, though this dosage may be maintained for several days. In order to keep the technique as simple and uniform as possible, the rule should be—not more than 2 doses of paraldehyde and dial together, plus one extra dose of paraldehyde alone during 24 hours, whether in single or double strength. Experience taught that increasing the dosage beyond this level or doubling the dose of one without the other, or giving smaller doses more often, complicates the technique without improving the result.

The normal hospital diet is given, but avoiding anything that might be difficult to swallow, such as bread crusts or roast meat. Mince, stews, mashed vegetables, eggs, soft bread and butter with jam are all safe. Also, the patient has two to three pints of egg and milk daily, and liberal glucose and lemon drinks. Solid food is taken as long as the patient can feed himself without difficulty in swallowing. If he cannot feed himself or there is the slightest dysphagia he is given fluids only.

Diet and medicine are given when the patient wakes up, not at fixed times. Very often, having eaten, the patient will fall asleep again. In any case the medicine should not be given until ½ hour after the meal, since giving it earlier increases the liability to vomit.

Insulin is not given so long as the patient can take solid food, which he generally can for the full course of treatment. If he is reduced to fluids only, 10 units of insulin, which may be increased if necessary, and a glucose drink are given with each dose of medicine.

Narcotic Effect.

Ninety patients were treated. The average time out of 24 hours spent fully asleep, drowsy and awake was $17{\cdot}2 \pm 1{\cdot}9$ hours, $2{\cdot}0 \pm 1{\cdot}5$ hours and $4{\cdot}8 \pm 2{\cdot}3$ hours respectively. The amount of sleep is particularly satisfactory, as 52 out of the 90 treatments were given to some of the most difficult patients in the hospital. A few patients were treated with paraldehyde alone, dial alone, and a mixture of paraldehyde 3 drm., pot. brom. 30 gr., and tr. opii 30 minims. The narcotic effect was not as good as with paraldehyde and dial, the highest average daily sleep being 14½ hours, and similar complications occurred.

Mortality.

Two of the 90 patients treated died. The first was a maniacal woman of 54. She had improved after a previous course of treatment, but a few weeks later developed a large carbuncle on a dangerous area of the scalp and became much worse mentally. She interfered with the dressings constantly. I regarded the consequent danger of the infection spreading as so urgent that I decided to repeat the narcosis in the hope of stopping her interference with the dressings and of improving her mental condition. She died suddenly on the fourth day. At the post-mortem there was lobular collapse of the lung such as is found after anaesthetic death from respiratory paralysis. No doubt the sepsis had made an otherwise safe dose dangerous, the mechanism possibly being a double upset of carbohydrate metabolism. The second patient was a hypomaniacal man of 70. His narcosis was stormy. After the treatment he was much quieter, in fact a little depressed. About 14 days later he became very over-active, restless and noisy. He had to be hand-fed. He died of broncho-pneumonia a month after the last day of treatment. One cannot exclude the presumption that had he not been weakened by the treatment he would not have got his fatal broncho-pneumonia at that time, so that the narcosis must be held at least indirectly responsible for his death. I have described these

patients in detail not for the sake of special pleading, but because the circumstances of sepsis and old age are exceptional; and I believe, in the light of experience, that similar deaths will not happen again.

Complications.

The complications are similar to those of other techniques. From the start there is a small fall in blood pressure, but on the whole, cardiovascular anxieties are rare. Nearly all the patients had a steady and regular pulse throughout. One patient only had a mild cardiac collapse on the fourth day, but recovered within an hour or two and finished the course without incident. Dysphagia and ataxia also were uncommon. *Vomiting* was the most troublesome complication. At first, liquor atropinae was not included in the paraldehyde mixture, and 15 out of 21 patients vomited. Out of 69 patients who had paraldehyde with liquor atropinae 21 vomited—a striking proportional improvement. Most of the vomiting was in the first three days (see Table I), which suggests that the cause is not intoxication, but the gastric insult of the mixture —quite understandable by those who have taken paraldehyde. Twenty-two patients were *restless*, particularly in the first half of the second week. Thirty-six patients had *pyrexia* scattered evenly over the fortnight. It rarely exceeded 100°, and, as with somnifaine, the temperature usually returned to normal if the next dose was omitted. Eleven patients had *albuminuria*. Four patients had to be *catheterized*. One patient, who had been a regular epileptic in the past, had a single *epileptic fit* two days after the end of treatment. One patient had a *Saturday night palsy* which made a full recovery. Many of the patients who had these complications had them once only.

TABLE I.—*Distribution of Complications according to Day of Occurrence.*

Complication.	Day exhibited.														Total occurrences.	Number of patients.
	1st.	2nd.	3rd.	4th.	5th.	6th.	7th.	8th.	9th.	10th.	11th.	12th.	13th.	14th.		
Vomiting*	7	10	5	1	2	3	1	1	0	3	1	2	1	0	37	21
Pyrexia	3	7	7	7	7	5	6	8	7	5	4	4	6	2	78	30
Restlessness	0	0	0	5	4	4	3	9	9	8	9	6	7	5	69	22
Albuminuria	0	1	3	2	3	3	3	3	5	4	3	4	4	3	41	11

* Excludes 15 out of 21 patients treated before liq. atropinae was introduced into the paraldehyde mixture.

Ketonuria and Glycosuria.

Only five patients had *ketonuria*. In three cases the patients were so restless that for several days they had not been able to take solid food, and had had fluids only. In two of these insulin was not given, and the ketonuria

ceased when the narcosis ended, and they began to take solid food again. It is not possible to decide whether the end of narcosis itself or the resumption of solid food caused it to disappear. The third patient first showed ketonuria on the 6th day. Thereafter he had 10 units of insulin with glucose with each dose of the mixture, but ketonuria appeared on the 9th, 10th, 15th, 16th and 17th days. He was restless and on fluids only throughout. A fourth patient had ketonuria on the 9th, 10th and 11th days, when acute otitis media was discovered and the treatment was stopped. The fifth patient had a trace of ketones in the urine on the 9th day. It disappeared without insulin and the treatment was successfully continued. She was menstruating at the time.

Six patients had *glycosuria*. One of them had glycosuria and ketonuria together on the 6th and 15th days. Two patients had a "faint trace" only on two occasions each, and the others no more than "a trace" once each. Except in the first patient there were no special associations with the glycosuria and it disappeared without special treatment.

These findings throw a little light on the problem of ketonuria during prolonged narcosis. Most patients had no insulin, and a good full diet was evidently enough to prevent the appearance of ketonuria. But though starvation may predispose to ketosis I cannot agree with Menzies (1937) that it is the sole cause of it. The appearance of glycosuria, remembering that the production of alimentary glycosuria is normally almost impossible, must be due to some upset of carbohydrate metabolism. Certainly, starvation cannot explain it. Many patients with acute peptic ulcer symptoms have no more to eat than patients on somnifaine narcosis with the Ström-Olsen technique, but have no ketonuria. Finally, since ketonuria appears at the same time as restlessness, confusion, pyrexia and other toxic signs, it is surely logical to assume that it is itself a toxic sign.

Weight.

Twenty-five patients gained weight, 42 lost weight, and 13 showed no change. The average change in weight was a loss of $1{\cdot}7 \pm 3{\cdot}4$ lb. The significance, if any, of weight change in prolonged narcosis has not yet been settled. Many authors ignore it, or mention it very vaguely. Some claim an increase in weight. On the other hand, Monnier, quoted by Gillespie (1939), reported a loss of 4–5 kg. with cloettal. "He regarded it as of therapeutic value in that it is a sign that metabolic processes are altered." Out of the 51 patients with attacks of less than two years' duration, those who benefited lost on the average $1{\cdot}05 \pm 2{\cdot}8$ lb., whereas those who had no improvement or only temporary improvement lost on the average $2{\cdot}1 \pm 3{\cdot}4$ lb.—just double. Statistically, however, the difference is less than twice the standard error of the difference. The subject is perhaps worth further investigation.

TABLE II.—*Results in 51 Patients in whom the Acute Phase was under two years' duration.*

Diagnosis.	Number treated.	No change.	Temporary improvement.	Lasting improvement.	Recovered.
Mania	26	13 (50%)	2 (8%)	3 (11%)	8 (31%)
Depression	19	7 (37%)	1 (5%)	3 (16%)	8 (42%)
Schizophrenia	6	5 (83%)	1 (17%)	0	0

RESULTS.

As many of the patients were chronic refractory cases, I have only included in the table of results cases in whom the acute phase was of under two years' duration—the type to whom narcosis is usually given. The criteria for assessing the results were similar to Palmer's (1937). The results closely resemble those obtained with somnifaine and other drugs. A male maniacal patient continued maniacal during the treatment, but two days after it ended suddenly became acutely depressed, and has remained so for the last 18 months. A second course of treatment made no change.

DISCUSSION.

I believe the treatment to be reasonably safe if used with normal caution. Most patients caused no anxiety. Only three treatments had to be stopped because of signs caused by the narcosis, two because of feeble pulse, and the other because of restlessness. The special virtues of the technique are simplicity and cheapness. The cost of the maximum daily dose of paraldehyde and dial is less than one-third of the cost of 4 c.c. of somnifaine. The difference for a hospital doing 50 treatments a year amounts to several pounds. The biggest disadvantage is the unpleasant taste. The memory of it is always vague, and most patients make little opposition to the medicine after the first two or three doses. But it must be admitted, the unpleasantness of it makes the treatment psychologically unsuitable for some patients. Its best use, perhaps, is for the treatment of acute phases in chronic manic-depressive patients and other types with acute manic excitement. Such patients are not distressed by the unpleasant taste; and simplicity of technique has additional virtue when the treatment is to be conducted in chronic or refractory wards.

SUMMARY.

The technique for prolonged narcosis with paraldehyde and dial is described. Used with the caution afforded to other techniques it is reasonably safe, but not foolproof. The complications and results are similar to those with somnifaine. The advantages are simplicity and cheapness. A disadvantage is the

unpleasant taste, which makes it psychologically unsuitable for some patients. It is most useful for treating periodic acute phases of excitement or depression in chronic patients.

It is a pleasure to thank Dr. R. Ström-Olsen, Physician Superintendent, for permission to use the clinical material of the hospital, and for much helpful advice.

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A NOTE ON THE USE OF THE 1937 REVISION OF THE STANFORD BINET VOCABULARY LIST IN MENTAL HOSPITAL PATIENTS.

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THE Terman vocabulary test is probably used in mental hospitals more often than any other single test for measuring intelligence. The 1937 Stanford Binet Vocabulary List contains only 45 words selected from the original hundred. There is therefore a temptation to use it in place of the old one on account of its brevity. But this may cause serious errors.

A hundred patients were given the original 100 word vocabulary test. All were fully co-operative, and none had any thought disorder or abnormality of the stream of mental activity. The results were scored in three ways. Firstly, they were scored according to the usual means for the various mental age levels, as used, for example, by Babcock (1930). Secondly, they were scored according to the mean vocabulary scores of adults of different mental age levels given by Terman (1918). Thirdly, the 45 words comprising the 1937 list were scored separately according to the 1937 revision. Average adult was counted 15 years, Superior Adult$_1$ 16 years, S. A.$_2$ 18 years, and S. A.$_3$ 20 years.

The mean chronological age was 56·02 $\pm$ 9·4 years, the range being 24 to 69 years. The mean mental ages in months on the three methods of scoring were as follows :

Method of scoring.	Mean M.A. in months of 100 patients.	Range.	Sigma.
1916 Terman . . .	185·7 .	120 to 240 .	24·71
1918 "Adult Standard" .	175·9 .	96 ,, 240 .	25·48
1937 Revision . . .	197·4 .	120 ,, 240 .	32·91

Both on the 1916 and "adult standard" scoring the group averages close to the average adult normal of 15 years. But the 1937 revision makes it appear distinctly superior. The difference between the 1937 revision mean and the 1916 mean is 11·7 months, which is 2·84 times the standard error of the difference. The difference between the 1937 revision mean and the "adult standard" mean is 21·5 months, which is 5·17 times the standard error of the difference. Thus the 1937 revision clearly and significantly exaggerates the mental age level.

In individual cases this appears even more strikingly. On the 1937 revision list no less than 28 patients achieved a score of S. A.$_3$, and 17 of S. A.$_2$, which

is absurd for a group of 100 patients in a public mental hospital. In five patients the 1937 revision gave a score of four or more M. A. years higher than with the "adult standard," and in a further 22 patients an exaggeration of between three and four years of M. A. All these patients had scores at or above A. A. Below A. A., exaggeration was not so common or so great.

Vernon (1937) has shown that even in children above the age of 12, the vocabulary level outstrips the Sanford Binet level, so that the vocabulary test over-estimates the true mental age. Moreover, in later life the vocabulary level increases with age, and especially so with persons of superior ability, while the general level remains stationary. Hence even the original vocabulary test exaggerates the true mental level in adults, especially in the superior group. Terman (1918) reported a difference of 1·73 Vocabulary M. A. years between adults and children of the same M. A. lying between M. A. 16 and 19. Add to this the still further exaggeration produced by the 1937 revision and it is easy to see that the results may be very misleading. For example; the clinician may be led to suspect thought blockage or other serious disturbance in a patient complaining of difficulty with his work when the reason is simply that the job is beyond his capacity. Conversely, in the case of a patient with a routine mechanical job and a high vocabulary rating, it may be wrongly supposed that the failure of the job to provide an outlet for his ability is a factor in his seeking satisfaction in phantasy life. Or, where a patient has a superior vocabulary, the discrepancy between his vocabulary score and his score on a test of general intelligence may cause a quite unjustifiable diagnosis of mental deterioration. Or, worse still, one may recommend an occupation beyond the patient's power, and so increase his maladjustment.

Summary and Conclusion.

1. One hundred co-operative mental hospital patients were given the Stanford Binet vocabulary test, which was also marked according to the mean vocabulary scores of adults of the different mental age levels. The 45 words comprising the 1937 list were marked separately according to the 1937 Stanford revision.

2. The 1937 revision of the Stanford Binet vocabulary list over-estimates the mental age level in adults, particularly at the upper end of the scale. All ratings on this test above A. A. and probably also those at A. A. and 14 years should be confirmed in other ways before any significance is attached to them.

I am indebted to Dr. Ström-Olsen, Physician Superintendent, for permission to use the clinical material of the hospital

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ASCORBIC ACID LEVELS IN PATIENTS SUFFERING FROM PSYCHOSES OF THE SENIUM.

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NUMEROUS workers (Plaut, 1935; Altaman, 1937; Monouni, 1937) have reported that the blood and spinal fluid ascorbic acid levels are low in the aged. No adequate explanation of this fact has been given. Wortis (1938) has suggested that, since oral administration increases the ascorbic acid level of the spinal fluid in the aged as in the young, defective absorption probably does not play a significant part. He believes that the lower values in older persons may be due to increased intensity of metabolic processes concerned with the elaboration of ascorbic acid. Friedman, in discussing this contribution, advanced the suggestion that in older persons there may be less need for ascorbic acid because metabolism is slowed.

In considering the possible explanations for a lowered ascorbic acid in the aged, it is clear that one may postulate that a low ascorbic acid may be due to inadequate amounts of ascorbic acid in the diet, to inadequate absorption from the bowel, or to increased utilization by the organism. In the present investigation preliminary questioning failed to reveal any uniform failure to take an ascorbic acid adequate diet, and consequently it was decided to investigate a second hypothesis, namely, that there might be an inadequate absorption from the bowel.

PROCEDURE.

Blood and spinal fluid specimens were obtained from a series of 15 patients suffering from psychoses of the senium. The patients showed memory defects and disorientation, and in the majority there was some nocturnal confusion; there was also some habit deterioration, but over-activity was present in only a small percentage of patients. The specimens were obtained within 48 hours after admission to hospital. Fourteen of these patients were put on a standard hospital diet which is calculated to contain 50–70 mgm. of ascorbic acid per day. The ascorbic acid examinations of blood and spinal fluid were repeated at the end of the week, and, during the second week, the same diet was maintained, save for the addition of 300 mgm. per day of ascorbic acid in tablet form. At the end of the second week final specimens of blood and spinal fluid were taken.

Ten of the 15 patients were carried through this second week. The ascorbic acid content was estimated by the method of Mindelin and Butler (1938).

Results.

It can readily be seen from Table I that the initial blood and spinal fluid ascorbic acid levels are considerably lower than normal. Wortis *et al.* (1938), using the Farmer and Abt technique, give 0·7 mgm. and 1·82 mgm. per cent., and Plaut and Bülow (1935) 1·97 mgm. and 2·53 mgm. per cent. as normal values for blood and spinal fluid respectively. It will also be noted that the spinal fluid values are on the whole disproportionately low. It was also found that on the ordinary hospital diet little or no rise in the blood or spinal fluid levels occurred, while on the ordinary diet plus 300 mgm. of ascorbic acid a very definite rise took place in both blood and spinal fluid levels, the rise being more marked in the former. No change in the behaviour of the patients was noticed as accompanying this rise in ascorbic acid levels. The disturbance of memory, the disorientation, confusion and habit deterioration showed no change which was consistent throughout the series.

Discussion.

From these results it is clear that the level of ascorbic acid in both blood and spinal fluid can be raised in aged persons by the addition of sufficient of the vitamin to the diet. Consideration of the conditions under which the ascorbic acid level is lowered shows that this occurs either where the metabolism is increased, as in hyperthyroid or toxic states, or where agents known to damage the mucous membrane of the gastro-intestinal tract, such as alcohol, have been taken in large amounts (Alexander *et al.*, 1938). From our knowledge of the basal metabolism in the aged (Benedict, 1935; Lewis, 1938; Matson and Hitchcock, 1934; Robinson, 1938), it would seem very improbable that the explanation of the low ascorbic acid levels is to be sought in this general factor. The suggestion advanced by Wortis, that there may be a lowering of the intensity of the metabolic processes concerned with the elaboration of ascorbic acid, seems difficult to validate in view of the fact that ascorbic acid is apparently assimilated unchanged. Similarly the concept advanced by Friedman to the effect that there is a lower ascorbic acid in the aged because the requirements are less seems rather to beg the question than to explain the mechanism. Our view is rather that there is a decreased ability to absorb the vitamin, but that this can be overcome if the concentration in the gastro-intestinal tract is sufficiently increased. Complete finality of statement as to whether low ascorbic acid content in the spinal fluid and blood in the aged is due to a decreased absorption or to an increased utilization must, however, await studies on the balance between ingestion and excretion of ascorbic acid.

The present findings tend to direct further attention to the fact that the ascorbic acid level is higher in the cerebrospinal fluid than in the blood. Since the spinal fluid level is disproportionately low and the blood level rises before the spinal fluid level, the question arises whether the high spinal fluid ascorbic acid level represents a reservoir.

Summary.

(1) Blood and spinal fluid ascorbic acid levels were estimated in 15 patients suffering from psychoses occurring in the senium. The levels were low as compared with normal non-senile adults.

(2) The levels could not be raised on an ordinary hospital diet containing 50–70 mgm. of ascorbic acid per day.

(3) The levels could readily be elevated by the addition of 300 mgm. of ascorbic acid to the ordinary diet.

(4) The spinal fluid levels were disproportionately low contrasted with the blood levels, and they rose more slowly in response to increased ascorbic acid administration.

(5) It seems probable that in aged psychotic patients there is a decreased capacity to assimilate ascorbic acid from the gastro-intestinal tract.

(6) No change in behaviour was noted to accompany the rise in blood and cerebrospinal fluid ascorbic acid levels.

Table I.

Patient.	Control.		Hospital diet.		Hospital diet + 300 mg. ascorbic acid.	
	Blood. mgm. %.	Sp. fl. mgm. %.	Blood. mgm. %.	Sp. fl. mgm. %.	Blood. mgm. %.	Sp. fl. mgm. %.
A. J—	0·0	0·16	0·0	0·12	0·68	0·77
P. R—	0·07	0·10	0·10	0·22	0·61	0·84
F. M—	0·09	0·14	0·03	0·05	1·01	0·71
M. S—	0·0	0·03	0·08	0·16	0·29	0·36
M. T—	0·05	0·14	0·10	0·0	0·05	0·16
J. W—	0·08	0·34	0·05	0·13	0·96	1·57
M. H—	0·28	0·83	0·15	0·16	0·71	1·34
S. C—	0·31	0·40	0·26	1·22	1·37	2·17
M. D—	0·12	0·36	1·22	1·01	1·24	1·12
S. N—	0·14	0·65	0·21	0·82	0·54	1·63
F. H—	0·26	0·76	0·18	0·81		
M. J—	0·05	0·26	0·14	0·21		
F. H—	0·14	0·47	0·14	0·68		
J. V—	0·13	0·37	0·23	0·64		
P. N—	0·0	0·16	0·12	0·19		

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Part II.—Reviews.

Knowledge and Character. By MAXWELL GARNETT, C.B.E., Sc.D. Cambridge: University Press, 1939. Pp. xii + 358. Price 18s.

This essay is an attempt to formulate psychological principles governing the practice and purpose of education. It is concluded that the aim of education is to mould character, and that a good character depends upon (1) a coherent neurographic pattern or single wide interest and (2) a strong will.

Believing that character formation is more important than the amassing of knowledge, Dr. Garnett holds that the old-fashioned form master is more likely to achieve this aim than the team of specialists, viz. the Dalton method. The form master is interested in the boys and their special problems, the specialist only in his subject. The form master will see to it that his teaching on varied subjects forms a coherent and meaningful whole. The specialist will be only interested to cram his pupils with his special branch of knowledge, divorced from all contact with other subjects. To the argument that, for instance, a classical master cannot teach mathematics, it is replied that the standard of mathematics required by the classical student would be more readily acquired from the form master, who is in sympathy with the boy's intellectual bent, than from the expert, who has long lost all interest in practical mathematics.

In the ultimate chapters the author is led on by his subject to describe the ideal commonwealth finally resulting from the application of his method of education. He gives us to understand that in this " world wide commonwealth of Christian people " there will be no conflict of opinion, and all will work together for the common purpose. He is careful to point out that his Utopia of robots has nothing in common with that of other ideologies, National Socialism, Fascism or Communism. S. M. COLEMAN.

The Clinical Treatment of the Problem Child. By CARL R. ROGERS. London: George Allen and Unwin, Ltd., 1939. Pp. xiii + 393.

The author, who is director of the Rochester Guidance Centre in the United States, brings a wide practical experience to bear on the many difficulties which the problem child presents to the clinic. The book is divided into four parts, dealing with ways of understanding the child, change of environment as treatment, treatment through modifying the environment and dealing with the individual.

In reading through the various therapeutic procedures described from Scout movement to deep psycho-analysis, we realize how highly developed the child guidance movement has become in the United States and what a lot we have to learn from them. At the same time the author very wisely is

careful to point out how the whole subject, including its delinquency aspects, is as yet only in its infancy, and that we must have many therapeutic failures before the subject is on a really sound and successful foundation. The treatment of the difficult child is applied from so many angles that there is unlimited scope for extension, but a word of warning appears necessary, for much time and money may be spent on therapeutic measures which appeal very strongly to the lay mind but may have little scientific basis or therapeutic value. G. W. T. H. FLEMING.

The Genetics of Schizophrenia. By Dr. F. J. KALLMANN. New York: J. J. Augustin, 1938. Pp. xvi + 291.

This monograph is based on the study of 1,087 cases of schizophrenia during a period of ten years. The subject of predisposition to tuberculosis and schizophrenia based on inherited inadequacy of certain tissues is discussed. Although the total fertility of the group was much below that of the general population, it was not low enough to lead to self-elimination. The hebephrenics and catatonics average only a little more than one child per person, while the paranoid group are almost up to the normal average, i.e. 4·6 per marriage. The author thinks that the practical effect of sterilization is so unsatisfactory that its general application does not seem to be advisable. Schizophrenia is an organic disease based on a specific predisposition which follows the recessive course of heredity and is therefore transmitted to all the children of schizophrenics.

We heartily support the writer's opinion that special attention should be directed towards borderline cases and the mild types of schizophrenia.

He points out that the ratio of frequency between the siblings and children of schizophrenics and again between the grandchildren and children is exactly the same for the expectancy of schizophrenia and for the mortality from tuberculosis. The primary and decisive hereditary factor in the genesis of schizophrenia and tuberculosis is neither a similarity in the physical structure nor some toxic-endocrine disturbance, but is presumably an hereditary inadequacy of certain tissues. The author considers that the most probable solution is an hereditary functional weakness of the reticulo-endothelial system.

G. W. T. H. FLEMING.

The Open Mind. By F. P. GAY. Chicago: Black Cat Press, 1938. Pp. xxiii + 324.

This is an account of the life and work of Elmer Ernest Southard, who is best known to us in this country as a very sound pathologist with a fine knowledge of psychology. He died in 1920 at the early age of 43.

The writer compares him with Sir Wm. Osler without his suffering greatly by comparison with a very great man. He knew him as a friend and writes sympathetically of his work with social science. Southard was a philosopher, and viewed his work in psychiatry and neuropathology from a philosophical angle. The philosophical tendency was apparent in his letters when he was only twenty years of age. There is a macabre tone to the book which rather spoils it. We read: "The convolutions of Elmer E. Southard's brain are well rounded, with the possible exception of the left first temporal." Without being sentimental we think we might have been spared this, but perhaps this viewpoint is merely a British one. G. W. T. H. FLEMING.

Selected Writings of Sir Charles Sherrington. Edited by D. DENNY-BROWN, M.D., F.R.C.P. London: Hamish Hamilton, 1939. Pp. xiv + 532. Price 25*s*.

This volume has been compiled as a testimonial by the neurologists who form the guarantors of *Brain*. The selection of Sir Charles Sherrington's writings is based on their importance from the viewpoint of clinical neurology. Many papers which are of importance but easily accessible are omitted.

The papers are devoted to the distribution of the motor and sensory nerve-roots, the sensory nerves to muscles, the spinal animal and the nature of spinal reflex activity, some particular features of spinal and bulbar reflexes, the anatomical course of reflex connections in the spinal cord, reciprocal innervation, the co-ordination of antagonists, postural reflexes, the motor area of the cerebral cortex, the nature of excitation and inhibition, and the quantitative management of contraction in lowest level co-ordination.

The presentation of a series of papers like this must give the present generation food for thought.

It is only a fraction of the work that Sir Charles published, but gives a splendid idea of the quantity and quality of work that can be done by a brilliant worker.

G. W. T. H. FLEMING.

Modern Clinical Psychiatry. By A. P. NOYES, M.D. London: W. B. Saunders & Co., 1939. Second edition. Pp. 570.

The author attempts to consider the major psychoses and neuroses as personality reactions to everyday social contacts. The classification adopted is that of the American Psychiatric Association. A chapter on psychiatry and general medicine is added at the end of the book. We would like to have seen this chapter at the beginning of the book and more emphasis placed on it. British psychiatry as a whole probably differs from American psychiatry in the emphasis put on the relationship to general medicine in this country and on reaction type in America. The chapter on psychopathic personality is well done, but the classification proposed by Kahn seems to cover all possible types of personality; we would like to see a much more circumscribed classification. Quite a number of the types would come under the psychoneuroses.

G. W. T. H. FLEMING.

Sleep and Wakefulness. By N. KLEITMAN. Chicago: The University of Chicago Press, 1939. Pp. xii + 638. Price 30*s*. net.

This is a very well-written book and proves a mine of information. It is divided into eight parts dealing with functional differences between wakefulness and sleep, the course of events during the sleep phase, periodicity, interference with the sleep-wakefulness cycle, spontaneous changes in the sleep-wakefulness cycle, means of influencing the sleep-wakefulness cycle, states resembling sleep, theories of sleep.

The most interesting section is the one dealing with the theories of sleep; this is divided into four chapters dealing with neural theories, humoral theories, sleep-centres and an evolutionary theory. The writer discusses the various neural theories, only to dismiss them all. Pavlov's theory receives short shrift, as does Claparède's theory of a sleep instinct. The biochemical, toxic and vegetative theories are all discussed, only to be rejected as insufficient.

The author regards wakefulness as one of the keystones of the building of sleep. He puts forward an evolutionary theory of sleep which is briefly that

wakefulness of necessity is a subcortical, probably hypothalamic function, whereas supplementary wakefulness of choice, as well as the diurnal sleep-wakefulness cycle, is a cortical function. The subcortical centre is regarded as really a wakefulness centre whose continuous activity is necessary to maintain a state of wakefulness. This centre is localized in the hypothalamus, extending perhaps into the mesencephalon and thalamus. Fatigue of the centre is not necessary for sleep; all that is necessary is for the afferent excitatory impulses from the periphery to cease. There are 1,434 references.

G. W. T. H. FLEMING.

The Language of Gesture. By MACDONALD CRITCHLEY, M.D., F.R.C.P. London: Edward Arnold & Co., 1939. Pp. 128. Price 5*s*.

A very interesting little book, which was written largely as a result of observing an aphasia which developed in a deaf-mute. The author found as time went on that there was a similarity between the system of gestures used by the deaf-mute and the sign talk of some aboriginal communities. Gestures are divided into two main divisions—those of obvious interpretation, and those which have a specific or artificial meaning. The instinctive gestures are more primitive than the symbolic. Speech and gesture have developed along parallel lines, not, as many would have us believe, speech from gesture,

G. W. T. H. FLEMING.

Hereditary and Environmental Factors in the Causation of Manic-Depressive Psychoses and Dementia Praecox. By H. M. POLLOCK, B. MALZBERG and R. G. FULLER. New York: State Hospitals Press, 1939. Pp. 472. Price $2.50.

This book is based on the study of 155 first admissions suffering from manic-depressive insanity and 175 suffering from dementia praecox.

The authors regarded the problem from the biogenetic view-point, abandoning all hope of ever finding a pathological foundation for either group.

We feel that the number of cases utilized was far too small to yield results of really convincing statistical value. It is not sufficiently realized that the normal population takes the greatest pains to conceal cases of mental instability of all degrees in the family history, whereas the relatives of a case of mental illness are much more willing to produce the family skeletons from their cupboards.

G. W. T. H. FLEMING.

The Nature of Thought. By B. BLANSHARD, B.Sc., Ph.D. London: George Allen & Unwin, 1939. 2 volumes. Pp.: vol. i, 654; vol. ii, 532. Price 32*s*.

These two volumes contain the results of many years of profound meditation on the part of the author. The reader is greatly assisted in his reading by a most detailed list of contents, chapter by chapter, covering twenty-eight pages in the first volume and thirteen in the second.

The two volumes are divided into four separate parts dealing with "Thought in Perception," "The Theory of the Idea," "The Movement of Reflection," and "The Goal of Thought." The author has attempted as a philosopher to combine psychology and philosophy into a more or less coherent whole. This is a very difficult task, and its successful accomplishment is beyond most psychologists and most philosophers. Prof. Blanshard must be admitted to

have come very near to the ideal. He takes us quietly and systematically through the devious pathways of psychology, gestalt and behaviourism, and through the more indefinite but none the less fascinating by-ways of philosophy.

The opening sentence of the book gives us food for considerable thought—"Thought is that activity of mind which aims directly at truth." This may be the view of the philosopher and a purely abstract ideal at that, but we doubt if it corresponds to the truth! So much modern thought aims anywhere but at truth, and as the years pass along civilization appears to be tending towards the definition that thought aims directly at untruth.

The two volumes make most interesting reading, and raise many problems which cannot be dealt with in a short review. G. W. T. H. FLEMING.

THE ROCKEFELLER RESEARCH BUREAU.

Owing to the war the Rockefeller Research Bureau of the Royal Medico-Psychological Association was for a time unable to fulfil its functions. It has now been found possible to reopen it, and it is hoped that full use will be made of the various facilities that it offers to research workers.

Attention is particularly directed to the scheme for aiding junior workers to pay short visits to other centres for help and instruction in methods of research and treatment by the allocation of small grants.

Arrangements can be made for interviewing any worker requiring special information at the offices of the Association.

Bibliographies and advice on technical points will be furnished on demand.

It is proposed to hold a short course, lasting a week, on methods of endocrinological research as applied to psychiatry and another on electro-physiological methods.

Those wishing to attend such a course are invited to write to the Secretary, Research Bureau, The Burden Neurological Institute, Stoke Lane, Stapleton, Bristol.

TWELFTH INTERNATIONAL CONGRESS OF PSYCHOLOGY.

Owing to the present war conditions the Twelfth International Congress of Psychology, which was planned to take place at Edinburgh, Scotland, in July, 1940. has been postponed, though not abandoned. The invitation of the City and University of Edinburgh is not withdrawn, and the Local Organization Committee hope that the Twelfth Congress may still meet in Edinburgh when circumstances permit.

James Drever,
Chairman.
Godfrey Thomson,
General Secretary,

Part III.—Bibliography and Epitome.

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AMER. J. PSYCHIAT.

VOL. XCVI. NOVEMBER, 1939.

Use of Metrazol in the Treatment of Acute Alcoholism.

The narcotic effect of alcohol has long been known. Primarily in small doses it acts on the cerebral cortex and depresses the inhibitory centres. Clinically this results in acutely agitated patients. When the narcosis is carried further, the patient lapses into a comatose state. In the present study the authors have chosen a group of patients who appear to fall into either of these classifications. The administration of metrazol to these individuals was followed by a marked improvement in the clinical state. Such improvement manifested itself in the arousal of the comatose cases, and sedation of the excited group. This improvement was not due to any changes of the concentration of alcohol in the blood. It is suggested that this apparent biphasic effect of metrazol is due to a direct stimulation of the narcotized cerebral cortex. In the mildly narcotized, or agitated group, the improvement is ascribed to a stimulation of the depressed inhibitory centres. Improvement in comatose cases is considered to be due to general stimulation of the central nervous system. (Authors' abstr.)

Nitrogen Inhalation Therapy for Schizophrenia. Preliminary Report of Technique.

Encouraging results from a year's experience in the treatment of schizophrenia in a small group of patients by nitrogen inhalation therapy have been noted.

The landmarks of treatment and the signs and symptoms of acute anoxia observed during these treatments are discussed.

As a result of the authors' experience with this form of therapy they believe that it can offer most promising and safest results if it is conducted by physicians well trained in the use of gas anaesthesia apparatus, cognizant of the signs and symptoms of acute oxygen want, and capable of instituting efficient resuscitating measures in the event of untoward reaction.

It appears that the most satisfactory results will obtain if the anoxia produced is severe and the time of the treatment limited to six minutes.

The use of nitrous oxide as a substitute for nitrogen or the employment of depressant drug sedation in conjunction with nitrogen inhalation therapy are contra-indicated. (Authors' abstr.)

The Results of Shock Therapy in the Treatment of Affective Disorders.

A follow-up study six months after discharge from the hospital of 37 patients who had shown affective disorders shows 41 per cent. as greatly improved and 76 per cent. definitely improved. Of 19 cases diagnosed involutional melancholia, 15, or 78 per cent., have been able to make a social and business adjustment. Moreover, this study shows that metrazol convulsions given with care can be used in patients in the fifth decade of life. The author found also that a few convulsions

when used in connection with other forms of therapy may produce satisfactory results in patients suffering from the mixed forms of depression, especially with the agitated depression accompanying the period of involution. (Author's abstr.)

A Comparative Study of Hypoglycaemic Shock Treatment and Control Observation in Schizophrenia.

A group of 100 patients of the predominantly chronic type of schizophrenia, equally divided by sex, underwent a course of hypoglycaemic shock treatment, while 69 patients—36 men and 33 women—were observed as controls. Fifteen other patients, eight men and seven women, improved spontaneously while in preparation for treatment. The report is based on the state of the patients eight months to two years after termination of treatment or control observation.

Various degrees of improvement took place in 36 per cent. of the treated patients—a lower percentage than generally reported.

The percentage of improvement in the control group was 21·7.

The percentage of improvement in the combined control and spontaneously improved group was 35·7, or about the same as in the treated group.

Relapses took place in 47 per cent. of the treated patients, in 33·3 per cent. of control cases, and in 24 per cent. of the combined control and spontaneously improved patients.

The treatment was the cause of death in 3 per cent. of cases.

" Recovery " occurred in only slightly over 7 per cent. among treated patients with psychosis of not more than 18 months' duration.

The same rate of " recovery " took place among the combined control and spontaneously improved patients with psychosis of less than six months' duration.

The percentage of " improved " ranged from 75·0 to 21·5 in the treated group, from 7·50 to 8·8 in the control group, and from 57·0 to 12·2 in the combined control and spontaneously improved group, in proportion to the duration of the psychosis.

" Lack of improvement " ranged from 12·5 per cent. to 78·5 per cent. in the treated group, from 25·0 per cent. to 86·8 per cent. in the control group and from 7·2 per cent. to 79·7 per cent. in the combined control and spontaneously improved group, in proportion to the duration of the psychosis.

The duration of the psychosis in the improved treated, improved control, and in the spontaneously improved patients was shorter than in the unimproved patients.

The highest percentage of relapses occurred among patients with psychosis of longer duration.

Both treated and control patients with psychosis of shorter duration had the longest lasting remissions. (Authors' abstr.)

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BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY.

PHILADELPHIA PSYCHIATRIC SOCIETY.

PHILADELPHIA NEUROLOGICAL SOCIETY.

Action Potentials of Muscles in " Spastic " Conditions.

Action potentials of muscles in patients presenting spastic conditions have been studied. A number of features apparently characteristic of spastic innervation have been described.

1. Voluntary innervation, whenever it is possible at all, is found to be weak both by ordinary observation and in terms of frequency and amplitude of the spike potentials produced. The management of innervation is revealed by comparison of motor unit and surface leads. Simultaneous motor unit leads show more or less complete synchronization in all muscles examined. This synchronization is considered a specific mechanism characteristic of the management of muscles in spasticity.

2. Spastic reflexes show a complicated pattern of tall spikes with after-discharges of irregular or occasionally regular grouping. They usually irradiate to

muscles served by other reflex arcs at other levels of the cord and may reach the other side of the body. This behaviour may be explained by a spreading of impulses in the intrinsic fibre systems of the cord. An impulse may be conducted over several " delaying pathways " and thus produce a repetition of spikes in a muscle whenever a " delayed " impulse returns. It may, on the other hand, run astray and reach other levels. Such an impulse may set up a long-lasting disturbance in a distant group of anterior horn cells, as in a case of amyotrophic lateral sclerosis. Both " direct " and irradiating reflexes produce synchronization of all activated units.

3. Clonus produces synchronization of motor units, as simultaneous and successive leads from whole muscles and pairs of coaxial electrodes show. The pattern of clonus is regular, indicating that in clonus a temporary centre is formed by which the alternating innervation of protagonist and antagonist is sustained.

4. No " spastic " innervation of a resting muscle was observed, and it is concluded that spastic " tonus " does not exist except as a reflex innervation, facilitated by the general hyperirritability. Spastic resistance is therefore probably to be considered a reflex phenomenon produced by stretching of a muscle either by the examiner or by the patient himself, when he tries to innervate an antagonist of the muscle in which spasticity is perceived.

5. Curare can be used to reduce spasticity. There are two possible sites of action: either on the neuromyic junction or on centres presumably in the cord. Curare does not appear to act by way of a Wedensky inhibition in spastic patients. With proper doses volitional innervation is not appreciably disturbed.

6. Management of muscles in spasticity is explained by the release of activity of the " old " motor system of the cord by total or partial loss of the corticospinal control. Synchronization of motor units and increase in reflexes are characteristic features of this mode of innervation. In case of subtotal loss of corticospinal control the remnants of the corticospinal systems suffice to set off the intrinsic system. Voluntary movement can thus be performed to a certain extent. This explanation of undifferentiated " mass movement " is preferred to the one by which it is related to circumscribed lesions of cortical areas. (Authors' abstr.)

Results of Experimental Removal of Pineal Gland in Young Mammals.

The pineal gland has been extirpated in young rats, cats and dogs, and adequate litter mate controls of each sex have been used for comparison of their development. As nearly uniform laboratory conditions as possible have been maintained during the growth period of these animals.

No behaviour changes were noted in the pinealectomized rats. Sexual maturity was attained at the same age in both control and lesion animals. There was some indication of increased somatic development in the males at puberty.

There were no differences in somatic or sexual maturation in the female control and the lesion cats. Both experienced normal estrus and both had normal pregnancies; but their offspring, sired by pinealectomized males, were weak, and of 24 kittens only 2 lived more than 48 hours. The pinealectomized mothers showed a lack of maternal instinct and lactated inadequately. The pinealectomized males matured sexually four to five months earlier than their controls and showed a precocious somatic development, still being larger than their controls at the time of full maturity of the normal cats. The lesion males were less playful, more aggressive and more belligerent than their controls.

Second generation cats, either as midterm or term foetuses or as cats several weeks of age, did not show any gross variations from the normal animal of the same age.

Serial sections of the cat brains did not show degeneration anterior to the habenular nuclei. No significant difference was noted between the mature control and the lesion animals in the histologic picture of the thyroid, adrenals and ovaries. The testes and hypophyses of the pinealectomized males were larger than those of

the control males, and the histologic appearance of these organs reflected the gross state.

One pinealectomized male dog outstripped his control both as to sexual development and body size before ten months of age.

This report sets forth the results of extirpation of the pineal gland in young mammals, the animals being allowed to reach maturity with continuous observation of their somatic and sexual growth, as well as of their behaviouristic and reproductive characteristics. This investigation is still in progress, and the data must necessarily change therefore from time to time. No arbitrary interpretation of our present results can be stated ; no statements of definite proof of any special function of the pineal gland can be made. It may be postulated, on the basis of the results here presented, that the pineal gland has a glandular function, probably endocrinal early in life in mammals, and that its function exerts through a yet undescribed process an influence on the sexual and somatic development of the immature animal. (Authors' abstr.)

Studies in Multiple Sclerosis : Serum Enzymes.

A manometric method is described which is more accurate and convenient than titration for determining the esterase, lipase and choline esterase activity of serum. The activity of these enzymes has been ascertained in normal persons, patients with multiple sclerosis and other patients, ethyl butyrate, tributyrin and acetylcholine being used as substrates.

Individual levels of activity are maintained nearly constant over long periods. Debilitation causes a pronounced lowering of activity of all these enzymes.

Quinine hydrochloride in vitro activates slightly the esterase, but inactivates the lipase and choline esterase of serum whether from patients with multiple sclerosis or from normal subjects.

No evidence of hydrolytic activity of any serum toward lecithin or various emulsions of brain fat has been demonstrated by this method.

No difference has been found in the behaviour of serum from patients with multiple sclerosis and serum from any other persons. Moreover, no change in the activity of these enzymes has been demonstrated during remission or exacerbation of the signs and symptoms of multiple sclerosis. (Authors' abstr.)

Effect of Phenobarbital on the Mentality of Epileptic Patients.

Psychologic tests performed before and after one year of treatment with phenobarbital showed no impairment in the mentality of 48 epileptic patients. The control group of 42 epileptic persons likewise did not deteriorate. Seven patients were tested before and after two years of phenobarbital therapy. On the whole, the slight changes after two years of treatment were in the direction of normality. In 13 cases the first year was used as a control and phenobarbital was given throughout the second year. There was some improvement in performance with the psychologic tests after the year of treatment. This study therefore indicates that phenobarbital in doses of 1½ gr. (0·1 gm.) two or three times a day can be given for two years without resultant deterioration of the intellect. (Authors' abstr.)

Relation of Anoxaemia to Early Activity in the Foetal Nervous System.

The earliest somatic activities of which cat embryos are capable made their appearance about 23 days after insemination. They were simple reflex responses to stimulation of the fore limbs or head.

Throughout the following ten days of the gestation period additional simple responses manifested themselves. Hand in hand with the appearance of simple movements there was progressive integration of the activities already laid down.

The nature of early foetal behaviour varied with changes in the respiratory metabolism of the foetuses. When deficiency in oxygenation or elevation of carbon dioxide became effective, the foetuses at first became more irritable to light tactile

or pressure stimuli and the individuality of responses was clearly defined. However, with further anoxaemia the individual movements became depressed, some, especially movements of appendicular muscles, being lost entirely; irritability decreased, and spontaneous movements of a fully integrated mass reaction resulted. Under conditions of anoxaemia stimulation of the foetuses resulted in mass movements. The greater the asphyxia, the more tonic and sustained were these mass responses. Severe asphyxia, however, ultimately led to breakdown of the total response and to depression of all activities.

Rhythmicity of certain movements, especially of the muscles to be employed in respiration after birth, appeared in foetuses about 30 to 31 days old under conditions of partial anoxaemia. With further increase in the carbon dioxide level or decrease of the oxygen in air breathed by decerebrate cats, it was possible to bring about participation in these respiratory-like rhythms of progressively more muscles until tonic, dyspnoeic gasps alone occurred.

It is concluded that behaviour develops by a process of integration of unit reflexes, which occurs with progressive growth of connections within the central nervous system. Experimental procedures usually disturb respiratory metabolic conditions so quickly that the individual movements are destroyed before adequate stimuli can be brought into play to elicit them, the mass reaction, i.e. Coghills total pattern, being the only form of behaviour remaining during partial anoxaemia.

(Authors' abstr.)

FEBRUARY.

Philadelphia Neurological Society.

Chicago Neurological Society.

Pick's Disease with Atrophy of the Temporal Lobes.

The study suggests that in Pick's disease the impairment of psychic functions occurs in a systematic manner, so that higher levels are disturbed before the more primitive levels. This would explain not only the characteristic dementia, but also the predominantly amnesic aphasia in cases of atrophy of the temporal lobes. The fact that amnesic aphasia frequently occurs as an initial phase in the course of other speech disturbances implies that it represents a systematic disturbance in the highest levels of the speech mechanism. Its prominence in Pick's disease, in which there is a general "loss of the categorical attitude," is in keeping with Goldstein's view that "amnesic aphasia is not a primary disturbance of the speech process, but a disturbance of the categorical attitude, which is a necessary condition for word finding." From an anatomic standpoint, the aphasia cannot be attributed to a specific localization, even though the restriction of the lesion to certain convolutions of the temporal lobes may have a determining influence. Thus, the involvement of additional areas, such as the insula, does not essentially alter the amnesic aphasia, as seen in our case. In other cases (Stertz), additional aphasic symptoms occur in spite of the similar localization of the lesions. Neither can the dementia be related to generalized involvement of the brain, since the latter is mild in cases of Pick's disease with atrophy of the temporal lobes, in contrast to that in diffuse degenerative disorders. It seems, rather, that the involvement in Pick's disease of genetically younger areas which are concerned with higher associative functions would result in the systematic disturbance in the highest levels of the speech and thinking mechanisms. (Authors' abstr.)

Variations in the Carbon Dioxide Content of the Blood in Epilepsy.

1. The carbon dioxide content of arterial and internal jugular blood drawn without relation to seizures was abnormal in 70 per cent. of 94 patients examined.

2. In patients subject to petit mal seizures, carbon dioxide values tend to be abnormally low, whereas in those subject to grand mal seizures they tend to be abnormally high.

3. Spontaneously occurring grand mal and petit mal seizures are preceded by abnormal fluctuations in the carbon dioxide content of arterial and internal jugular blood, the time relations being such as to indicate a causal linkage between the carbon dioxide content of the blood and the seizures.

These observations are consistent with electroencephalographic evidence that the type of cerebral dysrhythmia present in grand mal seizures is in contrast to that in petit mal attacks, and that carbon dioxide has a pronounced influence on cortical rhythms. All the available evidence indicates that carbon dioxide plays a significant aetiologic role in epilepsy. (Authors' abstr.)

Epileptogenic Lesions of the Brain.

The arteries of an aganglionic scar undergo periodic positive constriction. This may be due to the abnormal scar tissue which surrounds the vessels. It may be due to the more voluminous perivascular plexus of the arteries of the scar, or it may be that the lack of side-branches subjects the arterial trunk to abnormal stretch stimuli. (Stretch seems to be an adequate stimulus for producing local

constrictions of cerebral vessels, according to Echlin.) Such local irritability of the arteries of the central scar would produce the continuing destructive atrophy which is the universal histologic characteristic of epileptogenic lesions.

The authors are not in a position to say that such punctate destruction does not occur in scars which have not given rise to epileptic seizures. For the present they point out that this extremely slow, advancing destruction occurs at the frontier between the lesion and the functional cortex. This is the zone where electrical stimulation may reproduce a patient's habitual seizure. They do not suggest that a spontaneous seizure results directly from widespread vasoconstriction in this zone. The invariable accompaniment of epileptic discharge is local vasodilatation, which begins shortly after the onset of the discharge.

It is evident, however, that the scattered occasional vasoconstrictions that occur in this frontier zone produce progressive damage to scattered nerve cells. The phenomenon may well be an important mechanism in the charging process that periodically results in the explosive spreading discharge of ganglion cells that constitutes the physiologic bases of each recurring epileptic seizure.

(Authors' abstr.)

Adjustment of Acid-base Balance of Patients with Petit Mal Epilepsy to Over-ventilation.

The person with petit mal epilepsy responds to over-ventilation with a greater drop in the carbon dioxide content of the internal jugular blood, and maintains the low level reached for a longer period after the over-breathing has ceased than does the non-epileptic control subject. The corresponding changes in the acid-base balance are such that the epileptic patient has an acid-base loop of greater area than the control subject. These findings can be explained on the assumption that the mechanisms which regulate the physico-chemical state of the fluids of the brain are somewhat impaired in petit mal epilepsy, so that the person with such a condition is not able adequately to control or quickly adjust the acid-base balance when it is disturbed by over-ventilation. (Authors' abstr.)

Physiology of Concussion.

Apparatus is described for recording in animals changes in intracranial pressure produced by a blow to the head.

The intracranial pressure, at the time of a blow of sufficient force to cause unconsciousness in the dog, rises to a height considerably above the systolic blood pressure. After the blow the intracranial pressure returns immediately to the normal level and remains there.

There is loss of consciousness in the dog when the intracranial pressure is mechanically raised to a level above that of the arterial blood pressure, although this pressure is maintained for only one second.

At no time is consciousness lost in the dog when the intracranial pressure does not exceed the systolic blood pressure, even though the lower pressure is maintained for long periods (30 minutes).

Bulbar stimulation does not occur until the intracranial pressure reaches the level of the systolic blood pressure (Cushing).

There may or may not be a fall in arterial blood pressure after a blow to the head. The results in cases reported in which a fall was shown are in agreement with those reported by Cannon.

The loss of consciousness as a result of a blow on the head may possibly be explained on the basis of short lasting, complete cerebral anaemia (Cannon). It is agreed with Weiss and Baker that the rate of circulatory change is important in the production of unconsciousness.

Hypotheses are advanced to explain the "knock-out" blow of the prize ring and the allied condition, "punch-drunk." The suggestion is made that the syndrome "punch-drunk" may result from damage to the central nervous tissue from cumulative anoxia caused by repeated short-lasting anaemias. (Authors' abstr.)

Remissions in Epileptic Patients Treated with Sodium Bromide in an Out-patient Clinic.

1. Final remissions beginning with the institution of treatment or shortly after occurred in 47 of 98 cases, or 48 per cent.

2. Remissions were brought about in 80 of 98 cases.

3. In cases of idiopathic epilepsy there was a higher percentage of terminal remissions—49 per cent. as compared with 40 and 45 per cent. in cases of the focal and the organic type, respectively.

4. In 64 per cent. of the patients with *grand mal* alone a terminal remission occurred, while in 46 per cent. with both *grand* and *petit mal* a terminal remission was obtained. In patients having only major attacks it is easier to bring about a remission with treatment. (Authors' abstr.)

Evaluation of Metrazol Shock in Treatment of Schizophrenia.

One hundred schizophrenic patients have been treated with metrazol; there were 53 men and 47 women, ranging in age from 17 to 44; the duration of schizophrenia varied from five weeks to fifteen years, the average period being 34 $\frac{5}{16}$ months. A total of 2,697 injections were made. Patients had from 5 to 40 convulsive seizures of the *grand mal* type. There were 83 dislocations of the mandible and one fracture of the scapula; there were no deaths.

When the treatment was completed, 44 per cent. had improved and 56 per cent. were not improved. At present, three months to a year after completion of therapy (average seven months), 32 per cent. are improved and 68 per cent. are not improved.

There is a definite and persistent tendency to relapse in patients treated with metrazol shock therapy.

Catatonic patients with psychosis of short duration react in the most "dramatic" way to a few injections of metrazol, but catatonic patients always have been more apt to have remission.

Improvement is maintained longer in paranoid than in catatonic patients.

Metrazol shock therapy aids in achieving remissions earlier than routine treatment, thus reducing the duration of hospitalization; the method is convenient and economical.

Metrazol shock therapy may be utilized in preparing unco-operative, inaccessible patients for other therapeutic measures, such as occupational and recreational therapy and psychotherapy.

Metrazol shock therapy is of little or no value for patients with psychosis of long duration, unless previously they have shown a tendency to spontaneous remission.

Patients with psychosis of long duration with definite, marked deterioration fail to show any improvement; at best they become "better" institutional patients, and even then for only a short time.

Metrazol shock therapy does not seem to produce permanent and lasting recovery.

It is the author's impression that, while amelioration of psychotic symptoms occurs in many patients, the essential schizophrenic pattern remains unchanged. (Author's abstr.)

Effects of Ethyl Alcohol on the Cerebral Cortex and the Hypothalamus of the Cat.

By means of original modifications of the Horsley-Clarke technique, the effects of the intravenous administration of various concentrations of alcohol on the hypothalamus and the cruciate cortex of the cat were studied in 35 animals. The results indicate that:

1. The direct injection of alcohol in strengths of from about 0·02 per cent. may have a slightly stimulant effect on both the hypothalamus and the cruciate cortex, although the findings are not determinative. However, alcohol injected in a

concentration greater than 0·06 per cent. is definitely toxic to tissues of the central nervous system.

2. The intravenous administration of absolute alcohol in a dose of from 1 to 3 c.c. per kilogram has a depressant effect on the motor responses of the cortex to electrical stimulation, but in unanaesthetized animals the emotional mimetic reactions of the hypothalamus are unaffected or are actually increased in intensity and duration.

3. There is support for the view that whereas the cortex has an inhibitory function on lower centres, the reverse relationship also holds true, in that the cortex is likewise under the influence of the hypothalamus, and both structures are functionally interrelated in the neural mechanisms of emotional expression.

(Authors' abstr.)

Changes in the Electro-encephalogram during Metrazol Therapy.

A man, aged 33, who had been ill with schizophrenia for six years, was given 24 metrazol treatments, in which 20 convulsions were produced. An intensive electro-encephalographic study was made during and after the course of treatments, with continuous recording throughout each treatment.

Four stages of electrical activity of the brain during the convulsions and five stages following the convulsions are described as well as the associated clinical changes in the patient's behaviour. After convulsive responses to metrazol the patient invariably exhibited a clear mental state as the electro-encephalogram returned to normal.

The electro-encephalograms taken during the onset of a metrazol convulsion and the post-convulsive recovery were unlike those obtained in epilepsy. There was a similarity to the electro-encephalogram taken during the clonic phase of an epileptic convulsion.

The non-convulsive response of the patient, in which he was confused and disoriented, revealed in the electro-encephalogram a characteristic abnormal pattern and wave formation quite unlike the typical electrical pattern of petit mal epilepsy. This pattern was not seen after a convulsive response.

Unusual changes in the occipital electro-encephalogram were observed when the eyes were stimulated by intense light. This indicated that the brain tissue was in a highly irritable condition.

After the treatment was terminated the patient had alternate periods of hallucination and a clear mental state. Changes in the electro-encephalogram coincided directly with the hallucinatory manifestations.

With successive treatments a point was reached (after the eleventh injection) at which the normal physiologic functions of the brain tissue as represented in the electro-encephalogram appeared to be definitely impaired. Impairment then increased in degree with further treatments.

The patient improved temporarily, but did not maintain his early improvement; he began to regress during the latter part of the treatment. Six days after the last treatment he had regressed to his original condition.

A year later the damage or impairment of cerebral function as recorded by the electro-encephalogram remained. (Authors' abstr.)

ARCH. PSYCHOL.

VOL. XXXIV. SEPTEMBER–NOVEMBER, 1939.

ARQ. SERV. ASSIST. PSICOPAT. SAO PAULO.

VOL. III. NOS. 1–2. 1938.

Some Aspects of the Problem of Paranoia.

The author, after consideration of the chronic deliriant psychoses, recalled the great value of the work of Kraepelin in isolating the paranoia from the group of the former " Verrückheit " and making a clinical distinction.

He considers the major aspects of the monumental work of revision of Kraepelin's concept before the advent of the acquisition of modern constitutionalism, the analysis of structure and the deep researches of psychology.

He concludes in showing the notable improvements and clearer insight brought about by the investigations of the psycho-analytical school in the mechanism of defence of the " ego," and he affirms that the researches founded on clinical analyses and psychology are destined to clear up the difficult problems of the psychosis of paranoia. J. R. BEITH ROBB.

VOL. IV. NO. 1. 1939.

Treatment of Epilepsy by Intracranial Introduction of Air.

Therapeutic cisternal injection of air was performed on five epileptics.

Five of them were diagnosed as suffering from infantile cerebral lesions. Five others had had fits since infancy. Two had only developed fits in adult life and three others appear to have had very vague histories. All the cases exhibited various types of mental deficiency and abnormality.

Fifty to 100 c.c. of liquor was replaced by air using the suboccipital route, only one experiment being performed on each case. Improvement in the fit incidence was noted in twelve cases. Three cases became worse. The degree of improvement showed no relation to the type of epilepsy. J. R. BEITH ROBB.

The Treatment of Chronic Schizophrenia by Intravenous Injections of Ammonium Chloride.

A solution of 10 per cent. ammonium chloride was injected intravenously as a substitute for cardiazol in cases of schizophrenia. The initial injections were 2–5 c.c. and were increased to 10–18 c.c.

Immediately following the injection there is muscular relaxation accompanied by hyperpnoea when the face becomes congested, the pupils dilate and consciousness is simultaneously lost. The fit develops with a tonic phase—opisthotonic crisis

—and finally a clonic phase. The duration of the whole fit does not exceed ten minutes. Thirteen cases of chronic schizophrenia were treated. Each case received 20 or more injections. No accidents were noted in a series of a thousand injections. Only one case improved. J. R. BEITH ROBB.

NO. 2.

Juvenile Diffuse Psychotic Encephalosis.

The author refers to his attempt to define juvenile diffuse encephalosis in 1932. For purposes of histological examination material was obtained by cerebral puncture of the frontal lobe. The lesions found showed a primary neuronic degeneration without any trace of inflammatory reaction. The author considers that his findings justify the condition being termed an encephalosis. J. R. BEITH ROBB.

The Medico-legal Value of Post-mortem Examination of the Cerebrospinal Fluid.

The diagnosis of neuro-lues can be established by the Wassermann reaction, the Takata Ara reaction and the benzoin gum reactions as long as 24 hours after death. J. R. BEITH ROBB.

BRIT. J. EDUC. PSYCHOL.

VOL. X. FEBRUARY, 1940.

L'ENCÉPHALE.

VOL. XXXIV. MAY, 1939.

Convulsive Therapy by Cardiazol.

A series of 21 cases of non-schizophrenic psychotics were treated with cardiazol. The most striking results were obtained in a group of confusional cases, many of prolonged duration, and of whom 7 recovered and 3 were improved. The high percentage of recoveries was put down to the absence of any constitutional predisposition. Of 6 cases of delusional psychoses, 1 recovered, 3 were improved and 2 unchanged. Of 5 manic-depressives, 2 were improved and 3 unchanged.

S. M. COLEMAN.

Results of Insulin Therapy.

Report on 37 schizophrenics treated with insulin, 16 of whom were also treated with cardiazol. Of these, 9 showed complete remission, 6 social remission, 8 were improved and 14 were unimproved. Detailed charts are included, showing the syndrome, duration of illness and the hereditary incidence. Regarding technique, the writers find certain advantages in interrupting coma by intravenous glucose as a routine. S. M. COLEMAN.

GENET. PSYCHOL. MONOGR.

VOL. XXII. FEBRUARY, 1940.

Measuring Human Relations: An Introduction to the Study of the Interaction of Individuals. *Chapple, E. D.*

IL CERVELLO.

VOL. XIX. JANUARY, 1940.

JAP. J. APPL. PSYCHOL.

VOL. V. 1939.

JAP. J. PSYCHOL.

VOL. XIV. 1939.

J. ANAT.

VOL. LXXIII. JULY, 1939.

VOL. LXXIV. OCTOBER.

J. COMP. NEUR.

VOL. LXXII. FEBRUARY, 1940.

The Efferent Fibres of the Thalamus of Macacus rhesus.

1. The absence of degenerated fibres after lesions in the anterior and dorso-medial nuclei leads to the supposition that the majority of efferent fibres from these nuclei are unmyelinated.

2. The centre median nucleus is purely a thalamic association area sending its fibres to the surrounding thalamic nuclei.

3. Small lesions in the ventral nuclei indicate that the anterior portion of the ventral nucleus sends fibres in a diffuse manner to the frontal lobe, and that the posterior portion sends fibres primarily to the postcentral gyrus, but in addition to other regions of the parietal lobe and to the precentral gyrus.

4. The pulvinar has efferent connections to the post-parietal lobe and parastriate area of the cortex; and also sends fibres to the tectum and tegmentum of the mesencephalon. (Author's abstr.)

J. COMP. PSYCHOL.

VOL. XXIX. FEBRUARY, 1940.

J. CRIM. PSYCHOPATHOL.

VOL. I. NO. 3. 1939.

J. EDUC. PSYCHOL.

VOL. XXX. 1939.

J. EXP. PSYCHOL.

VOL. XXV. 1939.

J. GEN. PSYCHOL.

VOL. XXII. 1940.

A Quantitative Study of Certain Changes in Schizophrenic Patients under the Influence of Sodium Amytal.

1. As measured by the battery of tests employed, the performance of the schizophrenic patients was superior under the influence of sodium amytal. With reference to the Stanford-Binet test the following changes were found: (*a*) Increase in MA over the first and third tests; (*b*) decrease in the number of tests failed; (*c*) ability to pass tests at higher levels where failure had occurred in the first and third tests; (*d*) improvement in sub-tests involving memory, sustained attention, organization of activities and thought processes toward a goal, and increased organization of the thought processes into more meaningful and pertinent responses.

2. There was superior ability to organize disconnected elements into perceptual wholes in the Rorschach test, a reduction in both time and number of moves required in order to achieve success on form-boards and a greater degree of co-ordination on motor tests, with a tendency to vary less in the performance itself.

3. The Bernreuter personality inventory, while not diagnostic for most patients, tends to indicate a slight change in attitude toward those questions which are indicative of maladjustment. In this sense these patients tend to avoid somewhat, while under amytal, answers which are symptomatic of maladjustment.

4. Correlations between MA, organization score, and the performance boards during the first period are positive, although not all are completely reliable. Those patients with higher mental age are somewhat superior on the motor tests, but also slightly more variable on them. There is a tendency for those with higher mental ages to score lower on the neurotic scales, whereas those with a high time and move score on the form-boards tend to score higher on these scales.

During the second period, correlations between MA, organization score and performance boards tend to remain about the same. Correlations with the motor tests are lowered considerably. Correlations with the measures of variability indicate that patients with higher MAs become less variable under the influence of sodium amytal. Correlations with the neurotic scale are more negligible, but negative, indicating a tendency for those with higher mental ages to score lower on this scale. Those having high time and move scores on the performance board again tend to receive higher scores on the neurotic scale.

Correlations during the third period tend to be about as in the first period, with the exception of those form-boards which were too difficult to have discriminating power during the first period. Correlations between MA and variability scores are increasingly negative and indicate a return to greater variability. Those with higher MAs tended to receive lower scores on the neurotic scale, whereas those with high time and move scores on the performance boards scored higher on this scale.

5. Performance on all tests in the third period tended to revert more nearly to the level of the first period, indicating that the superior performances under amytal are the result of the condition produced by the influence of the drug.

6. The fact that the various changes found occur prior to narcosis would tend to substantiate the theory that sleep itself is not necessary to these patients, but rather that the drug is anti-inhibitory in nature. The removal of inhibitions appears to bring about the changes found. (Authors' abstr.)

J. GENET. PSYCHOL.

VOL. LV. DECEMBER, 1939.

A Developmental Study of the Bodily Reaction of Infants to an Auditory, Startle Stimulus.

An investigation of the bodily response of 14 infants during the first 20 weeks after birth to an auditory, startle stimulus—the dropping of a 2-lb. iron weight a distance of 3 ft. to a hard wood surface—shows a gradual breakdown of certain elements in the Moro response first elicited.

The pattern consists of an initial eyelid response; a primary extension of the upper extremities (involving lateral-wise abductive movement of the upper arm at shoulder, frequently to or near shoulder height) accompanied by extension of the elbow, supination of the lower arm, extension of the hands and fingers; and followed by a slower clasping movement (involving adductive movement in the shoulder and upper arm, flexion in the elbow, pronation in the lower arm), during which the whole arm describes an arc as the hands are brought to a mid-line position near the chest and head. During the course of movement the fingers frequently exhibit tremors. Coincident with the primary movements in the upper extremities, extensor movements in the head and trunk occur. Extensor, flexor, including secondary flexor and extensor movement in the knees and hips; turning in of the ankles; and plantar responses were observed as secondary responses in which flexor, extensor, or mixed responses appear.

This pattern, which frequently occurs in the incomplete form, persists over varying intervals of time, depending on the individual infant. The relative intensity of the response varies from individual to individual, and within the same individual from one observation period to the next.

The bodily reaction pattern gradually changes to one which is primarily flexor in character, in which the movements are less intense, and certain secondary movements (such as the subsequent clasping response of the arms) die out. Flexor forward movements of the shoulder and upper arms also gradually replace the early lateral-wise abductive, adductive movements as characteristic elements. By the twentieth week, in all subjects the primary response was generally flexor in character.

An explanation of the change in the general character of the pattern can in part be found in such neurological evidence as is at present available, which points to an imperfectly developed condition of peripheral nerves and muscles and the central nervous system during the early months following birth.

(Authors' abstr.)

J. NERV. MENT. DIS.

VOL. XCI. JANUARY, 1940.

Behaviour of Patients Undergoing Shock Therapy.

Observations on the actions of four schizophrenic patients, during the hypoglycaemic period, showed a progressive change of behaviour during the course of treatment in those who improved. Oral eroticism, sucking and biting movements, were found to be superseded by movements of a masturbatory character. The author is of the opinion that when genital eroticism has been aroused and maintained for several days, it is an indication for discontinuance of insulin.

S. M. COLEMAN.

Pick's Disease.

Clinical report with neurohistopathological findings in four cases of Pick's disease. In none of the four cases was a correct clinical diagnosis made prior to autopsy, despite a fairly long period of observation. S. M. COLEMAN.

Grasping and Sucking.

Grasping and sucking are inter-related in the newborn, so that the presence of one response facilitates the obtaining of the other and enhances its intensity. This relation is the expression of a basic physiological association of hand and mouth. In pathological states when grasping and sucking reappear, this relationship is again to be observed. The biological function of grasping is initially support; after hand to mouth activity has been established, it also serves for the approximation of subject and object. S. M. COLEMAN.

J. NEUROPHYSIOL.

VOL. III. MARCH, 1940.

Facilitation and Difficilitation Effected by Nerve Impulses in Peripheral Fibers.

At a discontinuity (block) in a nerve fiber created by anode polarization, a discontinuity that can be graded by varying the strength of the polarizing current, it is possible to demonstrate and to gauge the facilitation effected by blocked action potentials and to demonstrate a phenomenon, designated difficilitation, which probably is identical with "extinction."

The facilitating action of spikes at such an artificial synapse increases with their number and with their frequency. The facilitation per impulse declines slowly

with the number, but is demonstrable through at least 20 impulses. The facilitating action has not attained its maximum at impulse rates as high as 200 per second, nor its minimum at rates of 10 per second.

Once, in a tetanus, a spike succeeds in passing a block all of the succeeding spikes of that burst also will pass, notwithstanding the spontaneous variations in the excitability of a fiber. This effect is attributed to the supernormality that follows immediately the response of the post-fiber.

Difficilitation is demonstrable, when conduction has been established by facilitation, by interrupting this conditioning tetanus momentarily, the optimum period of interruption (under a specific set of conditions) being in the vicinity of 0·5–0·6 seconds, when, upon resumption of the tetanus, it may happen that spikes will no longer pass from the pre-fiber to the post-fiber (i.e. across the local discontinuity) as long as the tetanus continues. (Observations on this interruption of conduction have not been continued longer than 43 seconds.) But interrupting the second tetanus for a period of six seconds seems to permit the block to disappear.

Difficilitation, at least in its initial stages, is regarded as a manifestation of the subnormal phase of the excitability cycle in the post-fiber, a cycle that is started by the momentary interruption of tetanic stimulation; the spikes of the pre-fiber, with the resumption of tetanic stimulation, then no longer reach the threshold of the post-fiber.

Exactly the same phenomena of facilitation (recruitment) and of difficilitation (negative recruitment or " disbandment ") are demonstrable at the site of stimulation of a fiber with induction shocks, and it is concluded that both facilitation and difficilitation result from the spike's action as an electrical stimulus to the post-fiber. This holds not only with regard to the artificial synapse in the nerve fiber but, by inference, with regard to the actual synapse, as well.

The protraction of difficilitation which seems to be determined by continued tetanic stimulation of the pre-fiber is discussed, but no conclusion is reached regarding processes that might be determining it. (Authors' abstr.)

A Human Cortical Area Producing Repetitive Phenomena when Stimulated.

During the electrical exploration of a human cortex, an area was found which when stimulated produced perseveration of speech. The area (area X) lay on the mesial side of the left hemisphere, in area 6, probably just above the junction of that area with the posterior part of area 32.

The patient, under local anaesthesia, said the alphabet. At each application of the stimulus, and throughout the period of stimulation, the letter the patient was saying was repeated over and over again. The perseveration ceased instantly when the stimulus was stopped.

Area X is far from any known part of the speech zone. It influenced the function of distant neurons, and in such a way that these neurons were thrown into action again and again, as though the impulse were imprisoned in a given cell group, able to activate that group only, but unable to pass to another.

(Author's abstr.)

Effects of Eserine, Acetylcholine and Atropine on the Electrocorticogram.

1. The changes in the electrocorticogram in the cat and rabbit, induced by the local application of minimal amounts of 1 per cent. eserine, 1 : 10^5, 0·2–1 per cent. acetylcholine (ACh) and 0·2 per cent. atropine, were recorded by one or two cathode ray oscillographs.

2. Application to the cortex of 1 per cent. eserine causes a reduction in amplitude of the slow waves and of the large fast waves; these changes indicate cortical stimulation, since they are associated with motor effects.

3. Application to the non-eserinized cortex of 1 : 10^5–1 per cent. ACh evokes potential changes comparable to, though weaker than, those from 1 per cent. eserine. ACh in 0·2–1 per cent. solution applied to the previously eserinized cortex evokes the Es–ACh spikes; associated motor effects show that the spikes indicate

cortical stimulation. For the causation of these effects eserine must precede ACh, the reverse order being ineffective.

4. Atropinization of the animal precludes induction of the Es-ACh spikes and motor effects.

5. Pilocarpine locally is inert towards the electrocorticogram; further, it does not sensitize the cortex for ACh. The drug effects are not due to pH changes.

6. Eserine and ACh are believed to stimulate or facilitate synapses; eserine a synaptic sensitizer for ACh. The synaptic action of eserine may be partly direct and partly due to its inhibition of cholinesterase, with lessened destruction of effective (natural) ACh. Potential changes from eserine are believed due to unequal stimulation of synapses with consequent asynchronous firing of neurones. The Es-ACh spikes are believed due to powerful synaptic stimulation with synchronization of many neurones; the cells with short axons may be involved in this synchronization.

7. The hypothesis is proposed that, in consequence of stimulation of synapses by eserine and ACh, repetitive electrical impulses are initiated or accelerated across these junctions. (Authors' abstr.)

Cord Potentials in Spinal Shock: Single Volleys.

In cats, dogs and monkeys cord potentials and reflex responses to single afferent volleys have been recorded at intervals after spinal transection ranging from a few seconds to two months.

The latency of the cord potential is independent of the strength of the stimulus and long enough to indicate an internuncial origin.

The effect of transection upon the cord potentials is to reduce the amplitude and spread of the negative components and to abolish or almost abolish the positive components. These effects are far more severe and prolonged in the monkey than in the cat or the dog.

In the cat and the dog the threshold for cord potential and ipsilateral flexor reflex sampled in semitendinosus are equal and fall progressively during the first hour after transection, at the end of which they approximate that of the afferent nerve. In the monkey, on the other hand, though the cord potential threshold approximates that of the nerve within six hours, the reflex threshold for semitendinosus requires twelve days or longer to attain that level. Reflex responses from this muscle have never been observed even to maximal stimulation in an acutely spinal monkey. On the other hand, stimulation of dorsal roots has given feeble toe flexion and slight tail movement at thresholds approximating those of cord potential and afferent nerve in an acute experiment.

Hence, in the cat and the dog, spinal shock has been demonstrated only at the internuncial level. In the monkey, on the other hand, in addition to more severe internuncial depression, there is evidence of deep and prolonged shock to the motoneurones. (Authors' abstr.)

Cord Potentials in Spinal Shock: Multiple Stimuli.

In the spinal *Macaca mulatta* monkey, inhibition of the internuncial response to the second of two volleys to an afferent nerve is contingent upon the presence of a positive wave in the preceding cord potential. In the absence of such positivity, internuncial recovery from refractoriness is complete in 20 to 25 m/sec. Repetitive stimulation gives a series of internuncial potentials in which little positivity is added to that incident to the initial volley. Such a pattern contrasts sharply with that obtained from peripheral nerve, and hence suggests a perikaryal origin and different units for the sources of negativity and positivity respectively.

The acutely spinal monkey gives no contraction of semitendinosus in response to afferent stimulation by either single or multiple volleys. The chronic monkey yields a large contraction to single volleys to which little is added by further stimulation even at frequencies at which the cord potentials are but slightly reduced.

The view is advanced that in even the chronic monkey there persists a considerable degree of depression downstream from the internuncials recorded, presumably, at the motoneurones. (Authors' abstr.)

Cord Potentials in Spinal Shock : Crossed Effects in Monkey, Macaca mulatta.

In the spinal *Macaca mulatta* monkey the contralateral component of the intermediary cord potential is scarcely detectable in the acute preparation, is small at 12 days after transection, but has attained the magnitude of the ipsilateral component within two months.

In the chronically hemisected, acutely transected animal, the ipsilateral potential spreads farther up the cord when the stimulus is applied to afferents of the chronic side than when to those of the acute side. When the chronic side is stimulated, the threshold for the crossed cord potential is far higher and its latency far longer than that for the potential on the side of stimulation. When afferents of the acute side are stimulated, the thresholds for ipsilateral and contralateral potentials may be identical and the latter potential may approximate the magnitude of the former. From these data the following conclusions are drawn :

1. The contralateral cord potential is associated with the activity of perikarya or dendrites and not merely with that of axons.

2. Block of the crossed cord potential is due to a high threshold of the cells of the contralateral dorsal horn and not to lack of impulses playing upon them.

3. The above data yield evidence of the internuncial origin of the cord potential.

In the cat crossed inhibition of the internuncial potential parallels that of the flexor reflex, though usually it is somewhat less intense. In the chronic monkey, on the other hand, crossed inhibition of the reflex may occur without reduction of the corresponding cord potential. This indicates a locus of inhibition downstream from the internuncials recorded—presumably at the cells of the anterior horn. (Authors' abstr.)

An Attempt to Produce Sleep by Diencephalic Stimulation.

1. Destructive and stimulating electric currents were applied to the hypothalamus, thalamus, junction of the hypothalamus and thalamus, head of the caudate nucleus, septum pellucidum and region of the anterior commissure in waking cats.

2. Somnolence was produced by destructive action of currents when applied to the lateral hypothalamic area. Catalepsy tended to develop when the lesions involved the medial and caudal parts of the hypothalamus.

3. Somnolence was produced by destructive electric currents when applied to the lateral group of thalamic nuclei, but the strength and duration of the current was much greater than that in the hypothalamic experiments. It is possible that the effects were not solely thalamic.

4. Extensive lesions of the head of the caudate nucleus did not cause somnolence.

5. Stimulation of the structures mentioned above did not yield somnolence.

6. No evidence was obtained to support the theory that sleep is a phenomenon of active inhibition. (Author's abstr.)

Relayed Impulses in Ascending Branches of Dorsal Root Fibres.

This investigation was designed to describe in further detail the properties of the dorsal root reflex response recently reported by Toennies. Since the dorsal root fibres divide and send long branches up the dorsal columns to the nuclei of Goll and Burdach, it should follow that simultaneous with the passage of the reflex response outward toward the periphery, a relayed impulse should likewise pass up the dorsal columns. Cats were anaesthetized with dial and the cord was exposed. Stimulating electrodes were placed on the sixth or seventh lumbar dorsal root, and a recording needle electrode was placed in the homolateral dorsal column some distance cranial to the site of the stimulated root. In accord with the expectation

a relayed response was recorded following the direct afferent volley. The properties of the relayed response were found to be similar to the properties of the dorsal root reflex. Evidence was accumulated to show that the relayed response was carried by the ascending branches of the dorsal root fibres. (Author's abstr.)

Observations upon Diaphragmatic Sensation.

In the cat and dog these experiments show that nociceptive sensibility produced by stimulation of the central portion of the diaphragmatic peritoneum depends upon afferent conduction in sensory fibres in the phrenic nerve, independent of afferent fibres in the vagus and intercostal nerves and of efferent sympathetic pathways. Observations made on man by Dr. W. K. Livingston are presented to show that pain may be referred on stimulation of the central diaphragmatic peritoneum to a completely anaesthetized area of skin in the shoulder-tip region. Viscero-cutaneous reflexes are not essential for nociceptive sensation when the central diaphragmatic peritoneum is stimulated in the experimental animal or in man. (Authors' abstr.)

The Phasic Response to Cortical Stimulation.

Two types of response may be elicited in cats on cortical stimulation, depending on the depth of ether anaesthesia, etc. In one a new posture is assumed and held; in the other a pendular movement results. These are designated tonic and phasic responses respectively. The mechanism of the latter type was the subject of this study. This was investigated in the fore limb by determining the effect of (1) cutting the dorsal roots of the brachial plexus; (2) completely denervating the limb except for the twig to a single muscle, e.g. the biceps; (3) making a series of lesions in the dorsal and lateral funiculi of the spinal cord.

The results of these experimental procedures showed that, in so far as the peripheral nervous system is concerned, the phasic response was dependent upon inhibitory proprioceptive impulses set up in the contracting muscles themselves and conveyed to the cord by the dorsal roots. The central part of the mechanism was found to involve an uncrossed ascending path which corresponded in position to the ventral spinocerebellar tract. The complete mechanism responsible for the phasic character of the response would therefore appear to include the cerebellum. (Authors' abstr.)

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The Emotional and Somatic Response of Schizophrenic Patients and Normal Controls to Adrenaline and Doryl.

Emotional and somatic reactions of schizophrenic patients and normal controls are compared following intramuscular injection of adrenaline and doryl.

No significant difference was noted in the somatic response of the two groups,

although the schizophrenic group exhibited more variability of response to both adrenaline and doryl, tending to bear out the findings of others to the effect that the adaptive mechanisms of the schizophrenic to preserve the "steady state" are defective under stress.

Doryl injected intramuscularly produced an excellent peripheral autonomic response in both the schizophrenic and normal groups, but no emotional disturbance (anxiety or fear) in either group.

The clear-cut and definite failure of adrenaline to arouse anxiety or fear response in the schizophrenic as compared with the normal control group is significant, and points to a disordered emotional mechanism at a physiological level. We present experimental data which only indirectly localize this break in the chain of physiological response, and all explanations are highly speculative.

No claim is made of the efficacy of using adrenaline to differentiate schizophrenics from other mental disorders by means of their emotional response, although the findings reported would suggest possibilities for investigation in an effort to understand better the central emotional mechanism. (Authors' abstr.)

The Distribution of Commissural Fibres in the Corpus Callosum in the Macaque Monkey.

The presence and situation of commissural fibres in the corpus callosum, as shown by a study of degenerating fibres following cortical lesions, are described.

Areas studied in the frontal, parietal, occipital and temporal lobes were all found to contribute to the callosal system.

The position occupied by the fibres is discussed, with the general conclusion that the frontal fibres are spread over chiefly the genu and anterior third of the body, with some occupying the middle third, the occipital over the splenium and posterior third of the body, and the parietal and temporal over the posterior two-thirds of the body with those from the temporal occupying a position anterior to those coming from the parietal. The existence of commissural fibres from the temporal lobe crossing by way of the anterior commissure is confirmed. The amount of the Marchi deposit recorded suggests that, from areas of equal extent, the parietal cortex contributes relatively the greatest number of commissural fibres, and then the cortex of the frontal, temporal and occipital lobes in that order.

(Author's abstr.)

Behaviour and Mood Cycles Apparently Related to Parathyroid Deficiency.

Three parathyroidectomized monkeys kept on a low-calcium diet drank large amounts of a 2·4 per cent. calcium lactate solution, thereby alleviating their symptoms of insufficiency. Their intake of calcium lactate solution showed fairly regular cycles averaging 40 days in length.

A woman aged 56 suffering from a parathyroid deficiency showed quite regular cyclic variations in mood and behaviour with a duration of approximately 40 days. For the first half of each cycle she was depressed and slow, and for the second half she was fairly normal. After calcium therapy these cycles disappeared.

(Authors' abstr.)

Hypoglycaemic Shock and the Grasp-reflex. The Effect of Insulin Shock on Bulbocapnine Catalepsy in Monkeys.

1. Hypoglycaemic shock was induced in six monkeys. The phenomena observed are essentially similar to those seen in therapeutic hypoglycaemia in man.

2. The hypoglycaemia was accompanied by a reappearance of the neonatal grasp-reflex, which disappeared when coma became deep and reappeared briefly during the phase of recovery.

3. When bulbocapnine is given at different periods during the action of insulin, the general effects and those in regard to the hanging-response are a summation of the individual effects of the two drugs, except when the peak of action of both drugs coincides, when new phenomena appear.

4. These consist of disappearance of the tremors caused by the bulbocapnine and the appearance of spontaneous grasping, together with a grasp-reflex obtainable on light stimulation of the palm.

5. Hypoglycaemic shock has no effect on the cataleptic manifestations induced by bulbocapnine, nor does it itself produce catalepsy in the monkey.

6. Theoretical reasons are adduced from the experiments for the supposition that the action of insulin is predominantly a depressant one on the cerebral cortex. (Author's abstr.)

Degeneration of the Papillo-macular Bundle in Apes and its Significance in Human Neuro-pathology.

A spontaneous systemic degeneration of the papillo-macular bundle is frequently found in captive monkeys dying from different general diseases. In routine optic nerve examinations it has been observed in 8 out of 27 cases; most of these were of recent onset.

The optic nerve lesions which accompany most cases of spontaneous "encephalosis" and "myelosis" in monkeys (cerebral and spinal form of subacute combined degeneration) are also systemic degenerations of the papillo-macular bundle. They may be complicated by the appearance in the peripheral optic pathways of the same circumscribed, later confluent, patches of demyelimization which characterize the disease in the spinal cord and centrum ovale.

The frequency of the optic lesion and its often terminal character in different general diseases (generalized tuberculosis, gastro-intestinal troubles, cachexia, meningitis, etc.) suggests that its origin may be in a nutritional deficiency, and that this may also account for the lesions of subacute combined degeneration in monkeys.

Our actual knowledge of human papillo-macular bundle degeneration seems to support this hypothesis. (Author's abstr.)

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VOL. XXVI. NO. 5. 1939.

J. PSYCHOL.

VOL. IX. JANUARY, 1940.

Some Relationships Between the Urinary Excretion of Male Hormone by Maturing Boys and Their Expressed Interests and Attitudes.

Ten boys between the ages of 13 and 16 were observed over a period of six months. Rank-order correlations between the behaviour rating, scores on the questionnaires and male hormone activity indicated that only one of the questionnaires correlated high with both the observed behaviour and the hormone activity of the subject, and correlated low with the chronological age of the subjects. In a second group of 23 it was found that the degree of maturity of the expressed interests and attitudes of the boys correlated higher with hormone activity than they did with chronological age. Ten boys with a high hormone content showed a greater proportion expressing interest in heterosexual activities, personal adornment and strenuous competitive sports than did 13 boys with a low hormone content.

G. W. T. H. FLEMING.

J. PSYCHOL. NORM. PATH.

J. SPEECH DISORDERS.

NEOPSICHIATRICA.

VOL. V. MARCH–APRIL, 1939.

MAY–JUNE.

JULY–AUGUST.

NEUROBIOLOGIA.

VOL. I. NO. 1. JUNE, 1938.

SEPTEMBER.

A Contribution to the Study of the Early Manifestations of Schizophrenia.

The author has made a study of the early signs and symptoms of schizophrenia, and divides these factors into (1) those observed by the friends, (2) those observed by the physician.

In the first group he includes abandoning of occupation, idleness and inactivity, solitariness, silence, indifference to and lack of interest in other members of the family. The tendency to remain stationary, at times displays of extravagant actions without finality, the meaningless tears and laughter; the peculiar attitudes, the strange and pathetic gestures, negativisms, soliloquies, hallucinations, ideas and delusions of auto-reference, grandeur and persecution; the sexual indifference, fugues and attempts at suicide, the sum total of factors contributing to the physical appearance of the victim.

In the second group are included the following: The recognizing of a state of illness, amnesias, the transportation of personality, possession by strange bodily sensations, feelings of automatism and enforced movements, delirious ideas of influence, possession and auto-reference, the realization of impulsive movements without any reason, disturbance of perception (probably due to the change in the quality of reality), alterations of verbal expression with embarrassment, interruptions of thought, indifference and inactivity. These factors indicate a picture of depersonalization.

J. R. Beith Robb.

DECEMBER.

The Affective Dynamics of the Spoilt Child.

The author indicates the importance of the study of "emotion-belated" persons, i.e. individuals who he states are confined to an "infantile affective fixation."

In children the psycho-analytic method is used to investigate the child's sexual life. He remarks on the influence of the parents and family constellation on the character of the spoilt child. Types of spoilt children are found among the following: the only child, the first born, the last born, and the widow's child.

As a result of child spoiling affective fixations may persist into adult life.

With adults a comprehension of the psycho-analytical situation may be all that is necessary in treatment of slight cases.

In more severe cases a proper psycho-analytic examination is necessary, not only of the patient, but also of the parents, while environmental complications should be adjusted. J. R. BEITH ROBB.

Contraceptive Manoeuvres, Neurosis and Adultery.

Discussing etiology the author endeavours to establish a relationship between frustrate practices and the adultery which would be one expression of sex dissatisfaction, another being the neurosis resulting from the repression of adulterous impulses and impulses just hostile to the other sex mate.

He indicates that there are theoretical and practical difficulties in treating cases of this nature at a clinic. Further, where there is anxiety he stresses the difficulty in distinguishing between the anxiety of neurosis and that of hysteria, and of reconciling this syndrome with the divergent opinions of Freud, Stekel and Bleuler.

J. R. BEITH ROBB.

The Modern Treatment of Schizophrenia Compared with Routine Methods.

The author recalls that in the employment of the Meduna and Sakel methods for the treatment of schizophrenia one can undoubtedly make mistakes which on the whole cannot be avoided. He raises the issue of the different theories concerning schizophrenia, the possibility of spontaneous remission of these cases and the effect of previous medical treatment.

Since 1932 he had used routine methods in the Hospital of Juquery, S. Paulo, Brazil, in the treatment of 240 schizophrenics, of which 200 were his own personal cases. Of these selected cases 18 patients were fully recovered and 15 were improved, showing a percentage of 16·5 per cent. improved cases. Only where the usual methods were found to be unworkable did the author adopt the new methods. Out of the 200, 40 were thus treated—35 with convulsive therapy and 5 with insulin therapy. The total reported remissions following these methods numbered 14, and the improvements 11. Lasting improvement was obtained in 25 of the 40 cases, which is more than four times that obtained by the usual method.

The conclusion is that the newer methods give better results.

J. R. BEITH ROBB.

PSYCHIAT. QUART.

VOL. XIV. JANUARY, 1940.

Clinico-pathologic Study of a Case of Pick's Disease.

The authors describe a case of Pick's disease with the usual distribution of atrophy in the brain. The basal portion of the frontal lobe was more severely affected than the convexity. The orbital area was particularly shrunken. According to Spatz in this region is to be found the primary area of atrophy, and from a lesion of this area results impairment of the higher and more complicated psychic functions. Histologically the authors found the usual changes, but in addition there were large amounts of lipoid within the nerve cells. The staining reactions of these granules placed them in the lipochrome group, a group characteristic of senile nerve-cells. The extensive pigmentary deposit in the cells in the third and fifth layers of the cortex, the severe involvement of the dentate nucleus and the inferior olives agree well with the findings of Gellerstedt in senile brains. The authors conclude that Pick's disease represents a senile process limited to a determined zone of the brain. Angiospasm may play a role in the pathogenesis of the process. G. W. T. H. FLEMING.

The Effect of Metrazol Injections on the Electro-encephalogram.

1. On the basis of a comparison of potentials recorded from leads taken at various locations on the head, with electromyograms and with the movements as shown by ultra-high-speed motion pictures, an attempt has been made to separate the brain potentials from potentials caused by movement and muscle action currents.

2. The overt seizure shows in all stages, from the latent period to the end of the second clonic stage, an activity of 30 cycles per second in the motor region. An activity of 10 cycles per second was recorded from occipital leads during the latent period and the tonic stage. Motor-occipital leads recorded in the latent period showed some activity of 15 to 16 and 3 to 5 cycles per second.

3. The relaxation period shows low-voltage random activity.

4. If no seizure follows the metrazol injection the following changes in the EEG may occur:

(*a*) Drop in percent.-time alpha without appearance of abnormal potentials and return to normal activity within a minute.

(*b*) Appearance of random abnormal potentials with a slow return to normal activity after more than 45 minutes.

(*c*) Larval seizure, after which the activity returns to normal in less than 15 minutes. (Authors' abstr.)

PSYCHOANAL. QUART.

VOL. IX. JANUARY, 1940.

PSYCHOANAL. REV.

VOL. XXVII. JANUARY, 1940.

PSYCHOL. BULL.

VOL. XXXVII. FEBRUARY, 1940.

PSYCHOL. REV.

VOL. XLVII. JANUARY, 1940.

PSYCHOMETRIKA.

VOL. IV. 1939.

PSYCHOSOMATIC. MED.

VOL. I. OCTOBER, 1939.

The Hormonal Induction of Homosexual Behaviour in the Spayed Female Guinea-pig.

The induction of homosexual activity in spayed female guinea-pigs was attempted by means of injections of estrogens alone, estrogens and progesterone, and androgens alone or in combination with estrogens and progesterone.

Estrogen followed by progesterone was more effective than any single hormone or any other combination of hormones. It is postulated, therefore, that these hormones acting synergistically are responsible for mounting activity as well as heat in the normal animal.

Estrogen-conditioned animals were not stimulated to mount by animals which were mounting actively; and display of mounting in excess of that normally induced by estrogens depended on the injection of progesterone.

The highest percentage of animals was induced to mount when progesterone was injected 36 hours after the conditioning injection of estrogen. A diminishing percentage remained conditioned as long as seven days.

The extent to which mounting activity was displayed varied, but tended to be relatively consistent in individuals given repeated series of injections.

Animals which were refractory to the quantity of hormones which induced mounting in most animals remained refractory when given increased dosages.

In spayed immature animals the heat response was induced at an earlier age than mounting activity.

The similarities and differences between mounting activity and the heat response are enumerated. They suggest the working hypothesis that the two parts of overt behaviour are mediated by two effector systems, that both are stimulated by the synergistic action of estrogen and progesterone, but that each has its threshold, which varies independently from animal to animal. (Authors' abstr.)

The Correlations between Ovarian Activity and Psychodynamic Processes. II. The Menstrual Phase.

1. The simultaneous use of day-by-day study of vaginal smears and basal body temperatures on the one hand, and of the analysis of the recorded psychoanalytic material on the other hand, provided clear correlations between the physiological and psychological processes.

2. The investigation confirms the probability that in the adult woman, instinctual drives are related to specific hormone functions of the ovaries.

3. The premenstrual-menstrual phase of the sex cycle is one of diminishing progesterone and low, but variable estrone production. The metabolic gradient is generally downward.

4. Corresponding with the hormone levels, the instinctual tendencies are on the genital level when hormone production is relatively high; on the pregenital level when hormone production is very low.

5. Upon extinction of progesterone, eliminative tendencies appeared in the psychological material. This was most common in the late premenstrual period.

6. There is a semi-quantitative correlation between hormone production and psychic tension. (Authors' abstr.)

The Hypothalamus as a Thermostat Regulating Body Temperature.

As a result of experiments on cats the author concludes that the basal centre for the control of body temperature is composed of two parts. One is a heat-sensitive region located chiefly in the preoptic and supraoptic regions and connected through a descending pathway in the lateral hypothalamus with a motor centre for panting located somewhere behind the hypothalamus. The other part which reduces heat loss appears to be coextensive with the sympathetic centre in the hypothalamus. Its descending pathway enters the brain-stem dorsolateral to the mamillary bodies.

In the monkey, lesions in the anterior part of the lateral hypothalamus cause hyperthermia. It appears to be reasonable to conclude that the same part of the hypothalamus protects the body against chilling in carnivores and in primates.

G. W. T. H. FLEMING.

Alterations in the Hypothalamus in Mental Deficiency.

A histologic study was made of the diencephalon in 16 cases of mental deficiency, cases which did not show evidence of disease or injury to the cerebral cortex, and most of which at least could be classified as " primary amentia."

Pathological involvement of the third ventricle region was evident in all but two cases. Ependymitis and meningitis and distortion of the walls of the third ventricle were the most common findings.

The nucleus tubero-mammillaris was the only cell group in the hypothalamus which did not show a marked reduction in the number of cells. There was an average cell reduction of 27 per cent. for the paraventricular nucleus. In 15 cases the supra-optic nucleus showed an average cell loss of 35 per cent. The nucleus tuberis lateralis showed an average cell loss of 52 per cent. The average amount of cell reduction for the substantia grisea was 33 per cent.

The normal appearance of the cells in the hypothalamic nuclei suggests that the cell reduction occurred at an earlier period in the history of the patients.

Through its influence upon the hypophysis and the parasympathetic nervous system the anterior hypothalamus is probably concerned with the mobilization and discharge of energy. Hence it is believed that the alteration in the hypothalamus may play a role in the widespread physiological inadequacy and the abnormalities of growth and development, which are so common in mental deficiency.

(Author's abstr.)

Rorschach Manifestations of Improvement in Insulin-treated Schizophrenics.

There was, before treatment, a marked difference between the recovered and the unimproved patients with respect to their approach to the task of interpreting the ink-blots, a difference which disappeared after treatment. The recovered patient had been very inefficient before treatment; he became efficient after treatment. The unimproved patient had already been efficient before treatment; he remained so after treatment. The recovered patient's pre-treatment inefficient approach, or the great discrepancy between his potential and his actual functioning, can be recognized in his Rorschach record by the following signs: the lack of concentration upon the task and the making of numerous side remarks; the presence of good percepts accompanied by uncontrolled, extensive associations and by a great unevenness of performance; the abnormal distribution of colour interpretations, implying a disturbing influence of the emotions upon the reasoning processes. All these signs disappeared after successful insulin therapy. As regards the unimproved patient, on the other hand, his mental efficiency, or the lack of a noticeable disproportion between his potential and his actual functioning, can be recognized in his Rorschach record by the following: The earnest attempt on the part of the patient to do his best, his elaborations aiming at the completion and clarification of his ideas; the presence of poor percepts combined with controlled elaboration and with an even performance level; the presence of a colour response which implies that emotional factors did not interfere noticeably with the functioning of the patient's intellect.

(Author's abstr.)

REV. DE NEURO-PSIQUIATRIA.

VOL. I. NO. 3. SEPTEMBER, 1938.

The Cardiazol Test in the Diagnosis of Epilepsy.

The authors subjected epileptics and normal persons to injections of cardiazol. The administration of 2–3 c.c. 10 per cent. cardiazol produced an epileptiform convulsion in epileptics, but not in the normal controls except in a few cases. Further investigation, however, revealed that where a normal subject had had a convulsion a meal had been consumed prior to the test. In the same test cases when the stomach was empty the convulsion did not occur. It is recommended that the test subject should not take a meal on the day of test. It was also observed that there was a close relationship between the dose and the weight and sex of the subject.

The opinion is expressed that cardiazol is helpful in the diagnosis of epilepsy, but the author will not go so far as to recommend the test for medico-legal purposes.

J. R. BEITH ROBB.

DECEMBER.

Contribution to the Treatment of Schizophrenia with Insulin.

The authors treated 76 cases of schizophrenia with insulin. Results: 54 remissions, of which 45 were complete while 9 are described as social remissions. Five patients died, but in these cases the psychosis was of long standing. In another series of 41 cases, where the duration of the illness was less than six months, 36 complete and 3 social remissions were obtained.

The method of treatment was classical, but in cases with agitation or stupor, a modification in technique as proposed by Sakel was adopted. The "zigzag" technique of von Braunmühl and the method of minimal doses was also tried, the latter method receiving favourable comment.

During treatment observations were made relative to such factors as sex, form and evolution of the psychosis before treatment, total days of treatment, quantity of insulin used to produce the first coma, the average daily dose to produce shock, the frequency of coma, the total hours of coma and the number of epileptiform attacks, remissions and relapses.

With regard to the influence of the shock on mentation, will, perception, emotions, instinctive action, psychomotor activity, the opinion is submitted that there was no evidence to justify the hypothesis that during shock the psychosis regressed to an earlier phase of the illness.

Epileptiform attacks during treatment appeared to be associated with muscular states of hypotonus, and frequently in the pyknic type of subject. The suggestion is also advanced that insulin coma is more liable to be associated with states of muscular hypertonus.

In 32 cases during treatment a study of the vegetative system was made, and the authors indicate that insulin therapy will not only cause a remission in the psychosis, but will also stabilize the vegetative tonus. J. R. BEITH ROBB.

Psychiatric and Mental Hygiene in Brazil.

The author discusses the history of the mental services in Brazil. The following classification of the División de Asistencia a los Psicópatas is given :

Psychiatric Classification of the D.A.P.

1. Psychosis, infective.
2. Psychosis, auto-toxic.
3. Psychosis, hetero-toxic.
4. Schizophrenia.
5. Paraphrenia with chronic hallucinosis.
6. Paranoia.
7. Psychosis manic-depressive.
8. Psychosis, degenerative (senile and pre-senile).
9. Psychosis of organic brain disease.
10. Neuro-syphilis (cerebral syphilis, tabes psychosis).
11. General paralysis.
12. Epilepsies.
13. Psycho-neurosis.
14. Psychopathic personalities.
15. Oligophrenia.
16. Other types unclassified.

J. R. BEITH ROBB.

The Treatment of the Neuroses with Cardiazol.

The author reports on ten cases of hysteria treated with convulsant doses of cardiazol. The symptoms of hysteria in some of the cases, however, were not severe. Eight cases showed complete remission of the illness. No relationship could be observed between the efficacy of the treatment and the duration of the disease.

During treatment such symptoms as cephalalgia, asthenia and debility disappeared, while in one case chronic rhinitis was cured. In other cases there was modification of the personality, the individual becoming more adaptable socially. Results are claimed even when the cardiazol failed to produce a convulsion. The opinion is expressed that the factors responsible for a favourable result are outside the centres producing epileptiform convulsions.

Epileptics appeared to be more susceptible to the convulsant action of cardiazol than cases of hysteria, but cardiazol could not yet be used as a means of differential diagnosis.

In epileptics cardiazol did not intensify the spontaneous crisis, neither did it appear to awake latent epilepsy, but epileptics so treated became less irritable and the period between the fits lengthened. The paradoxical suggestion is made that epilepsy might be treated by inducing " epileptiform shocks."

J. R. BEITH ROBB.

REV. NEUROL.

VOL. LXXII. AUGUST, 1939.

SEPTEMBER.

RIV. DI NEUROL.

VOL. XII. DECEMBER, 1939.

RIV. PATOL. NERV. MENT.

VOL. LIII. MAY–JUNE, 1939.

VOL. LIV. JULY–AUGUST, 1939.

SEPTEMBER–OCTOBER.

NOVEMBER-DECEMBER.

SCHIZOFRENIE.

VOL. IX. DECEMBER, 1939.

Clinical Results of One Hundred Cases of Mental Illness Treated with Electroshock.

Of 56 schizophrenics treated with electroshock 10·7 per cent. were cured and 50 per cent. improved. Of 11 paranoid cases 54·5 per cent. were improved but none were cured. Of 24 manic-depressives 50 per cent. were cured, 41·6 per cent. were improved.

G. W. T. H. FLEMING.

TOKIO Z. PSYCHO-ANAL.

VOL. VII. NOS. 7–8. 1939.

Z. KINDERPSYCHIAT.

VOL. VI. 1939.

Z. TIERPSYCHOL.

VOL. III. 1939.

1. Pathology, Biochemistry, etc..*

Further Investigations on the Mechanism of the Formation and Destruction of the Chemical Factors of Nervous Stimulation. Koshtoyants, Kh. S., and Mitropolitanskaya, R. L. [*Compt. rend. acad. Sci. U.R.S.S.*, **23**, 955–7 (1939) (*in English*); *cf. C.A.*, **33**, 5492⁴.]

Investigations on the transmission of stimuli from the nerve of the cardiac muscle under conditions of carbohydrate metabolism, inhibited by the effect of glyceraldehyde on the heart of a frog, showed that after treatment of the heart with glyceraldehyde (0·02 M. solution) the typical response (stopping) to the excitation of n. vagus is absent. This is explained by the assumption that the disturbance of the normal glyceraldehyde led to the disturbance of the normal process of formation of acetylcholine-like substances. A. H. KRAPPE (Chem. Abstr.).

Cerebral Metabolism During Fever. Himwich, Harold E., Bowman, Karl M., Goldfarb, W., and Fazekas, Joseph F. [*Science*, **90**, 398 (1939).]

The brain metabolism of patients with general paresis was studied before and during fever produced by injections of typhoid vaccine or inductotherm therapy. Samples of arterial blood and of the return flow of the brain obtained from the internal jugular vein were analysed for O, CO_2, glucose and lactic acid. In every instance an increase of cerebral metabolism during fever was indicated.

FELIX SAUNDERS (Chem. Abstr.).

The Occurrence of Ovulation in the Rabbit as a Result of Stimulation of the Central Nervous System by Drugs. Marshall, F. H. A., Verney, E. B., and Vogt, Martha. [*J. Physiol.*, **97**, 128–32 (1939).]

Picrotoxin in a dose of 0·9–1·1 mg./kg. was injected intravenously into rabbits in heat. Follicle growth, development of batches of cystic and haemorrhagic follicles or ovulation ensued in a large number of animals so treated. No ovarian responses were obtained to the injection of a series of other substances, most of which were stimulants of the central nervous system.

E. D. WALTER (Chem. Abstr.).

* A number of abstracts in this section are reproduced from *Chemical Abstracts* by kind permission of Prof. Crane, of Ohio University, to whom the Editors wish to express their thanks.

The Duration of Life After Cerebrovascular Accidents. Newbill, H. P. [*J. Amer. Med. Assoc.*, **114**, 236 (1940).]

Sudden death (within two hours) from cerebrovascular accidents is the exception rather than the rule. The average survival period after thrombosis is approximately fifteen times as long as after haemorrhage or embolism. There was a marked difference in the survival period of the white (105 days) and the negro races (65 days), mainly confined to the thrombotic patients. Equally so between males (57 days) and females (129 days). G. W. T. H. FLEMING.

Nicotinic Acid Deficiency Encephalopathy. Joliffe, N., et. al. [*J. Amer. Med. Assoc.*, **114**, 307 (1940).]

The authors describe 150 cases of an encephalopathic condition distinguished by clouding of consciousness, cogwheel rigidities and uncontrollable grasping and sucking reflexes which may or may not be associated with polyneuritis, pellagra, or with the oculomotor signs of central neuritis.

Patients treated with nicotinic acid plus hydration showed a marked reduction in mortality. The authors consider the condition to be a nicotinic acid encephalopathy. G. W. T. H. FLEMING.

The Effect of Extracts of the Adrenal Glands on the Respiration of Isolated Brain and Liver Slices. Tipton, S. R. [*Amer. J. Physiol.*, **127**, 710–15 (1939).]

Extracts of the adrenal whole gland and cortex depressed the O consumption of brain and liver slices of normal and of three adrenalectomized rats. The R.Q. of the brain slices was not affected by the extract. An extract of beef brain also showed depressing effects on the respiration. Crystallized corticosterone in concentrations of the same magnitude as the solid matter of the adrenal extracts also showed marked depressing action. E. D. WALTER (Chem. Abstr.).

Sugar Tolerance of Alcoholic Patients. Bowman, Karl M., Wortis, Joseph, Orenstein, Leo L., and Goldfarb, Walter. [*Proc. Soc. Exptl. Biol. Med.*, **42**, 37–40 (1939); *cf. C.A.*, **33**, 7385[3].]

On admission there was a marked decrease in the sugar tolerance of a group of 18 alcoholic patients, probably because of undernutrition. After one week in the hospital on a normal diet the sugar tolerance was improved.

L. E. GILSON (Chem. Abstr.).

Encephalopathy Produced by Manganese. Grewel, Fr., and Sassen, E. [*Nederland. Tijdschr. Geneeskunde*, **83**, iv, 5464–71 (1939).]

Mn poisoning leads to simultaneous cerebral and liver disturbances.

E. BEUTNER (Chem. Abstr.).

Morphology of Glycogen Distribution and Transformation. III. Cytology of Glycogen Accumulation in the Motor Cells of the Normal Nervous System. Shabadash, A. L. [*Bull. biol. med. exptl. U.R.S.S.*, **7**, 353–7 (1939) (*in English*); *cf. C.A.*, **33**, 6373[5].]

The normal resting or recently recovered nerve cell contains glycogen (I), although variations in carbohydrate metabolism from one kind of nerve cell to another give rise to many types of I accumulation. All the motor cells of a definite level of the motor nucleus show the same typical degree of I accumulation at the same time. The granules of " normal " I are characteristic and readily distinguished from pathological I inclusions, which appear as large coarse structureless deposits which distort the shape of the cells. I is found as a normal component of the Nissl tigroid, where it is probably combined with protein.

IV. Glycogen in the Cells of the Gasserian and Spinal Ganglions of Normal Animals. Reentovich, R. V., and Shabadash, A. L. [*Ibid.*, **8**, 29–31.]

The normal pseudo-unipolar nerve cells of the Gasserian and spinal ganglions of mammals in a relatively quiescent state and under proper conditions of nutrition contain glycogen. S. A. KARJALA (Chem. Abstr.).

The Influence of Brain Metabolites on the Oxidation Process of Animal Tissues. Govorovich, E., and Tikhaya, M. [*Bull. biol. med. epxtl. U.R.S.S.*, **7**, 39–43 (1939) (*in French*).]

There are no differences in the action of brain metabolites isolated during rest or during induction coil excitation on the respiration of the brain, kidney, liver or muscles of cats. S. A. KARJALA (Chem. Abstr.).

The Influence of Brain Metabolites on the Secretory and Motor Functions of the Stomach. Guerchikova, K. A. [*Bull. biol. med. Explt. U.R.S.S.*, **7**, 315–18 (1939) (*in French*).]

The intravenous injection of small concentrations of the protein-free ultrafiltrates of brain metabolites into dogs causes an increase in gastric juice secretion, an increase in total acidity and free HCl, and a decrease in digestive capacity. Large doses decrease the secretion of gastric juice but have no effect on total acidity, free HCl or digestive capacity. In all cases gastric secretion was obtained only with the simultaneous administration of milk as a stimulant. Depending upon the functional state of the motor appearance of the stomach, injection of brain metabolite solutions may increase or decrease motor activity. If the stomach is in a state of relative rest the injections increase the activity, but if it is at maximum activity they decrease activity. S. A. KARJALA (Chem. Abstr.).

The Method of Direct Action on the Central Nervous System, and more Particularly on the Vegetative Cerebral Centres. Shtern, L. S. [*Bull. biol. med. exptl. U.R.S.S.*, **7**, 267–70 (1939) (*in French*).]

One of the determining factors of the functional state of the vegetative nervous centres of the brain is the K/Ca ratio. Increase of the ratio by direct injection of an extract of the posterior lobe of the hypophysis, adrenaline or K salts into the cerebral ventricles results in excitation of the nervous centres, while decrease of the ratio by the injection of kidney extract or Ca salts results in inhibition. Shock is accompanied by a decrease in K and inorganic P and an increase in Ca, and can be relieved by direct injection of K and P salts. Injection of the salts into the blood stream is not always effective because of the resistance of the haemato-encephalic barrier. S. A. KARJALA (Chem. Abstr.).

Calcium Ions Necessary to Synaptic Transmission in Parasympathetic, not in Sympathetic, Ganglia. Schafer, Geo. D. [*J. Pharmacol.*, **67**, 341–52 (1939).]

The parasympathetic paths to the sphincter pupillae of the cat are temporarily paralysed by proper injections of Na citrate, but the sympathetic pathways to the constrictor musculature of the visceral blood vessels, to the chromaffin cells of the adrenal medulla, to the dilator pupillae or to the retractor smooth muscle of the nictitating membrane are not. Perhaps the synapses in cholinergic ganglia are of two classes, Ca-cholinergic and K-cholinergic.

L. E. GILSON (Chem. Abstr.).

Cholesterolysis in the Blood Plasma of Individuals with Mental Disorders. Schube, Purcell, G., Raskin, Naomi, and Campbell, Eleanor. [*J. Lab. Clin. Med.*, **25**, 142–9 (1939).]

The rate of change of the total cholesterol concentration of the blood plasma of 26 male patients who were normal physically but mentally ill was studied over a period of 24 hours at room and ice-box temperatures. The results were similar to

those obtained on normal individuals (*C.A.*, 33, 1378[9]) but on a lower plane. The rate at which cholesterol aggregates are able to free themselves from the meshes of protein molecules is discussed as an important factor in cholesterolysis.

HOWARD W. ROBINSON (Chem. Abstr.).

The Influence on the Animal of Thyroid Metabolites Introduced into the Cerebral Ventricles. I. Their Influence on the Composition of the Blood and Cerebrospinal Fluid. Kassil, G. N., Plotitsina, T. G., and Volkoviskaya, Ch. [*Bull. biol. med. exptl. U.R.S.S.*, **8**, 51–5 (1939) (*in French*).]

The injection of thyroid metabolites and thyroxine (I) into the cerebral ventricles of dogs results in a reduction in the K/Ca ratio and a decrease in P in the cerebrospinal fluid and blood. I also lowers the concentration of reducing substances in the fluid and blood serum. The injection of diiodotyrosine (II) causes a lowering in K, Ca, P and K/Ca in the blood and a lowering in K and Ca, with an increase in P and a slight increase in K/Ca in the cerebrospinal fluid. The injection of small doses of metabolites, I or II directly into the blood stream results in an increase in reducing substances, P and K/Ca. S. A. KARJALA (Chem. Abstr.).

The Protein Fractions in Blood and Spinal Fluid After Poisoning of the Nervous System with Carbon Monoxide. Bakhtiyarov, V. A. [*Klin. Med.* (*U.S.S.R.*), **16**, 726–9 (1939).]

Chronic CO poisoning decreases blood and spinal fluid albumin, increases blood and spinal fluid globulin, and decreases the permeability of the haematoencephalic barrier. S. A. KARJALA (Chem. Abstr.).

The Effect of Monosaccharides on Water Absorption from the Sub-arachnoid Space. Bedford, T. H. B. [*J. Physiol.*, **96**, 392–6 (1939); *cf. C.A.*, **32**, 9297[9].]

Isotonic solutions of glucose, xylose and mannose were without influence on absorption when introduced into the subarachnoid space for one hour. Solutions twice the isotonic concentration caused a marked reduction in absorption after 30 minutes. These sugars have a similar action on water absorption and they are in all probability absorbed by a common process. No evidence was obtained of a specific absorption of glucose such as occurs in the intestine.

E. D. WALTER (Chem. Abstr.).

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2. Pharmacology and Treatment.

The Relationship of the Insulin Hypoglucaemic Reaction to Shock. Corwin, Warren C. [*J. Lab. Clin. Med.*, **25**, 169–74 (1939).]

Hypoglucaemic manifestations (" insulin shock ") were produced in dogs and rabbits by the injections of fatal and non-fatal doses of insulin. Determinations of the haemoglobin content and the number and volume of erythrocytes in the blood indicate that haemo-concentration does not occur incident to such hypoglucemic reactions. Visceral evidences of capillo-venous congestion and increased capillary permeability were not seen in the animals after death. The mechanism of death in " insulin shock " is not the same as that of shock (Moon, *Arch. Path.*, **24**, 642, 794 [1937]. HOWARD W. ROBINSON (Chem. Abstr.).

Neuro-Histopathology of Metrazole and Insulin Shock Therapy. Experimental Study in the Cat. Winkelman, N. W., and Moore, Matthew T. [*Trans. Am. Neurol. Assoc.*, 214–16 (1939).]

Insulin (I) caused severe damage of the neurones, while metrazole (II) produced practically no morphologically demonstrable change in the central nervous system

of the cat. These results may indicate the need for greater caution in the use of I in human subjects; II may be considered the safer drug.

J. PINCHACK (Chem. Abstr.).

Mechanism of Insulin Convulsions. III. Effects of Varying Partial Pressures of Atmospheric Gases After Adrenalectomy. McQuarrie, Irvine, Ziegler, M. R., Stone, W. E., Wangensteen, O. H., and Dennis, C. [*Proc. Soc. Exptl. Biol. Med.*, **42**, 513–14 (1939); *cf. C.A.*, **33**, 7385⁵.]

Breathing a mixture of 5 per cent. O_2 and 95 per cent. N_2 causes hypoglucemia in adrenalectomized dogs without insulin, and hypoglucemia in normal dogs. Insulin convulsions are prevented by anoxia of this degree even when the blood sugar falls to 9–14 mg. per cent. Breathing a mixture of 15 per cent. CO_2, 20 per cent. O_2 and 65 per cent. N_2 also tends to prevent insulin convulsions.

L. E. GILSON (Chem. Abstr.).

Action of Insulin on the Chronaxie of the Foot of the Snail. Cahen, Raymond. [*Compt. Rend.*, **209**, 447–8 (1939).]

Insulin, in relation to its hypoglucaemic action, stimulates the isolated heart and depresses the isolated intestines. Its effect on the isolated foot muscle of the snail was noted by measuring the chronaxie. Insulin increases the chronaxie, but the effect is not persistent, in spite of the maintenance of the preparation in contact with hormone. The rheobase was increased equally with the chronaxie. There is spontaneous cessation of the action of insulin after prolonged contact. It diminishes after 35 to 50 minutes, and tends to regain its initial value after 45 to 65 minutes. It is not due to a change in insulin, as a new amount of insulin added to the old again raises the chronaxie. In its effect on muscle, insulin acts as a potential poison.

DOROTHY A. MEYER (Chem. Abstr.).

Biochemistry of Hypoglucaemic Shock. I. The Chlorides in Plasma and Corpuscles. Romeo Filippo. [*Biochem. terap. sper.*, **26**, 325–37 (1939).]

The Cl in total blood as well as in the plasma is conspicuously increased, especially in cases with lethal prognosis. An increase of Cl in the erythrocytes persists to the end of shock in non-serious cases whereas there is a final decrease in grave cases. A theoretical discussion is given.

A. E. MEYER (Chem. Abstr.)

Physicochemical Equivalents in Shock. II. Surface Tension of Serum in Insulin Shock. Scimone, I. [*Arch. sci. Biol.* (*Italy*), **24**, 303–10 (1938).]

No appreciable difference in static and dynamic surface tension was found in the serum of schizophrenic patients subjected to insulin shock except a slight diminution when the serum was diluted ten times. P. F. METILDI (Chem. Abstr.).

The Effect of Metrazole by Perlingual and Enteral Administration. Kuschel, H. [*Klin. Wochenschr.*, **18**, 1131 (1939).]

Metrazole is readily absorbed by the mucosa of the tongue and gastro-intestinal tract. The duration of the effect is about three times that following intravenous injection. H. L. MASON (Chem. Abstr.).

Physiological Observations Following Induced Convulsions. Orenstein, Leo L. [*N.Y. State J. Med.*, **39**, 1921–3 (1939).]

A study was made of circulatory changes in 15 schizophrenic patients given intravenous injections of metrazole. After a mild metrazole convulsion the electrocardiagram also showed rapid rate, arrhythmia, T-wave elevation and depression of the S-T segment. After a severe convulsion the electrocardiogram also showed sinus arrest, shifting of the pace-maker, auricular and ventricular

premature contractions, coupling of beats, nodal escapes, and rarely a marked bradycardia. The blood pressure showed a rise in systolic and diastolic levels at the beginning of the injection, and generally a fall in the diastolic and an elevation in the systolic level after a convulsion. The cerebrospinal fluid after a metrazole convulsion showed a marked rise in pressure and no change in content. When the metrazole was given too slowly to cause a convulsion no notable effects were produced other than an increase in heart rate. E. J. C. (Chem. Abstr.).

Treatment of Multiple Sclerosis with Nicotinic Acid and Vitamin B_1. *Moore, M. T.* [*Arch. Int. Med.*, **65**, 1 (1940).]

Five cases of advanced multiple sclerosis in which many forms of treatment had been used without appreciably halting the progress of the disease and in which the patients were treated with nicotinic acid and vitamin B_1 are reported.

Nicotinic acid produces vasodilatation not only of the skin but also of the brain and spinal cord.

Nicotinic acid and vitamin B_1 (thiamin chloride) may be given parenterally in considerable doses (nicotinic acid, 120 mg.; thiamin chloride, 33·2 mg.) for prolonged periods without apparent harmful effects.

Subjective and objective evidence of continued improvement has followed the parenteral use of nicotinic acid and vitamin B_1 in the cases of multiple sclerosis here reported. (Author's Abstr.).

Effect of Analeptic Drugs on Hibernation in the Thirteen-Lined Ground Squirrel (Citellus Tridecemlineatus). *Pfeiffer, Carl, Foster, Mark A., and Slight, David.* [*J. Pharmacol.*, **67**, 307–12 (1939).]

The sympathicomimetic amines are the most potent analeptics against the hibernating state. During hibernation clonic convulsions are well tolerated and may not awaken the animal; spinal convulsions are poorly tolerated and sensitivity to spinal convulsions is greatly increased. Metrazole, picrotoxin and cocaine have high analeptic indexes in hibernation. Caffeine sensitizes the hibernator so that handling produces a tetanic convulsion which may be immediately fatal. Coramine is twice as toxic in hibernation and produces a sensitization lasting several days during which the animal, if touched, goes into clonic convulsions, which may continue two to three days (" marathon convulsions ") and kill the animal by exhaustion, but which can be stopped by ephedrine, which awakens the animal. Strychnine is ten times as toxic in the hibernating as in the awake animal. The hibernating animal is a good test animal for the study of acidosis and the effects of vaso-constricting and metabolism-stimulating drugs. L. E. GILSON (Chem. Abstr.).

Electrical Studies on the Pharmacology of Autonomic Synapses. III. Action of Ephedrine Analysed by a Study of its Sympathetic Central and Ganglionic Effects. *Marrazzi, Amedeo S.* [*J. Pharmacol.*, **67**, 321–9 (1939); *cf.* C.A., **33**, 4674[4].]

Increased preganglionic potentials show that ephedrine activates sympathetic cells within the central nervous system, while decreased postganglionic potentials show that it blocks sympathetic stimulation. The possible mechanism of the action is discussed. L. E. GILSON (Chem. Abstr.).

Effect of Cyanide on Cerebral Metabolism. *Fazekas, J. F., Colyer, Harriet, and Himwich, H. E.* [*Proc. Soc. Exptl. Biol. Med.*, **42**, 496–8 (1939).]

In dogs the intravenous or intracarotid injection of KCN causes a decrease in cerebral O consumption proportional to the KCN concentration. Concentrations which inhibit cerebral respiration cause no significant decrease in the O consumption of skeletal muscles. L. E. GILSON (Chem. Abstr.).

Consequences of Narcosis or of Asphyxia? Experimental Data on the Influence of Nitrous Oxide and of Oxygen-Lack on the Central Nervous System. van der Molen, H. R. [*Nederland. Tijdschr. Geneeskunde*, **83**, iv, 4921–9 (1939).]

Inhalation of a $N_2O + O_2$ mixture with less than 8 per cent. O_2 for several hours causes serious degeneration of the ganglion cells of the cerebrum. The same holds for a 100-hour-narcosis with a mixture containing 20 per cent. O_2.

R. Beutner (Chem. Abstr.).

Effect of Phenylisopropylamine (Benzedrine) on the Metabolism of the Non-anaesthetized Dog. Delaunois, A. L., and Marri, R. [*Acta Brevia Neerland. Physiol., Pharmacol., Microbiol.*, **9**, 242–3 (1939).]

Five fasting dogs were intramuscularly injected with 0·5–1·0 mg. benzedrine per kg. Ten minutes after injection both O_2 consumption and CO_2 output had increased markedly and R.Q. had fallen an average of 0·042. In about 45 minutes the values were back to normal. E. Curzon (Chem. Abstr.).

The Pharmacological Action of Deuterium Oxide. VIII. Action on the Central Nervous System. Herrmann, Julian B. [*J. Pharmacol.*, **67**, 265–75 (1939); *cf. C.A.*, **33**, 3884[4].]

Application of D_2O to the cerebral cortex produces a marked state of catalepsy in cats and monkeys. Injected D_2O disappears from the cerebrospinal fluid within 30 minutes. Encephalographic determinations parallel the objective findings of cerebral depression. Application of D_2O to the spinal centres of cats and frogs has no apparent effect on nerve impulse transmission. Application of D_2O to nerve or muscle or nerve-muscle has no obvious effect on nerve-impulse transmission or muscle contraction. L. E. Gilson (Chem. Abstr.).

The Effect of Sodium Bromide on the Nutrition and the Gastro-Intestinal Tract of Epileptic Patients. Arieff, Alex J. [*J. Lab. Clin. Med.*, **25**, 19–24 (1939).]

Few toxic cases were observed in these patients with blood bromide concentrations around 200 mg. per 100 c.c. When there was no anorexia or bromide toxicosis producing an inadequate caloric intake this blood level caused no weight loss, had no effect on nutrition and produced no abnormal change in the basal metabolic rate. Gastric analyses showed that the chloride ion was displaced by bromide from 25 to 50 per cent. In experiments in vitro HBr slightly retarded peptic digestion, but not enough to produce clinical symptoms and had no effect on trypic digestion.

Howard W. Robinson (Chem. Abstr.).

A New Method of Treatment of Alkaloid Addicts by Tetrodotoxin. Hsiang, Nai Shi. [*J. Oriental Med.*, **30**, 639–47 (*German abstr.* 179) (1939).]

From 1 to 2 c.c. of tetrodotoxin ($C_{10}H_{32}O_{16}$) mixed in 20 c.c. 20 per cent. glucose solution is given intravenously or orally to 18 subjects of opium and heroine habits, the number of dosages depending upon the severity of the symptoms, and oral treatment requiring a greater amount of the drug. Detailed data are given as to various symptoms before and after the treatment, confirming the authors' previous success with 1,500 patients. T. Sashiro (Chem. Abstr.).

The Synergism of Phenobarbital, Dilantin Sodium and other Drugs. Cohen, B., et al. [*J. Amer. Med. Assoc.*, **114**, 480 (1940).]

The authors found that the increase of phenobarbital dosage up to an average of 3 gr. a day, with due regard to individual effect, was followed by a great reduction in the incidence of seizures amounting to about 68 per cent. as compared with treatment by phenobarbital alone given in a routine way. Dilantin sodium was not as effective as adequate phenobarbital usage. Benzedrine has a favourable

effect on toxic symptoms of luminal and also on those of dilantin. The combination of luminal and dilantin is far more efficient than either drug alone; the reduction in fit incidence is at least 50 per cent. over the most favourable results obtained without combining the drugs. G. W. T. H. FLEMING.

The Local Anticonvulsive Action of Calcium Salts. *Beutner, R.* [*Proc. Soc. Exptl. Biol. Med.*, **42**, 547–9 (1939).]

In guinea-pigs the intramuscular injection of 100–200 mg./kg. of procaine-HCl caused clonic and tonic convulsions. Mixing $CaCl_2$ with the procaine-HCl greatly decreased the incidence of convulsions. Other Ca salts acted like $CaCl_2$, except Ca gluconate, which does not ionize. $MgCl_2$ counteracts the action of $CaCl_2$, probably by altering membrane permeability, and in the absence of Ca increases the convulsive action of procaine. L. E. GILSON (Chem. Abstr.).

Alcohol and Sedatives. *Peter, Helmut.* [*Deut. Z. ges. gerichtl. Med.*, **31**, 113–53 (1939).]

Impairment of attentiveness and concentration power paralleled the limits of motor performance and blood alcoholic level. Phenobarbital, 0·3 gm., had the same effects as alcohol, 1 g./kg. body-weight, when the subject was tested objectively. Sedormid impaired the motor ability of one case slightly. Cibalgin was effective only after exercise. Subjective tests showed that the effects of phenobarbital and alcohol can be differentiated. Together with alcohol even the relatively ineffective cibalgin produced a real narcosis; pyramidone produced a sense of well-being with no improvement in motor performance. FRANCES KRASNOW (Chem. Abstr.).

The Action of Some Indifferent Narcotics on the Acetylcholine Sensitivity of the Rectus Muscle of the Frog. *Emmelin, Nils.* [*Skand. Arch. Physiol.*, **83**, 69–70 (1939).]

Various alcohols (Me, Et, Pr, Bu, Am) increase the action of acetylcholine on the frog rectus muscle proportionally to their number of C atoms. Experiments with 3 isomeric Bu-alcohol show that the tertiary alcohol has a weak action while normal primary BuOH and isobutyl alcohol have a strong action. Neither glycerol nor ethylene glycol has any effect. The sensitiveness toward acetylcholine is also increased by Me, Et, Pr esters of carbamic acid, methylurethan having the weakest and propylure than the strongest action. Certain narcotics increase the sensitivity to acetylcholine, and their effect persists even after the complete paralysis of the choline esterase by physostigmine. S. MORGULIS (Chem. Abstr.).

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IMPORTANT NOTICE

The next Preliminary and Final Mental Nursing Examinations will be held on Monday, November 4, 1940.

The latest date on which entries will be received is October 1, and no candidates whose names have not been received by that date will, under any circumstances, be allowed to sit for the Examination.

H. G. L. HAYNES,
Registrar.

VI

R

By R. M. STEWART, M.D., F.R.C.P.ED., M.R.C.P.,
Medical Superintendent, Leavesden Hospital, Watford.

(Received March 16, 1940.)

A SINGLE small aperture connecting each lateral ventricle with the dorso-cephalic portion of the third ventricle provides the sole means of escape for cerebro-spinal fluid, and consequently it follows that any interference with its patency will seriously retard the outward flow of ventricular fluid. Complete, or even partial, closure of the foramen leads to a rapid increase in the volume and pressure of imprisoned ventricular fluid so that a condition of internal hydrocephalus is soon established. Usually both foramina are occluded, the hydrocephalus being therefore bilateral and the ventricles more or less symmetrically enlarged. In rare instances, however, only one foramen is obstructed, in which case the dilatation will, of course, be confined to the ipsilateral ventricle. Unilateral hydrocephalus of this obstructive type is commonly caused by inflammatory conditions in the neighbourhood of the foramen, or by pedunculated tumours attached to the choroid plexus which enjoy a degree of movement sufficient to permit intermittent or permanent blockage of the foramen of Monro. It is, however, possible to find examples of unilateral hydrocephalus in which the outflow of cerebro-spinal fluid through the foramen of Monro is unimpeded, and in these the cause of the ventricular dilatation is to be sought in some diseased condition of the cerebral wall which has become so weakened as to be unable to resist even normal ventricular pressure. Such expansion may be either limited to one part of the lateral ventricle, or general, involving the entire body with its horns.

In illustration of this second non-obstructive type of unilateral hydrocephalus the following two cases may be quoted :

CASE 1.—When admitted to hospital on 2.ix.14, A. W—, a female, aged 14, was noted to have the physical development of a child of five ; unable to articulate or to occupy herself in any way, dirty in habits and subject to severe epileptic fits, she was a typical example of profound idiocy. In 1924, when transferred to Leavesden Hospital, she was found to have spastic paralysis of right upper and both lower limbs. Corneal clouding on both sides and traces of notches on the upper central incisors suggested the presence of congenital syphilis, and after a course of novarsenobillon her fits became less frequent, but otherwise no improvement was noted. Ten years later the paralysis had become more marked, especially on the right side ; the pupils reacted normally, the deep reflexes were exaggerated and the plantars could not be obtained. The Wassermann reaction was negative in the blood and cerebro-spinal fluid ; the pressure of the latter was normal. On 21.xi.34 the patient had a succession of fits, the movements being almost confined to the left side. Death occurred at 7.20 p.m. on 24.xi.34.

An autopsy was performed on 26.xi.34 at 10 a.m. The body was that of an undersized adult female. The limbs on the right side were smaller than on the left, the right arm showing contracture at the elbow-joint, and the right leg a marked degree of talipes equino-varus. The calvarium was increased in thickness and density, but showed no asymmetry. The dura was normal. The brain was microcephalic, weighing 870 gm. The pia-arachnoid showed intense congestion over the frontal and parietal gyri of the right cerebral hemisphere, but without thickening or opacity. On the opposite side it showed neither congestion nor thickening, having, indeed, an almost normal appearance.

On the right cerebral hemisphere the convolutions were simple, but showed no atrophy. Those on the vertex of the left hemisphere were of a yellowish-brown colour, flattened to a marked degree and pressed tightly together (Figs. 1, 2). Their staining and flattening into ribbon-like areas was particularly marked in the territory supplied by the middle cerebral artery. On palpation the convolutions had an almost leather-like consistence. Division of the attenuated corpus callosum allowed the escape of a large quantity of clear cerebro-spinal fluid and when the two hemispheres were separated the left lateral ventricle was seen to be enormously dilated and to have lost all semblance of its normal shape (Fig. 3). As is usual in hydrocephalus, the white matter had yielded more readily than the grey, being hardly recognizable, and thinned to a mere shell which in some areas was actually translucent. In the neighbourhood of the frontal, temporal and occipital poles the grey and white matter were of an almost normal thickness, the convolutions in these localities being relatively well formed. The ependymal lining of the ventricles was for the most part smooth and shiny, but here and there it presented a wrinkled appearance ; the choroid plexus was thickened and bound down. The right lateral ventricle showed a very slight degree of dilatation, but with a perfectly normal ventricular lining. The third and fourth ventricles were normal and the Sylvian aqueduct connecting them showed no dilatation. No evidence of recent or old inflammation could be found at the base of the brain and in this situation the arteries showed no evidence of disease. The cerebellum showed marked asymmetry, its right hemisphere being notably smaller than the left. In the medulla the right pyramid and the left inferior olive were reduced in size.

Microscopic appearances.—Sections of cerebral cortex were made from the frontal and parietal regions of both cerebral hemispheres and stained for nerve cells, glia and myelin sheaths.

In the right cerebral hemisphere little abnormality could be found. There was no obvious disturbance of the cyto-architectonics, but in all laminae of the pre- and post-central gyri the nerve cells were poorly developed and fewer than normal (Fig. 4*a*). Apart from some increase in glial nuclei, no evidence of gliosis could be found.

Over the left cerebral hemisphere the pia mater showed slight thickening; it contained numerous fibroblasts but no inflammatory cells and its vessels were normal.

In the left pre- and post-central gyri cortical devastation was almost complete, the total depth of the grey matter being about one-quarter of the thickness of the corresponding gyri on the opposite side (Fig. 4*b*). No nerve cells could be found

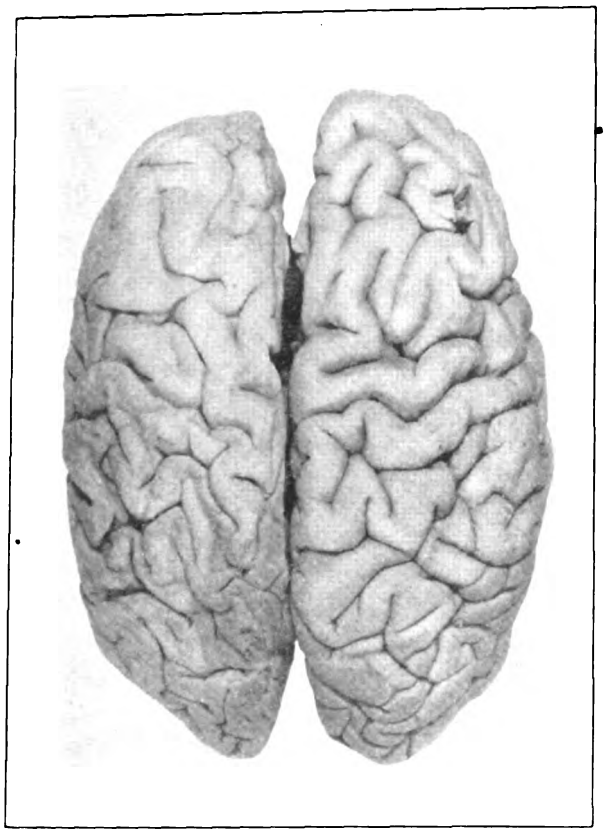

FIG. 1.—Cerebrum. The left hemisphere is smaller than the right and its convolutions markedly flattened. $\frac{2}{3}$ actual size.

except in the deeper layers and here those which survived were immature, many of them resembling neuroblasts. Rod cells were numerous.

In the molecular layer numerous yellow pigment granules could be seen lying scattered between a horizontal row of dark staining neuroglial nuclei.

The white matter was likewise much reduced in thickness and contained a great excess of glial nuclei.

Sections stained by Holzer's method revealed an intense degree of gliosis (Figs. 4*c*, 5*a*). Immediately beneath the pia a thin superficial stratum of fine interlacing fibres could be seen merging into dense strands and sheaves at a deeper level.

In the white matter the degree of gliosis, stronger and denser than in the grey matter, was most striking. Gliosis was also dense in the ependymal lining of the

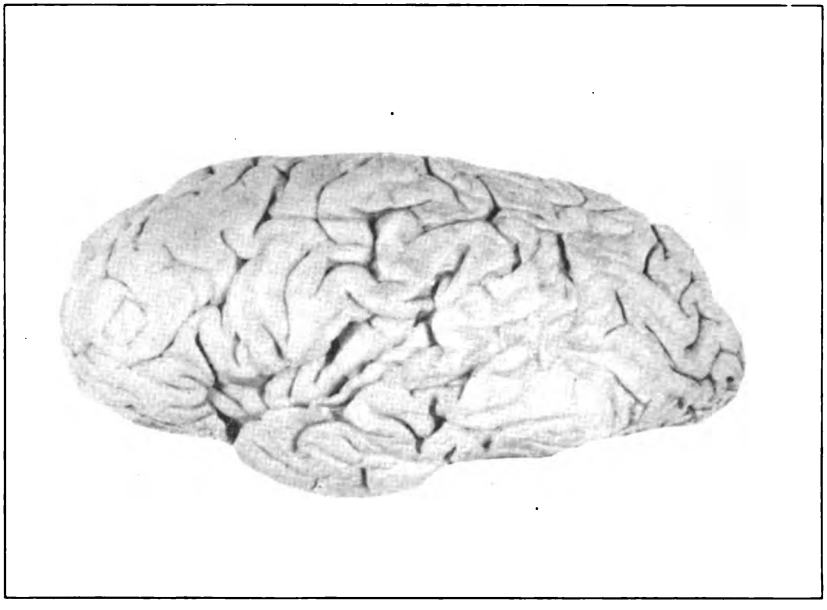

FIG. 2.—Lateral view of left cerebral hemisphere showing the flattened, shrunken gyri. Note exposure of insula.

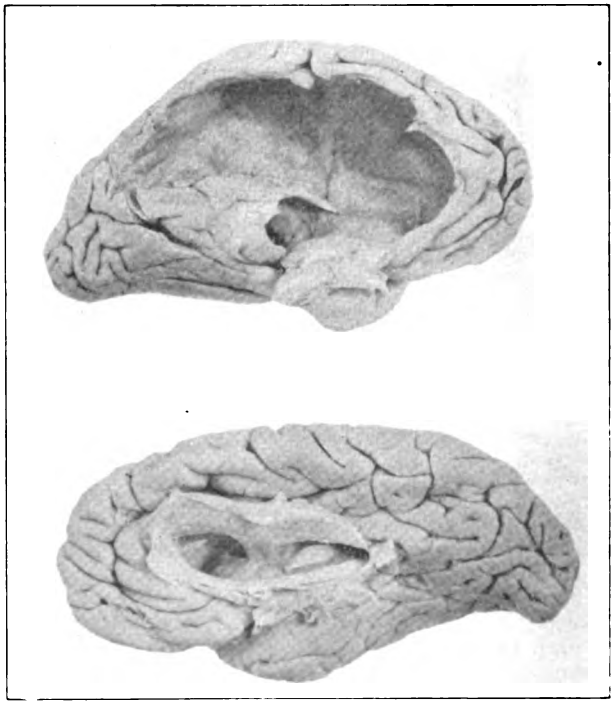

FIG. 3.—Mesial aspects of the two hemispheres. The left lateral ventricle is enormously dilated, the right very slightly dilated.

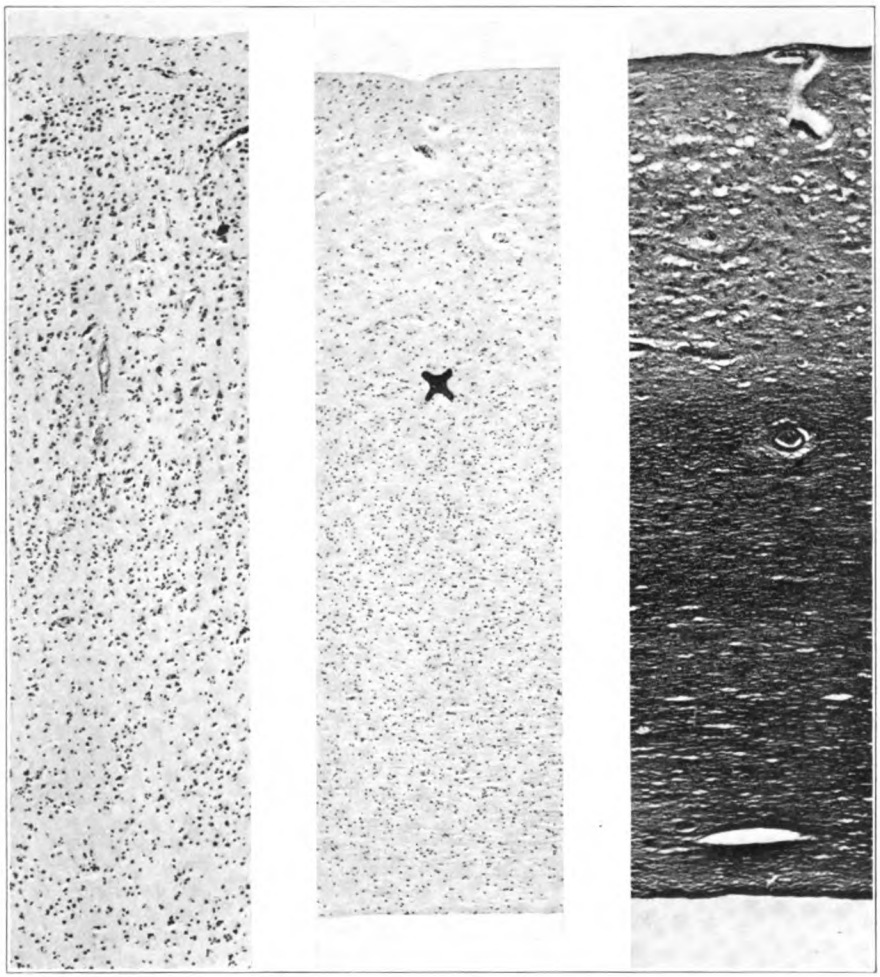

FIG. 4.—(*a*) Section of right post-central gyrus. There is a paucity of nerve cells though their lamination is preserved. Tol. blue. × 65. (*b*) Section of left pre-central gyrus. The grey matter is shrunken and devoid of nerve cells. *X* marks transition between grey and white matter. Compare with (*a*) of similar magnification. Tol. blue. (*c*) Similar section stained by Holzer's method. Note superficial gliosis and the dense character of the glial overgrowth in the white matter. × 65.

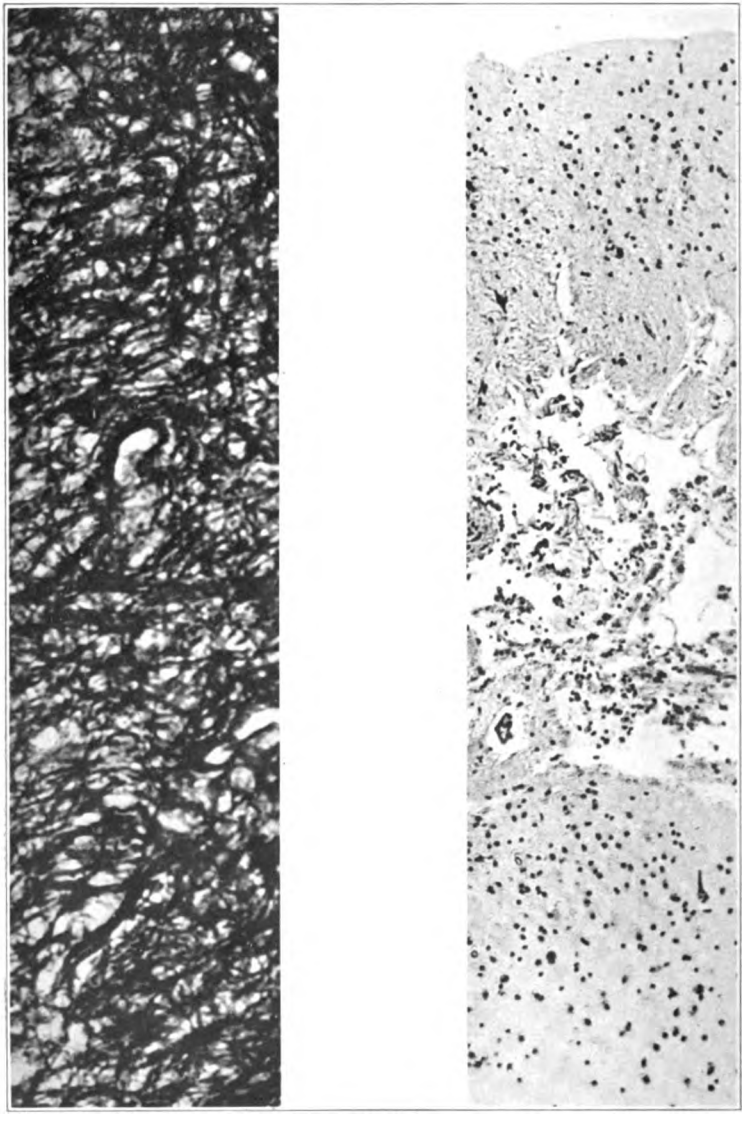

FIG. 5.—(*a*) Gliosis of white matter under high magnification. × 665. (*b*) Section of left post-central gyrus showing status spongiosus. Haem. and eosin. × 125.

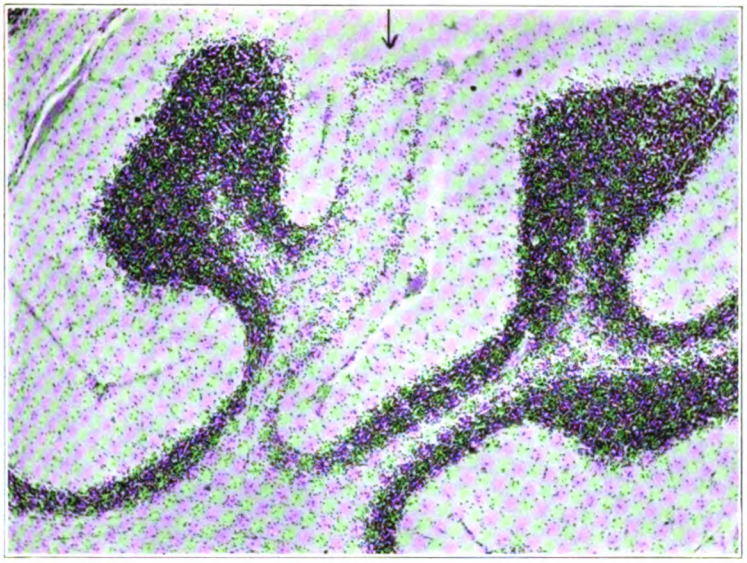

FIG. 6.—Cerebellar cortex showing atrophy limited to a single folium. Tol. blue. × 35.

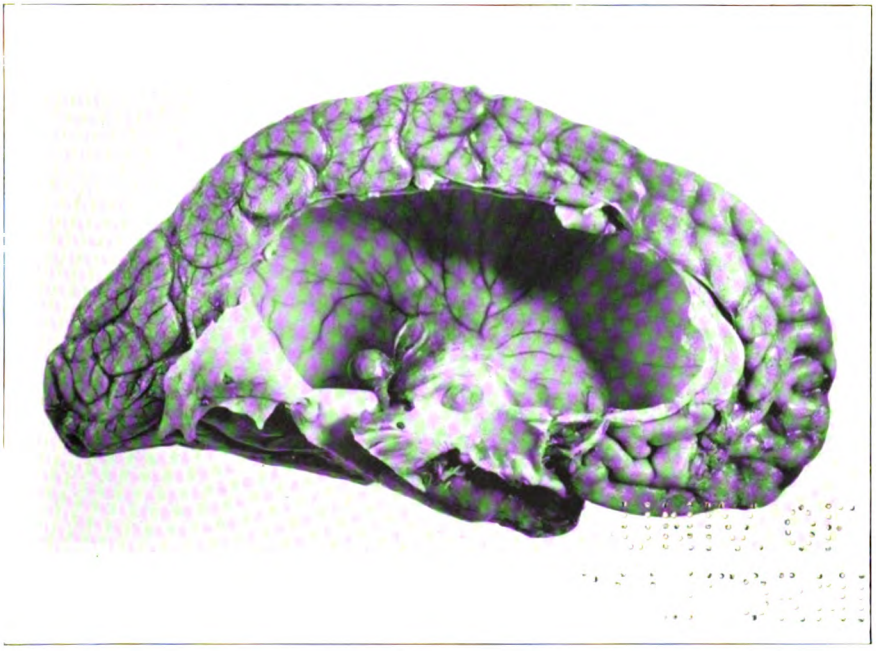

FIG. 7.—Case 2. Lateral view showing degree of ventricular dilatation. Note tumour attached to choroid plexus.

ventricle. The blood vessels in the grey matter appeared to be fewer than normal, but showed no structural abnormality.

In certain areas other changes were found. Thus, in the convolutions lying anterior to the precentral gyrus many areas could be found in which a loss of all components of the nerve parenchyma in the second and third cortical layers was accompanied by an imperfect replacement by fibrous glia and the establishment of numerous holes of varying size; the appearances were, in fact, typical of status spongiosus (Fig. 5*b*).

In the more normal convolutions of the temporal and occipital poles it was possible to find areas in which nerve-cell lamination was retained, but even here a marked degree of gliosis was present.

Cerebellum.—The two unequal lateral lobes showed no obvious changes. For the most part the molecular and granular layers were well developed and the Purkinjë cells had suffered no numerical loss, but here and there areas existed (Fig. 6) in which all three layers had undergone a striking degree of atrophy, while contiguous folia were completely preserved.

Medulla oblongata.—The right pyramid tract showed a marked degree of sclerosis, no myelin sheaths being found in Weigert-Pal preparations. The left inferior olive was more slender and contained fewer nerve cells than the right.

The blood vessels of the medulla and ependyma lining the fourth ventricle were normal.

Summary of microscopic appearances.—The convolutions of the right cerebral hemisphere showed a marked poverty of nerve cells, but no disturbance of lamination and no gliosis. Those of the left cerebral hemisphere showed an almost complete destruction of nerve cells, associated with a replacement fibrillary gliosis and the establishment of status spongiosus.

CASE 2.—The second case was that of a male idiot aged 19, who, from an early age had shown weakness of the right arm. In addition he displayed the clinical features of osteochondro-dystrophy, or, as it is now called, dysostosis multiplex. The pathological findings of this case have been fully reported elsewhere (Ashby, Stewart and Watkin, 1937), and it is only necessary here to refer to the findings in the cerebrum.

The brain was of normal consistence and after fixation weighed 1,043 gm. The cerebral hemispheres were asymmetrical, the left being broader and flatter and 102 gm. lighter than the right. Occupying the stem of the Sylvian fissure and the gyri surrounding it and covered by thickened and opaque pia-arachnoid a large area of cortical atrophy could be seen.

The right cerebral hemisphere showed two small areas of thickened pia-arachnoid, but without cortical atrophy, one occupying the horizontal ramus of the Sylvian fissure and the other in the prefrontal region. On division of the two hemispheres a condition of unilateral hydrocephalus was revealed, the left lateral ventricle showing a very marked degree of dilatation affecting equally the body and its horns (Fig. 7). Save for a small area overlying the caudate nucleus there was no evidence of ependymitis. Attached to the choroid plexus in the body of the ventricle was a small firm rounded tumour about the size of a hazel nut, and from its position it was obvious that it could not have blocked the foramen of Monro. Another tumour, occupying the same position and of the same size, was present on the choroid plexus of the otherwise normal right lateral ventricle.

A vertical coronal section through the left cerebral hemisphere in the plane of the middle commissure showed that the area of softening was sharply confined to the cerebral cortex, with, however, marked thinness of the underlying white matter. On this side, too, the basal ganglia were much smaller than in the opposite hemisphere.

The cerebellum was symmetrical with a normal fourth ventricle. Microscopic examination of the area of cortical atrophy showed a complete absence of cortical cells and a marked excess of fibrous glia. Elsewhere the changes, which bore a close resemblance to those of amaurotic idiocy, were similar in both hemispheres.

Review of Cases Previously Published.

The earliest reference to unilateral hydrocephalus is to be found in a communication by Von Mohr (1842). In his first case, a mentally defective girl who had acquired a right-sided hemiparesis in infancy, there was a history of epilepsy. Death occurred in her twenty-first year. Examination of the brain revealed an atrophied left cerebral hemisphere with an enlarged lateral ventricle; that of the right hemisphere was slightly dilated. The wall of the left lateral ventricle was very thin and its ependymal lining thickened. The foramen of Monro was unobstructed.

His second case was that of an insane woman who died in her sixty-first year. For many years she had had a right-sided hemiparesis. At the autopsy the left lateral ventricle was found to be much enlarged, its wall thin and compressed. There was also cystic degeneration of the posterior portion of the left corpus striatum with enlargement of the descending ventricular horn. The right lateral ventricle was normal and there was no obstruction of either foramen of Monro.

White (1901) recorded the case of a woman, aged 74, with a history of recurrent attacks of hemiplegia of short duration. On the left side an internal unilateral hydrocephalus was found, with marked poverty of cortical nerve cells, glial overgrowth and other degenerative changes. The ventricular wall was thickened and the choroid plexus enlarged with a firm mass in its substance containing numerous hyaloid bodies. The foramen of Monro was unobstructed.

In another case of unilateral hydrocephalus reported by Spiller (1902) the patient, a female idiot, showed a left-sided paresis. Death occurred at the age of fourteen. The left cerebral hemisphere was normal. On the right side there was marked ventricular dilatation, the walls being extremely thin, so that the whole hemisphere was a mere sac. The dilatation appeared to be due to inflammatory changes which had partially closed the right foramen of Monro.

Two cases of partial dilatation of one ventricle were reported by Cramer (1905). In the first, an idiot with right-sided hemiplegia had been epileptic since his seventh year; death occurred at the age of twenty. At the autopsy a marked chronic leptomeningitis was found which was most noticeable over the left frontal and temporal lobes. The left anterior horn was very large and had expanded the wall of the hemisphere into a thin shell. The author assumed that in this case a meningo-encephalitis had weakened the cerebral substance, thus permitting dilatation of the horn.

The second case was that of a man, aged 23, who had been ill for three months with symptoms of increased intracranial pressure. There was a marked right hemiparesis and some weakness on the left side. Decompression afforded no relief. At the autopsy the right temporal lobe and the descending horn were

found to be much enlarged. The dilatation was attributed to the presence of an inflammatory mass which had completely closed the entrance to the temporal horn. Though tubercle bacilli were not found, a tuberculous origin was suspected.

Weber (1906) in a study of hydrocephalus in general refers to five cases, none of which was entirely unilateral. In the first, a chronic diffuse leptomeningitis with cystic degeneration of the hemisphere wall had resulted in atrophy of the brain-tissue over the anterior horn.

In the second case a subcortical encephalitis, probably syphilitic in origin, had softened the wall of one lateral ventricle.

The third case showed encephalitis and softening in the neighbourhood of the dilated ventricle.

The fourth case showed a chronic diffuse leptomeningitis with adventitial overgrowth and sclerotic areas, especially over the left lateral ventricle. This was probably a case of congenital syphilis.

In the fifth case there was also chronic leptomeningitis with areas of gliosis and softening external to the dilated ventricle.

In each of these five cases the foramen of Monro was unobstructed. Weber believes that two factors operate in the production of this type of hydrocephalus —diminished absorption of cerebro-spinal fluid owing to the presence of a chronic leptomeningitis and disease of the hemisphere wall which permits the ventricle to enlarge.

Hunt (1916) records the case of a woman, aged 78, who had a left-sided weakness of 25 years' duration. The report is fragmentary, no information being given as to the state of the foramen of Monro.

Dandy (1919) reported a case of the obstructive type in which a pedunculated tumour was suspended in the left ventricle and periodically closed the foramen of Monro.

Dott (1927) describes a case of unilateral hydrocephalus which appears to be the first of its kind. A progressive unilateral hydrocephalus was found to be due to obliteration of the left foramen of Monro by scar-tissue. In this case an active infective process had become localized and shut off in the ventricular system. Cure was effected by excision of a window in the septum lucidum, the normal right foramen of Monro thus providing an exit for the cerebro-spinal fluid from both lateral ventricles.

Hinrichsmeyer (1922) records a case of local atrophy of the brain substance with a corresponding enlargement of one lateral ventricle. The patient was a feeble-minded boy with epilepsy and a left-sided paresis dating from birth. An operation performed in his tenth year revealed a hydrocephalic enlargement of the right ventricle. Marked thinning of the brain substance was found in the frontal region, the island of Reil being completely destroyed. The foramen of Monro was normal on both sides.

Much more informative is the paper by Winkelman and Eckel (1924).

Their patient was a man, aged 62, with a history of intense alcoholism and a paralysis of four years' duration.

On admission he was found to have a right hemiplegia, motor aphasia and definite evidence of senile deterioration. He improved, but after an interval of two years was readmitted in a state of semi-stupor and with even greater spasticity than before. Death was caused by another paralytic "stroke." The more important autopsy findings were: generalized arteriosclerosis, interstitial myocarditis and chronic nephritis. The brain was soft with fluctuation and recent areas of thrombotic softening in the left parieto-occipital region, flattening of the convolutions and a generalized shrinkage of the left hemisphere. The pia-arachnoid was slightly thickened and the vessels were sclerotic. On sectioning the brain after hardening the right ventricular system was found to be dilated but not more than usually found in a senile brain. On the left side the posterior horn was markedly dilated and the cortex surrounding it thinned out. No actual obstruction was found, although the foramen of Monro was slightly narrower than on the opposite side. The anterior portion of the left ventricular system and the descending horn were moderately dilated. On microscopic examination the characteristic findings of an arteriosclerotic brain were found. The cortex on the posterior portion of the left hemisphere was much narrowed and so altered as to be unrecognizable. In some areas there was complete replacement by a glial scar, in others the replacement was less complete. The condition of the pia-arachnoid varied; over a comparatively normal portion it showed a moderate fibrosis without cell infiltration, while over the posterior horn of the lateral ventricle it showed both inflammatory and proliferative changes. In some areas there was adherence of the cortex to the pia-arachnoid with proliferation of glial fibres in the form of sheaths. The vascular changes were those usually found in senile brains.

Under the title, "A Case of Cerebral Hemiatrophy or Unilateral Hydrocephalus," Wilson (1925) relates the case of a Chinese imbecile girl, aged 22, who was reported to have had frequent epileptic seizures and impulsive outbursts. The neurological signs were: microcephaly, right hemiplegia with wasting and contractures, right homonymous hemianopia and dysarthria.

Death was due to pulmonary tuberculosis. At the autopsy the skull, dura mater, right cerebral hemisphere, cerebellum, pons and medulla were normal; the right lateral ventricle was of normal size. The membranes of the left cerebral hemisphere were thickened, opaque and almost devoid of blood-vessels. They could be stripped with difficulty, disclosing the remains of the convolutions as "little dimples." It was impossible to make out any distinction between grey and white matter, the substance presenting a white, jelly-like appearance. The lateral ventricle was enormously distended; the ependyma was quite smooth. No mention is made of the condition of the foramen of Monro. The left cerebral hemisphere weighed 3¾ oz., the right, 17 oz.

A somewhat similar case was described by Noronha (1925). A mentally defective Hindoo, aged 30, subject to periodical epileptic fits, followed by mental excitement, showed paralysis of the right half of the tongue, the face and upper limb. Speech was slow, slurring and interrupted. On post-mortem examination the dura mater was found to be thickened, and on incision an unusual quantity of cerebro-spinal fluid escaped. The right cerebral hemisphere was of normal consistence and the structures forming it well defined. The whole of the cortex of the left cerebral hemisphere formed the wall of a huge saccular cavity, filled with milky white fluid. Though not well marked the convolutions were easily distinguished, and when the contained fluid was allowed to escape, the hemisphere collapsed like a half-inflated football.

Diaz y Gomez (1933) has recorded a case of fibroma in the posterior cerebral fossa which, by occluding the foramen of Monro, caused internal hydrocephalus on the left side. Recovery after surgical intervention in unilateral hydrocephalus is reported by Tinel, de Martel and Guillaume (1932) in the case of a child aged 10, the dilatation resulting from an inflammatory process affecting the foramen of Monro.

Discussion.

From the pathological standpoint two distinct types of unilateral hydrocephalus may be recognized. In the first, which differs but little from the bilateral form, there is obstruction of the foramen of Monro; in the second type there is no obstruction, but disease of the hemisphere permits a passive ventricular dilatation on the affected side. Dott (1927) considers that the term "unilateral hydrocephalus" should be reserved for those cases in which one ventricle, or part of it, becomes dilated by reason of an obstruction affecting its cavity or its outlet, and he suggests that the term is a misnomer when applied to conditions in which one lateral ventricle has become passively enlarged by reason of local atrophic shrinkage of the adjacent brain-substance, inasmuch as the accumulation of fluid maintains normal pressure conditions within the cranium and is therefore actually beneficial.

He does not, however, suggest an alternative title for the non-obstructive type, and it is obvious that if the term is to be restricted to ventricular dilatation of obstructive origin a general revision of the nomenclature of all pathological states to which the prefix "hydro" is employed will be necessary. Thus, since there is little evidence to show that the cerebro-spinal fluid contained in a dilated central canal of the cord is under increased pressure, the term "hydromyelia" will have to be discarded.

It may be remarked, too, that it has yet to be proved that there is no increase in intraventricular pressure at the stage when the pathological process involving the cerebral wall is active. Meningitis and encephalitis are frequent causes of hydrocephalus, and in their acute phases some rise in cerebro-spinal

fluid pressure is invariable, so that the presence of a normal ventricular pressure, perhaps years after the onset of the disease, does not necessarily rule out the possibility of increased pressure at the time when the inflammatory process was active. Moreover, that such a rise in unilateral hydrocephalus does occur is suggested by the not infrequent presence of a slight degree of ventricular dilatation on the side on which there exists no cerebral atrophy or other evidence of gross cerebral damage. This was present in the first case now reported. To the writer it seems unwise to limit the use of a term so long sanctioned by usage, especially if it be employed merely as a descriptive term, unfettered by implications regarding the mode of production of the hydrocephalus.

Concerning the cause or causes of the weakening of brain substance in this form of hydrocephalus it is difficult to speak with any degree of certainty. It is possible that either the whole or part of the brain may be weakened by an encephalitis occurring in utero, while similar processes of perhaps syphilitic or tubercular origin may develop in early life.

However produced, the general shrinkage of brain substance is probably never sudden but extends over a long period of time, so that the changes found at autopsy may represent the end-results of a process sustained many years previously. Consequently, the absence of all signs of inflammation does not necessarily mean that they may not have been present at one time. In some instances, as in Case 1, a clue to the duration of the hydrocephalus is afforded by the presence of a crossed atrophy of the cerebellum, for such a finding is a clear indication of a congenital or early post-natal origin. That the hydrocephalus in Case 1 was probably acquired in childhood and not in infancy is shown by the absence of cranial asymmetry, for its development in early life would almost certainly have been associated with yielding of the membranous bones on the affected side.

The presence in certain areas of status spongiosus affords belief for the view that destruction of all components of the nerve parenchyma must have been both rapid and intense, but the cause of this destruction remains obscure. Certain clinical features—and notably the corneal clouding and notching of the incisors—strongly suggested a syphilitic origin, yet neither in the nervous system nor in the visceral organs were there changes indicating such an infection. In particular, the meningo-vascular tissues, which in neurosyphilis so often bear the brunt of the damage, showed no residual signs of inflammation. It is, of course, possible for the nervous system to escape luetic involvement even when stigmata of congenital syphilis are obvious, and it may be assumed that this case was of such a character, for neurosyphilis being "an extensive disease of slight intensity," it would be difficult to understand how a syphilitic process which destroyed so large an area of one hemisphere could fail to implicate the other.

The second case is of interest in that the presence of a small tumour attached to the choroid plexus at first glance suggested hydrocephalus of the obstructive

type, but the presence of another tumour occupying the same position and of the same size on the choroid plexus of the otherwise normal lateral ventricle on the right side indicated that the cause of the dilatation was to be sought elsewhere. As already described, the convex surface of the left cerebral hemisphere was occupied by a large area of cortical atrophy covered by thickened and opaque pia-arachnoid, but its extent seemed hardly sufficient to account for the uniform dilatation of the whole cavity, unless one assumes that the lessened resistance of the hemisphere wall extended much further than the area of cortical degeneration.

Summary.

Unilateral hydrocephalus may result from obstruction at the foramen of Monro or from disease of the hemisphere wall which permits a passive dilatation of the ventricle. The clinical and pathological features of two cases of the latter type are described.

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PHYSICAL TYPES AND THEIR RELATIONS TO PSYCHOTIC TYPES.

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(*a*) PROBLEM AND DATA.

THE object of this paper is to test the following two hypotheses :

1. That the physique of female adults can be regarded as the resultant of two independent modes of variation, one determining differences in size or bulk, and the other determining differences in proportion or type.

2. That a relation exists between schizophrenia and manic-depression, on the one hand, and differences in physical proportion or type, on the other.

As regards the first theory, prior analyses of the physique of normal and abnormal males have disclosed the presence of two factors governing variation in bulk and shape respectively. These factors were found in the case of a young group, of average age 21·80 years, S.D. 3·61 years, and in the case of an older group of average age 42·05 years, S.D. 12·54 years (Cohen, 1938, 1940). In an earlier investigation by Burt (1938), in which factor analysis was first applied to anthropometric measurements, the results suggested three separate and independent factors, the first being a general factor, presumably governing growth in all directions ; the second determining disproportionate growth in the long bones ; and the third (mainly in adults) governing increase in breadth, thickness, girth, and weight (Burt, 1938). It appears, however, that the second and third factors of Burt may be regarded more simply as the positive and negative aspects, respectively, of one bipolar factor.

As regards the second hypothesis, many attempts have been made to substantiate the claim that temperament and physical shape are closely related. There seems to be little doubt that many of these claims, at any rate in the way they are formulated, are highly exaggerated. The general assumption behind typological work seems to be that genetic influences exist which determine an individual's physical proportions, his temperament, and also his tendency (if any) to a specific mental disorder. The search for empirical types has generally implied that type differences are fundamentally innate. However,

although there is a certain amount of evidence that differences in physique and physical segments are inherited according to Mendelian principles, no one has yet demonstrated that temperament is transmitted according to the known laws of heredity. Nor is there any uniformity of view among psychiatrists as to the importance of heredity in the aetiology of mental disorder.

Stature is believed to be determined by a large number of genes (Fisher, 1918). The different segments of stature, such as head and neck length, torso, sitting height and fibula, are genetically determined according to Davenport (1925). Ateleiotic dwarfism is most probably the result of two dominant genes (Hogben, 1932).

In a recent paper Burt (1939) seems to imply that the factor of general emotionality underlying "primary conative tendencies" is inheritable, and that differences in this factor are primarily inborn. He is careful to point out, however, that this simply means "there is a demonstrable correlation between a child's behaviour soon after birth, and his behaviour later and all through life, and that there is a demonstrable correlation between the behaviour of members of the same family such as could not be explained by environmental influences."

In an early paper Burt (1912) had stated that well-marked temperamental characteristics were frequently associated with definite physical characteristics, and "that the combination often seemed to run in families." More recently (1939) in a fuller discussion of the problem he points out that the correlation between physical and mental signs of temperament, even in selected groups of neurotic and unstable adults, is small and not always significant.

(*b*) The Data, Means and Standard Deviations.

The sample consists of 62 Jewish female patients of average age 34·89 years, S.D. 11·23 years. The patients were drawn from working and lower middle classes.* Twelve anthropometric measurements were taken of each patient; the means and standard deviations are given in the following table (Table I). Of the 62 patients, 31 were schizophrenes, 22 were manic-depressives, and 9 were mixed cases.

As a matter of interest the means and standard deviations there are also given in Table I*a* of the measurements of another group of 33 English (non-Jewish) female psychotics. These measurements will be further analysed in a later section of this paper.

(*c*) The Variability of the Measurements.

The coefficients of variation are given in the following table (Table II). The coefficients of variation obtained from the measurements of the other group of 33 English female psychotics are also shown in the table.

* The measurements and diagnoses were taken at the Friern Hospital by Dr. Emanuel Miller, to whom I am much indebted for the data.

TABLE I.—*N.* = 62.

Traits.	Means (cm.).	S.D. (cm.).
Stature	153·37	7·26
Leg length	80·58	4·93
Sitting height	80·69	3·59
Arm length	54·27	3·01
Trunk length	45·59	2·64
Pelvic breadth	26·91	1·93
Shoulder breadth	30·18	1·67
Chest breadth	23·23	1·97
Chest depth	17·80	1·78
Head circumference	53·09	1·48
Head length	18·02	0·67
Head breadth	14·66	0·61

TABLE I*a*.—*N.* = 33.

Traits.	Means (cm.).	S.D. (cm.).
Stature	160·09	5·86
*Leg length	74·88	5·45
Arm length	53·33	2·60
Trunk length	45·52	2·29
Pelvic breadth	27·64	1·60
Shoulder breadth	30·73	1·70
Chest breadth	23·02	1·45
Chest depth	18·96	2·02
Head circumference	53·94	1·49
Head length	18·37	·62
Head breadth	14·73	·62

* Measured from the great trochanter to the lower end of the external malleolus; in the Jewish group leg length was measured from the inferior iliac spine downwards.

The following two sets of co-efficients vary for the same reasons; the correlation between them is ·945 (p.e. ± ·20).

Chest depth, of all the traits, seems to vary most in both groups. Indeed, with the exception of chest breadth among the Jewish females, the variability for chest depth stands out as significantly larger than that of any of the other organs measured.

The greater variability of chest depth may be attributed to the fact that it is the only sagittal measurement; in women it is the only measurement

TABLE II.—*Coefficients of Variation.*

	62 Jewish females.	33 Non-Jewish females.
Stature	4·74	3·66
Leg length	6·12	7·28
Sitting height	4·45	..
Arm length	5·54	4·88
Trunk length	5·79	5·03
Pelvic breadth	7·18	5·79
Shoulder breadth	5·54	5·53
Chest breadth	8·49	6·30
Chest depth	9·99	10·65
Head circumference	2·80	2·76
Head length	3·70	3·38
Head breadth	4·13	4·21

which would include muscle, and particularly fat, as well as bony development. It is also probably influenced by individual differences in lung capacity.

In both groups, breadth measurements vary more than measurements of length. Similar results have been obtained with groups of males, as will be shown below.

The variability of the head measurements appears small as compared with the rest of the measurements. It may be argued that this is due to the difficulty of getting accurate measurements of variability on so small a part of the body, especially in view of the fact that head measurements would presumably be influenced by the presence of differing amounts of hair. Nevertheless, many anthropometrists agree that measurements taken on the living have practically the same precision as the corresponding measurements of skulls (Fisher, 1936; Le Gros Clark, 1939.) Possibly the fact, as Prof. Burt has suggested,* "that the head is a round box, while the rest of the bones are more like sticks, would tend to alter the type of variability shown." Moreover, since, according to the antero-posterior principle of growth, the head attains most of its ultimate size at an earlier age than other bodily parts, it may be subject to less influences during the later period of development. Most of the growth of the head, relatively speaking, takes place pre-natally and in the earlier years of infancy. The adult head is twice the length of the head at birth, whereas the adult legs, for instance, are about five times as long as they were at birth. Thus, taking size at birth as 100, then at the age of 21 months head length is 150, and at the adult stage 200, whilst leg length is only 200 at 21 months, and 472 at maturity (Burk, 1898).

However, the assertion that head measurements are in reality less variable than other bodily parts must be treated with considerable caution for reasons

* Private communication.

soon to be given. Most probably the observed discrepancy can be accounted for on statistical grounds, namely, that in measuring small objects the measurements will fluctuate too frequently towards the positive side of the true mean, the effect being to reduce the variance.

Now, it is frequently alleged, in discussing "racial" differences, that variation in cephalic index is much more completely determined by hereditary influences than is stature, and that in stature, pre- and post-natal environment plays a relatively larger part in determining the observed differences between individuals. For this reason the cephalic index is regarded as a better measure of "racial" differences than stature. Stature is said to be unstable and an undesirable measure of "racial" differences, whilst the cephalic index is said to be stable (Morant, 1939). It is alleged also that distributions for stature and for cephalic index appear to be independent (*op. cit.*, p. 51), and although variation in stature takes place after maturity has been reached, the effect of environment upon the cephalic indexes of adult people may be neglected in practice.

In criticism of this view it may be stated, first that neither head length nor head breath are independent of stature or of any other external measurement of the body. Secondly, as has been shown elsewhere by the writer and will be substantiated in the present paper, variation in head measurements is mostly due to a factor affecting magnitude or growth in all bodily parts, whilst the residual variation is due to a factor making, among other things, for excessive stature and dolichocephaly or, on the other hand, for short stature and brachycephaly. This appears to be true both of males and females, though it may not be true of all ethnic groups: that is to say, the positive association between stature and dolichocephaly may be present in some, but not in other ethnic groups (Huxley and Haddon, 1935). Moreover, there is much evidence for the belief that the correlation during adolescence and early maturity between head length and stature is invariably greater, sometimes as much as seven times greater than that between head breadth and stature (e.g. Schuster, 1911). In some samples there is actually a negative correlation between head breadth and stature (in adults) and a positive correlation between head length and stature. In addition, according to a recent report of Wissler (1939), adult males show a regular increase in head length till the 76–80 years age group and a decrease in stature and in head width after the 36–40 years age group, which would evidently raise the correlation between stature and dolichocephaly. The upshot of this argument is to imply that the use of the cephalic index as a measure of racial differences is open to practically the same criticisms as stature, because the two measures are closely related.

It is worth noting that the Jewish females are consistently more variable in shoulder, chest and, particularly, in pelvic breadth. This may reasonably be attributed to some ethnic difference between the two groups. On the other hand, the difference may not be statistically significant. Moreover, in the

case of the males, the English vary more in breadth than the Jewish, as may be seen below.

The variability of the traits may be summarized as follows :

TABLE II*a*.—*Mean Coefficients of Variation.*

	62 females (Jewish).	33 females (English).	86 males (Jewish).	114 males (English).
Five length traits (stature; trunk, arm and leg length; sitting height)	5·33	5·21 (sitting height omitted)	4·79	5·25 (sitting height omitted)
Three breadth traits (shoulder, chest and pelvic)	7·07	5·87	6·13	6·70
Chest depth	9·99	10·65	8·30	8·55
Three head measurements (length, breadth and circumference)	3·54	3·45	4·04 (head circ. omitted)	3·65 (head diagonal instead of head circ.).

(*d*) THE ANALYSIS OF THE MEASUREMENTS.

In order to answer our first question the twelve traits were inter-correlated and factorized. The use of correlations rather than of co-variances* may be justified for the following, among other reasons : Since the physical measurements are expressed in different units from the mental diagnoses, and since it will be necessary for the purpose of the second hypothesis to correlate the former with the latter, it is necessary to render the physical measurements independent of the units in which they are expressed by putting them into standard measure. Secondly, in analysing co-variances, the wide variation in a large characteristic such as stature would tend to swamp the variations in the smaller characteristics such as head length and head breadth.

The correlation co-efficients are given in Table III.

Out of 66 co-efficients only one is negative, and that one is not significant. Assuming the true value of the correlations to be zero, then with $N = 62$, the standard error is $\pm$ ·127. Forty-one coefficients in the table out of a total of 66 (or about 60 per cent.) are greater than twice the standard error (2 s.e. $= \pm$ ·254).

As a first approximation, the summation method of analysis (Burt, 1917) was used to obtain the factor saturations. The insertions in the diagonal cells

* The analysis of the co-variances were actually worked out, and were found to give results very similar to those obtained from analysing the correlations.

TABLE III.—*Intercorrelations.*

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.
Stature .	1	·728	·483	·467	·547	·182	·244	·110	·162	·042	·266	—·033
Leg length .	2		·429	·646	·568	·222	·324	·119	·224	·180	·198	·022
Sitting height	3		*	·379	·568	·326	·279	·170	·240	·252	·362	·207
Arm length .	4				·255	·220	·213	·210	·264	·364	·373	·343
Trunk length	5					·438	·480	·416	·327	·238	·177	·175
Pelvic breadth	6						·351	·363	·359	·414	·194	·328
Shoulder breadth	7							·466	·321	·331	·201	·132
Chest breadth	8								·445	·394	·290	·301
Chest depth .	9									·364	·189	·219
Head circumf.	10										·805	·709
Head length	11											·473
Head breadth	12											—

$N = 62$ $\bar{r} = ·305$. p.e. for a zero correlation $\pm$ ·0857.

were the largest correlations in the respective columns, as suggested by Thurstone (1935). The reflection of the residual correlations was also carried out by Thurstone's method (*op. cit.*).

As a further refinement, Burt's Least Squares method of analysis (Burt, 1938) was also applied to the first correlations in the following way. The diagonal insertions in the first matrix were the squares of the saturations obtained by the summation method. Using these same saturations as weights on the first matrix, a second set of weights was obtained and the process was repeated with the second weights to obtain a third set. The third weights (which hardly differed from the second ones) were then divided by the square root of the sum of their squares, and then multiplied in turn by the root of the total variance to obtain the first factor saturations.

The procedure was repeated on the first residuals to obtain the second factor saturations. The diagonal insertions for the residuals were obtained in this way ; in the column yielding the largest sum, the largest co-efficient in the column was inserted ; in the column yielding the smallest sum, the smallest co-efficient in the column was inserted and the remainder were graded accordingly.

The results are shown in Table IV.

The first factor (least squares) contributes 34·77 per cent. and the second factor 25·46 per cent. to the total variance.* The least squares method has the advantage of minimizing the errors and of bringing out more clearly, at each stage in the analysis, the tendency to hierarchical order present in the matrix.

The significance of the second factor may be evaluated in terms of the number of significant co-efficients in the residual matrix, after the first factor has been eliminated. Assuming the true residual correlations to be zero, then the standard error will be $\frac{1}{\sqrt{n-1}} = ·128$.

* With the summation method the contributions are 34·75 per cent. and 12·53 per cent. respectively.

TABLE IV.—*Saturations.*

Traits.	Summation method. Factors. I.	II.	Least squares method. Factors. I.	II.
Stature	·558	·634	·549	·821
Leg length	·623	·668	·627	·756
Sitting height	·618	·267	·633	·384
Arm length	·622	·255	·619	·557
Trunk length	·676	·134	·696	—·020
Pelvic breadth	·545	—·247	·556	—·500
Shoulder breadth	·541	—·152	·549	—·448
Chest breadth	·533	—·381	·535	—·690
Chest depth	·506	—·261	·506	—·471
Head circumference	·682	—·280	·676	—·329
Head length	·616	·070	·598	·187
Head breadth	·521	—·348	·492	—·243

Seven co-efficients are greater than twice the standard error (2 s.e. = ·256). The probability of a correlation of the magnitude of ·256 occurring by chance is ·05. One would therefore expect about three or four such residual correlations in a table of 66 coefficients to occur by chance. The observed number of significant residual correlations exceeds the number to be expected by chance at the 5 per cent. level of significance. There was therefore a justification for proceeding to take out a second factor.

The saturations for the two factors are plotted in Figs. 1 and 2. Factor I is represented by the vertical axis and Factor II by the horizontal axis. All the traits appear in the two upper quadrants because all the first factor saturations are positive.

(*e*) INTERPRETATION OF RESULTS.

The saturations of the traits in the first factor are all positive, indicating that if any individual has a positive measurement in any particular trait, it may be inferred that his measurement in all the other traits will be positive. If we assume that there is a general tendency for all these traits to increase together in the course of physical growth, then the general result would be positive correlations between all the traits so affected. The first factor may thus be regarded as determining general female body growth or size.

Judging by the narrow range of variation among these saturations, there is, apparently, little to choose among the traits as indexes of female size or growth. The saturations range from ·492 (for head breadth) to ·696 (for trunk length).

It is otherwise with male physique, where traits vary much more in their value to discriminate and predict body magnitude. Among males some traits are much more informative of the general growth or size of the body than others. In one analysis by the writer (1938) of measurements of male patients the

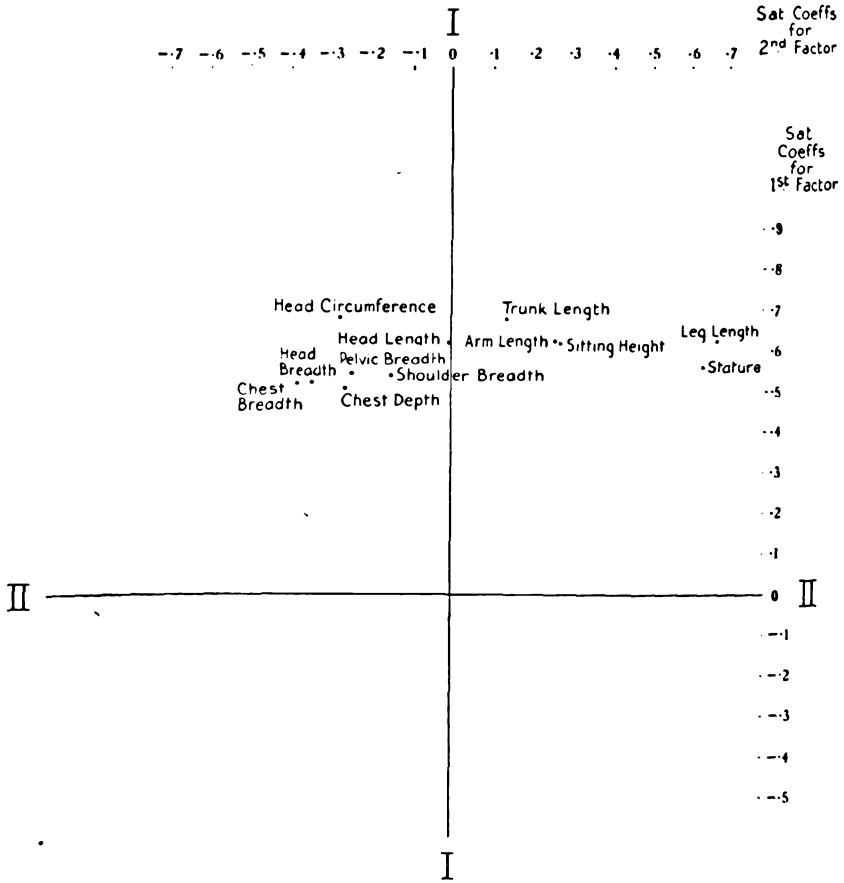

FIG. 1. N = 62 females (summation method).

factor saturations ranged from ·188 (for stature) to ·835 (for pelvic circumference), and in another analysis of normal males (1940) the saturations ranged from ·406 (for trunk length) to ·815 (for waist circumference). Among females, however, the twelve traits studied here are more or less equally informative in this respect.

However, it is necessary to mention that the comparison is not entirely justified for the following reason: The measurements for the males include three circumferential measurements which are not present in the female

measurements. Likewise, sitting height is present among the female traits and absent from the male traits. Thus the measurements of the females are measurements of characteristics that seem to be determined solely by growth of bones.

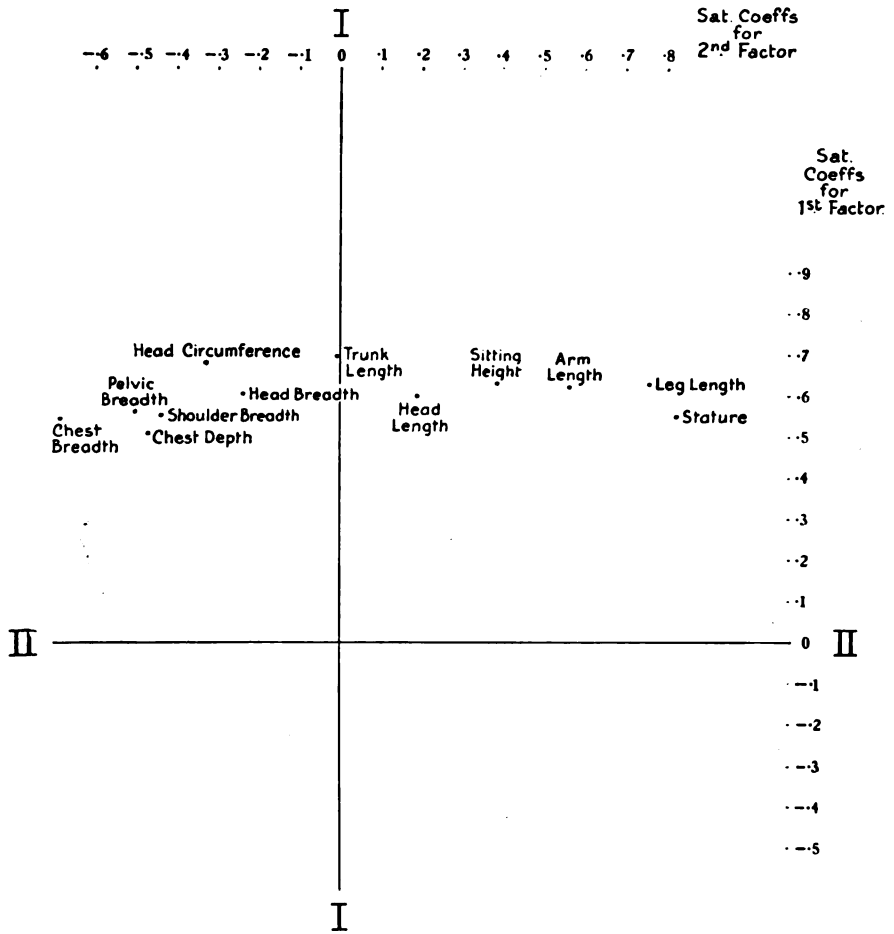

FIG. 2.—N = 62 females (least squares method).

On the other hand, the measurements for the males extend the meaning of growth to include growth of fat and muscle as well as growth of bone. Hence, it is possible that all the bones grow at approximately similar rates, but that muscles and fat grow at different rates. This is to some extent borne out by the fact that when the three circumferential measurements and the three head measurements are omitted from the analysis of the male traits the first factor saturations of the remaining eight traits range from ·303 (for stature)

to ·613 (for pelvic breadth). Turning to the second factor (Table IV), we find that it is bipolar with positive saturations for length measurements, stature, leg length, arm length, sitting height and head length and negative saturations for the breadth measurements, pelvic, shoulder, chest and head breadth, and for chest depth and head circumference. The negative saturation of ·020 for trunk length can hardly be regarded as significant.

The saturations for this second factor reveal the intercorrelationship of the traits when all the individuals are reduced to the same average scale of size and the bipolarity of the saturations indicate the presence of two antithetical and contrasting types, one denoting a tendency to disproportionate development in length traits and the other a tendency to disproportionate breadth development, including a rather deep thorax.

Conceivably, when the first factor was eliminated, there might have been no significant second factor residuals. If this had been the case, all the differences between the individual females would have been attributed to differences in general bulk or growth. The presence of a significant second factor points to the existence of an additional, relatively independent impulse to increase in specific length or breadth development. Thus, regardless of differences in general magnitude, if a woman is relatively tall, with more than average length of arm, leg and head, she will tend to have relatively narrow shoulders, pelvis, and head, and a flat and narrow chest. Conversely, when there is a relative absence of length development, a woman will tend to show much more breadth and sagittal development. In the earlier studies of males it was shown that growth in breadth is closely related to growth in circumference. So far as we have eliminated differences in general bulk, it must follow that excess of breadth or circumferential measurement must be accompanied by diminished vertical measurement.

(*f*) Correlating the Physique of Males with Mental Disorder.

In the writer's analysis of the measurements of male mental patients (1938), the results were given showing that the individuals differed both in respect to size, and in respect to shape, but no results were given of the relation between the measurements and the type of mental disorder to which the patients belonged. These results will now be given. Altogether there were 64 patients, consisting of 25 manic-depressives, 22 schizophrenes, and 17 other cases. We are only concerned here with the manic-depressives and schizophrenes.

It is required to know whether any relation exists between the physical proportions of these patients and their particular mental disorder. According to Kretschmer's theory (1925) manic-depressives tend to have relatively short arms and legs, and to show marked tendencies to obesity, whilst the converse is supposed to be true of schizophrenes. We shall therefore see whether there is any significant relationship between manic-depression and schizophrenia on

the one hand, and leg length, arm length and waist and pelvic circumference on the other.

On testing the significance of the difference between the means of the traits of the two groups of patients, the following results were obtained :

Trait.	Schizophrenes. Means (cm.).	Manic-depressives. Means (cm.).	Diff.	t.	P.
Leg length	81·614	80·440	1·174	·779	·5
Arm length	58·364	57·300	1·064	·840	·4
Waist circ.	71·045	76·100	−5·055	2·750	·01
Pelvic circ.	78·204	83·780	−5·576	3·120	·01

So far the differences between the means of the circumferential traits are significant, whereas the differences between the means of the length traits are not significant, since the observed values of t could be obtained by chance in about one in every two experiments.

But the non-significance of the differences between the length traits could be attributed to the small numbers involved in the samples. So another estimate of t for these traits was made in which the standard error was based on three more groups of patients for whom measurements were available. The precise method will shortly be explained. By this second method the value of t for the difference between the means of the groups for leg length rose to 1·891 with $P = ·1$; and the value of t for arm length rose to 2·701 with $P = ·01$. However, these values may still be influenced by effects of differences in general magnitude. Hence, it is necessary first to eliminate the general factor for size and see whether significant differences still remain.

The crude measurements were now expressed in standard measure $\left(\frac{\chi - \bar{\chi}}{\sigma}\right)$ and then weighted by the saturations of the traits in the second factor, i.e. every value of $\left(\frac{\chi - \bar{\chi}}{\sigma}\right)$ was multiplied by r_{ig} where r_{ig} represents the saturation of a trait in the second factor.

A combined weighted measure of the four traits leg length, arm length, waist circumference, pelvic circumference was now obtained. This combined weighted measure was correlated with manic-depression and schizophrenia.

Since there were 47 values of the compound physical measurement and only two values (manic-depressive and schizophrenia) of the mental measurement, the ordinary product moment formula was adjusted for the present case.

In general, when one variable is continuous and the other dichotomous, r_{xy} may be calculated by the formula $\frac{\sqrt{n_1 n_2}}{n_1 + n_2} \times \frac{d}{\sigma_x}$.

In the present instance,

n_1 = number of manic-depressives;

n_2 = number of schizophrenes;

d = difference between the means of the weighted physical measurements in the two groups;

σ_z = the standard deviation of the weighted physical measurements for the total group of 47.

The resulting correlation between physical proportions and mental type was ·413. Converting r into z we get ·436 with a standard error of ·151. $\frac{z}{\text{s.e}_z} = 2{\cdot}884$, which is above the ·01 level of significance. Hence, regardless of differences in general magnitude of body-build, male manic-depressives clearly tend to exceed male schizophrenes in waist and pelvic circumferences, whereas the latter exceed the former in leg and arm length.

The actual compound weighted measurements are given below:

Manic-depressives.		Schizophrenes.
—·205	.	—·202
—·209	.	—·153
·337	.	·695
—·790	.	·232
·049	.	1·772
—·952	.	2·396
—2·511	.	—1·024
—1·471	.	·375
—1·875	.	2·081
·442	.	—·542
·417	.	·089
—·685	.	1·092
—2·100	.	·979
1·598	.	—·038
—2·653	.	1·071
2·156	.	1·280
—·562	.	·134
—·420	.	·440
1·525	.	1·897
—·657	.	—1·057
·045	.	·389
—·143	.	1·111
—2·979	.	
·835	.	Mean ·592
—·138		
Mean —·438		

Histograms of the weighted measurements are shown in Fig. 3. A word of explanation is required making clear the assumptions underlying the use of the formula for correlating the physical characters with the dichotomous mental classification.

If our group of psychotics could be regarded as normally distributed, that is, if it could be supposed that the trait responsible for manic-depression or schizophrenia is normally distributed in the present sample, then other formulae

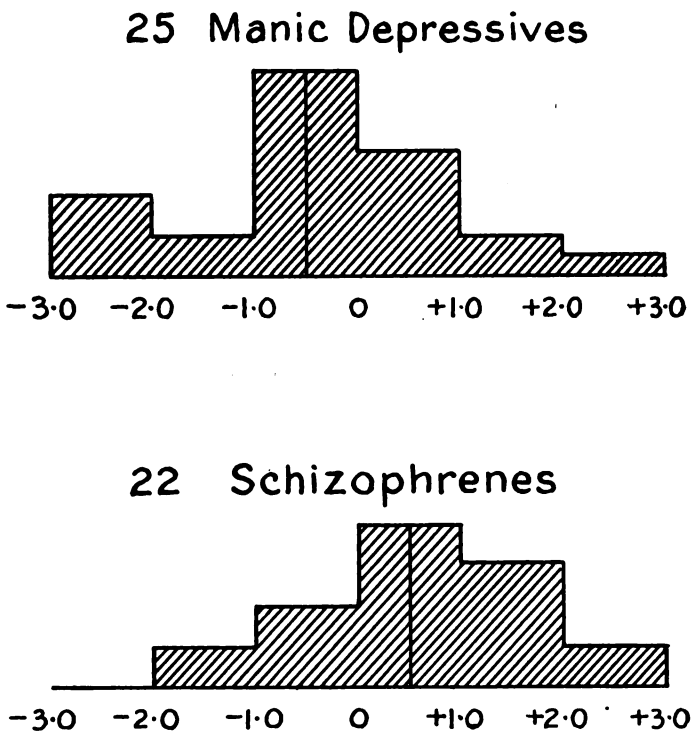

FIG. 3.—Histograms of compound weighted measurements of English male patients.

(e.g. that of Kelley [1923], p. 248) would be appropriate. It is assumed here, however, that while the trait responsible for the diagnosis of psychoses is a bipolar uni-dimensional factor, whose distribution is normal in the general population, the two groups of patients in the present sample only form the extreme positive and negative tails of this distribution. It is necessary to make this assumption in order to test Kretschmer's hypothesis, but it is not implied that all psychiatrists would accept it. It may indeed be maintained that while schizophrenia represents true mental disorder, manic-depression simply shows, in an accentuated form, the mood cycles common to all normal

people. However, according to Kretschmer, schizothyme, schizoid and schizophrene tendencies (like those of the cyclothyme, cycloid and manic-depressive) exhibit the same basic temperamental structure.

By omitting the vast majority of normal persons of cyclothyme or schizothyme temperament and selecting only the extreme cases from either tail of the distribution, the variability of the sample is very greatly increased, and this increase in variability as a result of selection increases the apparent value of the correlation between the physical and mental characters. It must therefore be made clear that evidence is only provided of significant correlations between physical shape and mental diagnoses in psychotic samples, but not in the general population of normal people.

(*g*) Correlating the Physique of Females with Mental Disorder.

Of the 62 female psychotics whose measurements were factorized, 31 were schizophrenes, 22 manic-depressives, and the rest were mixed cases. The following table gives the values of t obtained when the differences between the means of the groups (20 in each case) were tested.

Differences between Means of Measurements of 20 Schizophrenes and 20 Manic-Depressives.

Measurement.	Schizophrenes. Means.	Manic-depressives. Means.	Difference between Means.	t.	Levels of significance P.
1. Head breadth	14·630	14·670	—·040	·221	·9
2. Head length	17·865	18·200	—·335	1·736	·1
3. Head circumf.	52·715	53·345	—·630	1·500	·2
4. Chest depth	17·050	18·225	—1·175	2·322	·05
5. Pelvic breadth	26·700	27·275	—·575	·946	·4
6. Chest breadth	23·075	23·175	—·100	·137	·9
7. Shoulder breadth	29·925	30·100	—·175	·321	·8
8. Trunk length	45·225	45·175	+·050	·065	·9
9. Leg length	79·375	81·000	—1·625	1·034	·4
10. Arm length	53·250	54·850	—1·600	1·523	·2
11. Stature	150·625	154·160	—3·535	1·208	·3
12. Sitting height	79·800	80·525	—·725	·635	·6

Only the difference between the means for chest depth is so far significant. Since, altogether, measurements of four pairs of groups were available, that is, of three other pairs of psychotic groups (English females and English and Jewish males) besides the Jewish female manic-depressives and schizophrenes,

Prof. Burt suggested that the differences between the means could be judged in terms of the standard errors based upon the four pairs of groups combined. In this way we could discover whether any differences were non-significant simply because of the small size of the samples on which they were based. In general, the precision of a measure increases with the square root of the number of cases. The modified standard error, based upon the four groups combined is, according to Prof. Burt :

$$\frac{\sqrt{m_1\,\sigma^2_{n_1} + n_1\,\sigma^2_{m_1} + \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots m_4\,\sigma^2_{n_4} + n_4\,\sigma^2_{m_4}}}{\frac{1}{2}\,(n_1 + m_1 + n_2 + \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots m_4)}$$

where $m_1,\ n_1,\ \sigma^2_{m_1},\ \sigma^2_{n_1}$

. . . .

. . . .

$m_4,\ n_4,\ \sigma^2_{m_4},\ \sigma^2_{n_4}$

are the numbers and variances in each pair of groups.

As a result the following additional significant values were obtained :

	t.	*P.*
Head length .	3·764 .	·01
Leg length . .	2·617 .	·01
Arm length. .	4·061 .	·01
Stature . .	3·941 .	·01

The *t* for chest depth also rose from the ·05 to the ·01 level of significance. These results may, of course, be attributed to differences in general magnitude of bodily bulk between the two groups. It is worth noting that the manic-depressive females exceeded the schizophrenes in all the measurements except in chest depth and in trunk length (which last difference is not significant). There seems to be some " racial " factor at work here, for both male and female English schizophrenes are taller than manic-depressives, whereas the reverse is the case with Jewish males and females. Paterson (1930) pointed out that in Kretschmer's data the pyknic females were taller than the asthenic ones.

The measurements in the four traits, leg length, stature, chest breadth and pelvic breadth were standardized and weighted with the saturations of the traits in the second factor (least squares). The combined weighted measurements were then correlated with manic-depression and schizophrenia using the same formula as in the case of the males. A correlation of ·099 (p.e. ±·085) was obtained. Although this coefficient is not significant it is consistent with a correlation of about ·30 in a very large population, but inconsistent with a higher correlation. However, when we limit ourselves to the two traits, pelvic breadth and chest depth, we get more significant results. Standardizing and combining these two traits we get a correlation of ·557 with manic-depression and schizophrenia. Converting *r* to *z* we get a value of ·633 with a standard

error of ·141. $\frac{z}{\text{s.e.}_z} = 4{\cdot}48$, which is a highly significant value. We may therefore say that there is a very marked tendency for the manic-depressive females to have deeper chests and broader pelves than the schizophrenic ones and this difference is independent of differences in general magnitude of body build.

Compound Physical Measurements (Chest Depth and Pelvic Breadth).

Manic-depressives.	Schizophrenes.
—·346	·451
—·087	—·078
—·865	·710
·404	·202
—1·113	·710
1·477	—·429
—·616	—·586
—·217	·710
·586	—·735
·591	·109
—·616	·191
—·735	·202
·312	·332
1·379	—·606
—·876	1·249
·048	·461
—·057	·710
—2·061	—·606
—·337	·461
·451	—1·135
·596	·710
·332	·969
	1·467
Mean —·134	·461
	·312
	·980
	—1·404
	·191
	·182
	·860
	—·900
	Mean +·198

(*h*) A Further Analysis of the Measurements of Two Groups of Females.

In this section we shall limit ourselves to eight representative traits, and compare the results of analysing the measurements of the group of Jewish females with those of 33 English females referred to in section (*c*). The three head measurements were omitted for reasons already given in section (*b*), and measurements of sitting height were not available for the English group.

The intercorrelations of the traits are already given for the Jewish group in Table III, and Table V gives the intercorrelations between the traits for the English females.

Table V.—*Intercorrelations.*

	1.	2.	3.	4.	5.	6.	7.	8.
1. Stature	.	·648	·644	·233	·432	·527	·131	·094
2. Leg length			·607	·185	·239	·346	·188	·275
3. Arm length				—·011	·169	·353	·108	·100
4. Trunk length					·092	·131	·448	·238
5. Pelvic breadth						·057	—·042	·264
6. Shoulder breadth							·388	·148
7. Chest breadth								·412
8. Chest depth								—

$N = 33$. $\bar{r} = ·264$ s.e. for a zero correlation $\pm ·174$.

The summation method of analysis was used in both cases. For the Jewish group of 62, the initial diagonal insertions were the communalities obtained from the analysis of twelve traits in section (*d*) above. On eliminating the general factor, the residual matrix was bipolar and the traits, pelvic breadth, shoulder breadth, chest breadth and chest depth were temporarily reflected to obtain the second factor saturations. Negative signs are, of course, attached to the saturations of the reflected traits. The diagonal insertions for the residual table were obtained by putting the largest coefficient in the column containing the largest sum, the smallest in the column containing the smallest sum, and the rest graded accordingly.

The diagonal insertions for Table V and its first residuals were also obtained by giving the column with the largest sum its largest coefficient, the column with the smallest sum its smallest coefficient, and the remainder graded according to the squares of the sums of the respective columns. Here, again, the residual matrix was bipolar and the same four traits were reflected as in the previous analysis.

The resulting factor saturations are given in the following table:

TABLE VI.—*Saturations.*

	$N = 62$ factors.		$N = 33$ factors.	
	I.	II.	I.	II.
Stature	·654	·517	·809	·328
Leg length	·760	·566	·725	·429
Arm length	·566	·213	·554	·334
Trunk length	·727	—·062	·352	—·191
Pelvic breadth	·516	—·281	·302	—·104
Shoulder breadth	·563	—·253	·547	·010
Chest breadth	·531	—·485	·448	—·330
Chest depth	·503	—·335	·415	—·479
Variance	2·973	1·126	2·374	·790
Contribution to total variance	37·16%	14·08%	29·68%	9·88%

The saturations for each factor are plotted for the two groups separately in Figs. 5 and 6. It is clear from the contributory variances that the larger group (Jewish) varies more both in size and shape than the smaller group (English). The smallness of the correlations for the English females may be attributed to the fact in such a relatively small sample, errors of measurement etc., play a bigger part. Also, the Jewish group may be "racially" more heterogeneous. As regards differences in general magnitude, as may be seen from Figs. 5 and 6, the main divergences are in pelvic breadth and trunk length, in which traits the Jewish females vary more among themselves than do the English females. Pelvic breadth, trunk length and, to some extent, chest breadth, are more informative of general bulk in the Jewish than in the English group. On the other hand, stature is a better index of general magnitude in the English group than in the Jewish group. Turning to differences in proportion (Fig. 6), we find that leg length is, in both groups, the trait most informative of excessive length development. As an index of disproportionate "non-linear" development, chest depth is the first and chest breadth the second most informative trait in the Jewish group, and chest breadth first and chest depth second in the English group; that is, if we considered the most extreme variations in traits, we would observe that the long-legged English woman would have a very narrow chest, and a long-legged Jewess would have a very flat chest.

The 33 English females consisted of 19 manic-depressives, 13 schizophrenes, and one mixed case. When the measurements (of chest depth and pelvic breadth) of the 32 are standardized, weighted by the appropriate second factor saturations, and correlated with mental diagnosis, we get a coefficient of ·284.

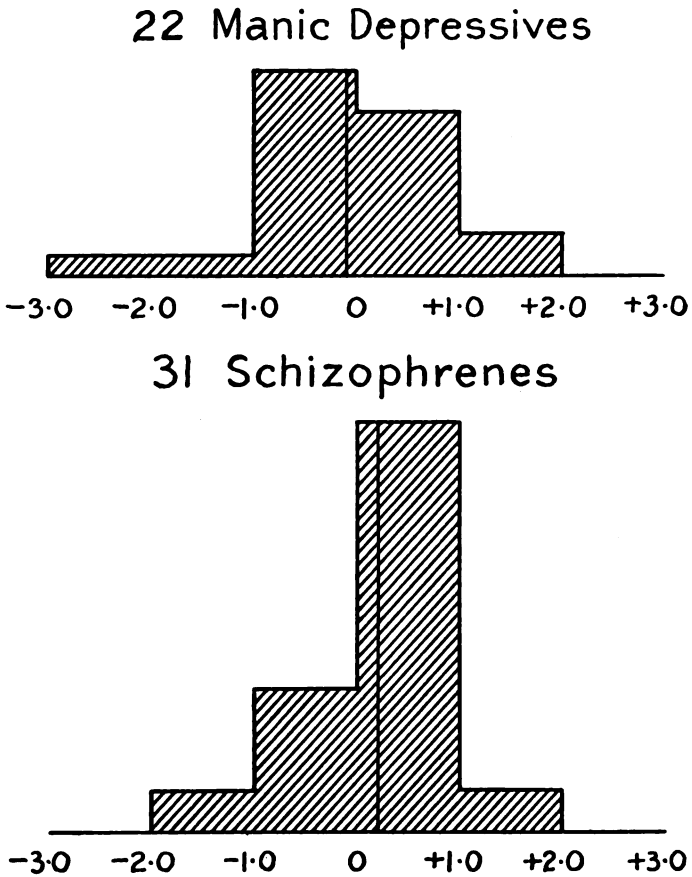

FIG. 4.—Histograms of compound weighted measurements of Jewish female patients.

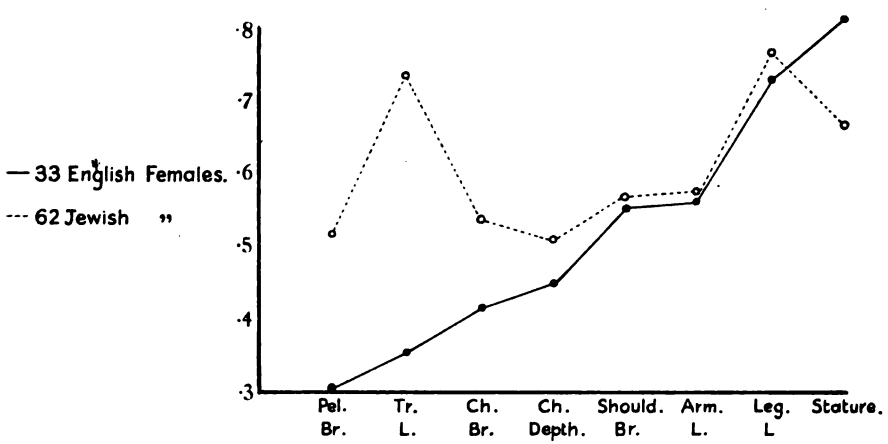

FIG. 5.—First factor saturations.

Converting r to z, we get ·292 with s.e.$_z$ = ·186 and P roughly about ·1. Although this value is not strictly significant, it is consistent with a much higher value in a larger population and with the significant value obtained earlier with the group of 62 females.

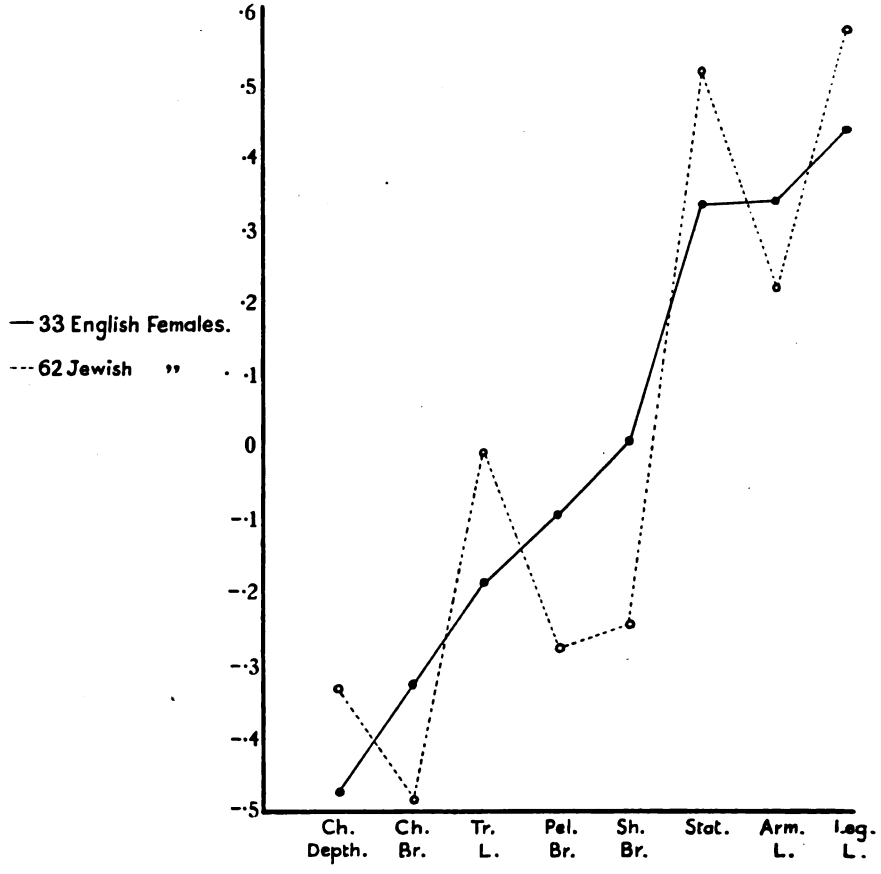

FIG. 6.—Second factor saturations.

(*i*) SUMMARY OF CONCLUSIONS.

1. An analysis of the anthropometric measurements of two groups of female patients revealed the presence of two factors, one governing general growth or magnitude, and the other governing differences in proportion. On eliminating the general factor, a bipolar factor remained with positive saturations for stature, leg length, sitting height, arm length and head length, and negative saturations for breadth of pelvis, chest, shoulder and head, and for chest depth

and head circumference. These results confirm the earlier work on measurements of males.

2. A statistically significant relationship was established between physical proportions and diagnosis of mental disorder. In the case of a group of 47 English male patients a significant correlation of ·413 was obtained between a combined weighted measure of arm length, leg length, waist circumference, pelvic circumference, and manic-depression and schizophrenia. In the case of a group of 51 Jewish female patients a significant correlation of ·557 was obtained between a combined weighted measure of chest depth and pelvic breadth and manic-depression and schizophrenia.

My grateful acknowledgments are due to Prof. C. Burt for his guidance and to Dr. Emanuel Miller for his valuable data.

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A FOLLOW-UP STUDY OF HYPERKINETIC CHILDREN.

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and

MILDRED CREAK, M.R.C.P.

(Received March 16, 1940.)

IN a study on chorea, tics and compulsive utterances, Creak and Guttmann (1) discussed some problems of the inter-relation of organic neurological and neurotic symptoms. They showed that residuals, latent or manifest, of neurological diseases of the motor system may be instrumental in shaping the clinical picture of neuroses. There is generally no difficulty in demonstrating such interrelations, if the neurological anomalies are of a well-known type and clear cut in onset. Pareses, peripheral or central, or aphasic disorders, are generally not difficult to recognize where they are the nucleus of a neurotic picture, and not much objection is encountered if one tries to assess their importance, pathogenetic or pathoplastic, in a given clinical picture. This, however, is difficult where less well known syndromes are concerned, such as apraxic or agnosic pictures, or where beginning or end are gradual and the whole picture less clearly defined, as in disturbances of the extra-pyramidal motor system. To recognize an early stage of Parkinsonianism within a depression or other "neurotic" illness is not easy. The same is true of mild extra-pyramidal hyperkinetic states, partly because they may be so similar to normal movements (pseudo-purposeful), and partly because the milder anomalies as seen in early or later stages (and in abortive cases) are little known.

This study was undertaken therefore because of the interest aroused in the whole problem of hyperkinesis by this earlier work. It was clearly seen, however, that many children with abnormal movements are not choreic and never have been. This has led to the institution of a more detailed examination of the motor behaviour and co-ordination as part of the routine examination of all children attending the Maudsley Hospital with psychiatric problems. Many of these cases show, in a mild form, the changes which are so often associated with organic motor disorders of the nervous system, for example, "twin" movements, spread of movement from the active side to the opposite passive limb, mild twitching and tremors. These are often seen in excitable and unstable children, apart from any demonstrable structural disease.

Arising from this came the idea that a useful background to these cases might be afforded by a study on these lines of cases which were noted to be in

any way fidgety, or who suffered from any form of nervous movements, when they first attended hospital. Cases were chosen from a number of years, sufficiently far back to allow of an independent follow-up study which covered an interval of years. The original notes had not been directed particularly, at the time of taking, to the motor system, and it was therefore supposed that any mention of nervous movements in itself suggested that these were of a fairly obvious kind. If the child was noted as fidgety, it was because there had either been special mention of this as part of the anamnesis, or it had been noted by the physician who took the case.

In previous follow-up studies the frequency of milder sequelae after chorea was proved, but the investigation of the families of the choreics pointed to a complication. There is a constitutional disposition for motor disturbances which may be made manifest by other nocuous stimuli than the causative agent of rheumatic chorea. In other words, the constitutional and the acquired predisposition may have a very similar significance within a clinical picture. This suggested a review of motor disturbances without limiting the field to a special aetiological group. Children were chosen, because the paediatrists give more attention to motor disorders than general physicians, psychiatrists or neurologists. The knowledge of the final outcome of such clinical pictures is limited in the literature on children's disease.

Winnicott (2), for example, in his "Clinical Notes on Disorders of Childhood," has a special chapter on fidgetiness, where he distinguishes between common fidgetiness due to anxiety, repeated movements, tics and chorea. He makes some interesting observations which have some bearing on our problem of the difference between fidgetiness and chorea. "In a typical case of common fidgetiness, the restlessness is part of the child's nature. It is the whole child that is affected. . . . On the contrary, a careful inquiry into the history of the onset of chorea will usually reveal the fact that a more or less normal child on a fairly definite date *became* fidgety." "Chorea, untreated, nearly always clears up." But it is well known that the end of a choreic attack is often very poorly defined, and it is then that it may be difficult or impossible to say whether the fidgetiness is still "organic," or whether it is entirely functional, kept up by hysterical or other psychological mechanisms, or whether there is behind it a permanent structural alteration, leaving a predisposition of the choreic motor pattern to appear, whenever the C.N.S. is exposed to some strain, mental or physical.

The condition underlying common fidgetiness, according to Winnicott, is anxiety. "Such a fidgety child is a worry, is restless, is up to mischief if left for a moment unoccupied, and is impossible at table, either eating food as if someone would snatch it from him, or else liable to upset tumblers or spill the tea. . . . Sleep is usually restless. . . . these children are over-excitable, or 'nervy' rather than nervous (of things, people, the dark, being alone). However, these children are often happy, though irritable if

restricted in activity. Picturing such a child one remembers countless children of between five and ten years old, thin and wiry, quick in the uptake, and eager."

Winnicott says nothing about the further development of these children, and the text-books and manuals of pediatrics do not give much more information. The type in question is described, e.g. by Gött (3), but he fails to say anything about the prognosis : " Restlessness and instability of voluntary musculature of which the child is not conscious is a purely nervous anomaly, though psychic influences tend to increase it. Such a child is fidgety, it cannot stand still, plays with its fingers or its clothes, grimaces, turns its head right and left, licks the corners of its mouth. This behaviour is intensified by emotion and is often reminiscent of early chorea. Often the tongue cannot be kept still when put out ; on closing the eyelids a slight tremor is noticeable, and the spread-out fingers exhibit a moderately fine tremor." Hassin (4) speaks only about the prognosis of tics : in ordinary localized tics the prognosis is fairly good : in generalized tics, especially in the form of Gilles de la Tourette, it is less good, though they may recover. (Oppenheim.)

The course is chronic and painless, without incapacitating the patient to any great extent. Thus it seemed worth investigating the outcome of patients who had been treated for motor anomalies. As the total number was small, and it was anticipated that a considerable proportion of the cases would not be traceable several years after treatment, all cases were selected in which some motor disturbance was complained of by relatives or teachers, not only those which were diagnosed as " motor " cases.

In this way 39 cases were collected out of the total of those discharged during 1930, 1931 and 1932. Fourteen of them could not be traced. Out of the 25 remaining, ten attended the Maudsley Hospital for re-examination ; in addition, relatives were interviewed by a social worker or the writers. Seven cases were interviewed by a social worker, who also obtained information from friends and relatives. In three cases only relatives could be seen by the social worker, where the patients themselves were not available for interview or examination. Finally, in five cases only written information could be obtained ; this group includes the report on one patient who died.

The ages of the 25 patients on whom this paper is based ranged from 5 to 15 at the time of their admission. Eight were under 10, the others 10 or over. There were no mental defectives among them. 20 were psychologically tested. The I.Q. ranged between 89 and 136, 16 being 95 or over. This point is mentioned to emphasize that we are not dealing with hyperkinetic (erethic) mental defectives. Although the problem of the nature of the hyperkinesis so common in idiots has some bearing on our topic, our cases provide no material for the discussion of the significance of the abnormal motor behaviour within the clinical picture of mental deficiency. It may be regarded as certain that not all hyperkinetic pictures in idiots are of the same origin ; Earl's catatonic psychosis

in mental deficiency (5) is an example of one clinical entity which can be differentiated out of the mass of hyperkinetics. Kramer and Pollnow (6) described a peculiar hyperkinetic disease of children which they have good reason to assume is an encephalitic process (post-mortem in one case), at any rate due to an organic disease process in the brain. A follow-up of their cases by M. Lamper (7) showed that all cases had permanent symptoms, though not of the kind so well known after epidemic encephalitis. Their hyperkinesis had improved to a variable extent, but even in those cases which showed practically no motor symptoms a striking "lability" of motor reaction was demonstrable. They showed a sort of "potential" hyperkinesis, revealed when they were upset, excited, cheerful or worried.

Two of our cases, 5 and 19, who developed organic signs in the course of their illness—hemiplegia, generalized epileptic fits—may be related to Kramer and Pollnow's disease, which, however, is not very clearly defined clinically. Family histories were available in twenty cases. In three of them serious heart disease and in one chorea were reported in near relations. One schizophrenia, one juvenile chronic mental hospital case (? schizophrenia), three epileptics, two suicidal depressions, three nervous breakdowns were mentioned. Only in two families was none of the near relations said to be nervous or mentally ill. In five cases motor symptoms, stammer, twitching were reported in the original records (i.e. without special questioning in this direction). The cases are reviewed here in four groups—Tics, Generalized Tics, Chorea and Fidgetiness. One case (4) was diagnosed hysterical shaking, and this patient still suffers from hysterical manifestations of a motor type.

Tics. [Cases 13, 17, 21, 19, 15, 9 and 10, 5.]

Three cases, (13), (17), (21), on which our information is based on letters only, had no symptoms to complain of at the time of the follow-up. But the information obtained in the three other cases suggests considerable reserve in accepting their statements as entirely correct. Patient (19) developed a hemiplegia after an infectious illness and, in addition, he is described as restless and fidgety. There is the possibility of some intellectual deterioration (due to cerebral illness ?). Both the other cases kept up the predisposition for motor reaction under stress. Case 15 lost his tics only two years ago ; he had them for at least six years after his admission, and at the time he had an attack of restlessness when his spasms were very bad. In the other case (9) the retrospective history obtained on the occasion of the follow-up made it likely that his tic was choreic in origin, and the tic is still present, i.e. about twelve years after the acute attack.

In the group "Multiple Tics," one (10) made a good recovery. Only when he closes his eye is a slight unsteadiness of his head to be noticed, reminiscent of the head-shaking which was his prominent symptom. It is interesting to note

that his paternal grandmother is described as "shaking and jumping" at the slightest sound. The grimaces complained of in the other case (5) may have been epileptic equivalents, though not recognizable as such on the first examination. Still, he was noticed to be "vacant" at times even then, and subsequently he developed *petit mal* and in the last few years major epileptic attacks. There is no doubt now that he suffers from some sort of organic epilepsy.

Chorea. [Cases 24, 12, 2, 25, 7.]

Five cases of chorea which occurred in this series were followed up in order to increase the material previously collected by the writers (1). There is no need to repeat here the discussion on how far this material from a psychiatric hospital is a selected one, particularly severe and particularly neurotic. It may be mentioned, however, that all these cases were out-patients.

Of the five cases, one (24) died of rheumatic heart disease five years after discharge. Another one (12) has mild recurrent attacks of rheumatism and chorea, a third (2) a loud systolic murmur very suggestive of a mitral regurgitation, well compensated. This last patient, however, has recovered very well as far as concerns his motor system. The same is stated in a written report on the health of the fourth patient (25), whereas the fifth (7) shows very characteristic motor residuals which are well under control; but they are clearly demonstrable if the patient is upset. They are of the kind which would condition the patient's neurotic reactions should she succumb to some emotional stress.

Fidgetiness. [Cases 3, 6, 22, 16, 8, 20, 18, 23, 11, 14, 1, 4.]

This group, which mainly interested us, consists of ten cases. In three of them a history of chorea was given (3), (6) and (22); in one more case (16) one would, in retrospect seriously consider that diagnosis. Important as this differential diagnosis is, it is not possible to be certain about it retrospectively, and it matters little in relation to our topic, as the attack in question was over when the child came under observation. The description at that time does not differ from that of the "fidgety" children. Two of them who were examined made a good recovery, that is to say, they have not had since their discharge any nervous symptoms, especially no such signs of restlessness or anxiety on account of which they had been treated. They still show, however, some signs of motor anomalies—twitchings when upset, marked movements of embarrassment—similar to those observed a long time after practical recovery from chorea. The third case is "quite well," according to a letter from his father which does not allow of any conclusion as to the fine disturbances which interest us here.

When Case 16 was originally examined the physician in charge appears to

have had in mind the diagnosis chorea *v.* fidgetiness, and he finally decided for the latter. The sudden onset and end would retrospectively suggest chorea rather than mere fidgetiness, and one might try to account for the "fidgety" rather than choreic movement by assuming that the manifest picture was a reaction to the physical disease and coloured by it in the expression of the anxiety. Another interpretation, however, would be that the predisposition to this particular kind of anxiety reaction could be found in the boy's constitution; his mother had suffered from chorea and pericarditis when she was young. The follow-up by letter did not allow of a closer analysis.

In Cases 18 and 20 the follow-up is not satisfactory. In both instances the informants mention that the patients are still shy or timid, and it cannot be assumed what the motor expression of this psychological state is and how far it comes under the heading of motor anomaly. Case 8 still complains of nightmare and anxiety attacks; he also shows jerky movements during the interview. He fits in best with those cases of common fidgetiness in which, according to Winnicott, the motor restlessness is the expression of anxiety. It is interesting to note that his mother has similar motor habits. It is, of course, impossible to decide how far imitation plays a part in the causation of the habits.

The last sub-group consists of four cases with definitely "bad" outcome (23), (2), (14), (1). Case 23 is described in a written report as restless and overactive. He is also dishonest and untrustworthy. Case 2 is still a nervous and jumpy child; she suffers from periods of excitement during which she cannot sit still, and she has many more anxiety symptoms eight years after admission.

Case 14, a girl, admitted because she appeared to be "on the verge of St. Vitus's dance," is, according to a short history and record obtained at the time, a characteristic representative of this group. The after-history could be obtained only by letter owing to the patient being so far away. She is, however, described as being still very nervous, and her aunt spontaneously mentioned her obsessions. The relationship between hyperkinetic and obsessive compulsive phenomena has been discussed in our previous paper on "Chorea, Tics and Compulsive Utterances" (1). Case 1 contributes some more material for the discussion on this subject. He was sent for treatment because of fits of temper; he was described as nervous, difficult, uncontrolled. He could not sit still, kept on going in and out of the room and touching everything. He was over-talkative and stammered. Now he shows no more motor anomalies; but he has numerous hypochondriacal symptoms, he is full of superstitions, phobias and obsessions. He is untidy and somewhat fatuous, and his affect is not quite in keeping with all the fears he is describing.

The result of this follow-up study can be easily summarized in a general way, though a statistical evaluation is impossible because of the small numbers in each group, and the different weight which has to be attached to the individual

observations owing to the different amount and quality of the information collected.

Tics, as such, have a good prognosis, i.e. after a number of years the patients do not complain of them. But a large proportion of them keep on having a predisposition for " motor " responses to individual strain. Our material also demonstrates impressively that tics may be the initial sign of organic neurological disease.

The post-choreic fidgetiness is illustrated from two angles in our material: the follow-up history of choreics shows residual motor instability, and the retrospective histories of cases of " general fidgetiness," " nervousness," suggest that some of them are post-choreic conditions. In these instances one may find afterwards more or less marked motor instability ; but on the whole their prognosis appears to be better than that of the " genuine fidgetiness." In all cases followed up (with one exception) we found the " motor signs " still present in a pathological degree, not only a predisposition for motor reactions as in the other instances. The case which was the exception shows the severest clinical anomaly now. The mixture of obsession, compulsion and hypochondriacal symptoms may signify an early schizophrenia, or it may be a later sequela of the same disease process which was manifested primarily in the hyperkinesis, and the history may lend itself to such an interpretation. Schilder (8) found in seven cases of obsessional neurosis definite organic signs reminiscent of those observed in epidemic encephalitis. He does not think, however, he is dealing with cases of mild encephalitis ; constitutional, early traumatic, toxic or infectious processes may be responsible. This follow-up study gives some idea of the origin and development of motor anomalies in a small group of patients. It is meant to be a contribution to the study of individual motor behaviour in general, and forms part of a larger investigation in this field.

It is only comparatively recently that the " motorium " as a characteristic feature in a person's individual make-up has been recognized, and the methods of describing and studying it are still in an embryonic state, and the knowledge collected by various workers is still poorly integrated. Still, we know that even simple movements, such as flexion, and/or extension of a finger reveal differences in speed and co-ordination (Isserlin). More complicated movements and their analysis, such as lately carried out by Peters and colleagues (9), allow the definition of motor types which may be correlated to the subject's psychological make-up. The habitual tempo of repetitive simple movements (tapping), the capacity to repeat and to keep up rhythms have been studied with the view of obtaining data to characterize the individual motor type of a person without having yet yielded clear-cut results. Rough classifications such as Earl's (5) over-movers and under-movers still convey the most vivid impressions of what is meant, and they certainly leave room for closer analysis. Enke (10) employed a set of actions (rather than movements) to describe the

motor behaviour of his subjects in a standardized setting, and thus was able to correlate the types found with the physique and, consequently, the character of his subjects.

Ozeretzki's (11) scale for characterizing the motor development of children uses both movements and actions. It has not been introduced into clinical use as widely as such a test would deserve (though Heuyer and others (12) have employed it), possibly because its standardization is not exact enough. Another objection which the present writers think important is the lack of knowledge as to how far upbringing, training and practice influence the results. It has therefore seemed more promising to use facial movements for such a test, as they are so much less subject to training. Kwint (13) worked out a scale of the development of motor ability in the facial region; in the writers' experience, the tests published do not allow such a sharp classification as claimed but the method certainly deserves elaboration. Each of these methods, if employed in the original examination of such patients and in their follow-up, would help to define more clearly the degree and type of abnormality of the "motorium" and the correlation between the variation of motor and mental symptoms.

For permission to publish these cases we are indebted to the late Prof. E. Mapother, Medical Superintendent of the Maudsley Hospital, where this work was carried out.

The Editors regret that owing to the cost it was found impossible to print the case-records; they are available at the Maudsley Hospital.

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THE DIFFERENTIATION OF NEUROSES AND PSYCHOSES, WITH SPECIAL REFERENCE TO STATES OF DEPRESSION AND ANXIETY.

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THE problem of the differentiation between neurosis and psychosis has given rise to much confused literature and discussion. This is particularly true of those cases in which anxiety or depression is the outstanding feature of the illness, and which do not show any gross symptoms of psychotic illness. Such confusion as exists appears to be due to a variety of causes. For example, the social implications of psychotic illness tend to favour a diagnosis of neurosis in many of the milder cases. Again, the same diagnostic terms are often used with quite different meanings by different workers. An even more potent cause of difficulty is the temptation to search for fixed disease entities in psychiatry which can be sharply separated one from the other.

This is a cardinal error, and it has often stultified attempts to introduce orderly methods of classification. It is, no doubt, dangerous in all branches of medicine to think in rigid diagnostic terms, since once the case has been suitably labelled, important individual differences may easily be overlooked. In psychiatry the complication and variability of the factors involved make the setting up of such fixed categories particularly harmful. Certain broad principles may, however, be found which enable us to group together a series of cases under a common heading. This heading, if it is to be of value, should help us to appreciate the factors which are similar in the series without losing sight of individual differences. It is in this spirit that we have to approach any problem of psychiatric classification.

The problem under discussion must first be formulated as clearly as possible. It is really a twofold one. Firstly, whether there is any essential difference between a neurosis and a psychosis. Secondly, whether there is any essential difference between that group of cases commonly termed psychoneurotic anxiety states, anxiety neuroses or anxiety reactions and that group commonly termed depressions. Unfortunately the problem is made even more complex by the fact that the first group is frequently termed neurotic and the second psychotic, this differentiation being made by previous definition of the groups and not by any appeal to clinical judgment.

It may be said that there are those who regard the concept of neurosis in

general and anxiety neurosis in particular as valuable and important, to be differentiated carefully from psychosis and psychotic depression. There are also those who regard these differences as incidental, misleading, and often quite unimportant. A few references from recent literature will serve to illustrate the difficulty.

In this country T. A. Ross has been a leading exponent of the view that there is a fundamental difference between anxiety reactions and depressions. His definition of the anxiety reaction may be accepted as a good one (1927), i.e. " Those patients whose chief symptom is either frank mental anxiety or its somatic manifestations, of which palpitations, sweating, flushing and tremor are the chief." It will be noted that he does not mention depression in this definition, and in another place (*The Common Neuroses*, chapter upon the " Symptomatology of Anxiety States ") he does not record it as one of the symptoms of the illness at all.

He lays stress upon the differentiation from the group of depressions for various reasons, among which prognosis, therapy and suicidal risk may be mentioned. In his view the diagnosis may be established by a number of indications. In the history of the case the depressive attack frequently comes out of the blue ; there may be a story of previous attacks of depression, and the personality of the patient may be surprisingly normal between the attacks. The neurotic, on the other hand, is seldom completely well between his attacks, which are closely related to psychological difficulties. The depression itself is of a different type in the two disorders. In the psychotic it is independent of the environment ; in the neurotic, environment makes a great difference. The psychotic tends to blame himself for his troubles, the neurotic tends to blame others. Other notable differences, according to Ross, are rapid variations of mood in the neurotic, retardation of mind and body and lack of insight in the psychotic.

If the differentiation to be made was truly one between anxiety on the one hand and depression on the other, most of this differential diagnosis would be beside the point. Ross is clearly, however, accepting the fact that in practice the diagnosis may have to rest, not upon the separation of anxiety and depression, but at least in some cases upon a distinction between two different types of depression. His reluctance to speak of the symptom of depression in connection with the anxiety reactions may perhaps be due to the tendency already mentioned to regard depressive illnesses as properly belonging to the psychoses, whereas all the cases he has in mind should, in his view, be regarded as neuroses. A possible source of confusion is here evident, since cases in which depression is the leading feature of the illness may be forced into the category of anxiety states in order to emphasize their relationship with the neuroses.

Gillespie, among many others, has attempted to solve this problem by setting up a group of psychoneurotic depressions closely allied to the anxiety states, but in which depression and not anxiety is the leading symptom.

These he differentiates from psychotic depression in various ways, but chiefly by their greater " reactivity." By reactivity he implies the variability of the affective condition in relation to internal or external factors (topics of preoccupation) of a conscious kind. In this respect Gillespie is, of course, following in the footsteps of many other writers (notably J. Lange), who have attempted to make a clinical differentiation from the classical endogenous manic-depressive insanity of Kraepelin.

Thus a consideration of the views of these two writers leads to the conclusion that there exists a complex group of cases marked by symptoms of anxiety or depression and belonging essentially to the neuroses. These can be differentiated from a group of depressions which belong to the psychoses.

These views have been strongly endorsed by other writers. For example, Yellowlees (1932), speaking of this type of case stated : " Neurotics generally are made, not born. I believe it to be far otherwise with the psychoses, the causes of which are more deeply and more mysteriously biological. Psychotics are born, not made." Again (1930), in a similar context, there is " a difference in kind as well as a difference in degree." Crichton Miller contrasts the group of cyclothymic depressions (psychotic) with the group of neurotics. He says, " The true cyclothymic varies for endogenous reasons, and all other explanations are fallacies of lay observation."

Quite contrary views have, however, been put forward by other writers, whose opinion must now be recorded.

In the 1937 edition of Price's *Textbook of Medicine*, Mapother and Lewis place the anxiety states under a sub-heading in the group of affective reactions, and consider the diagnosis and treatment of this group along with the rest of the affective states. They state, " The distinction between neurosis and psychosis is at times convenient, but without substance." An anxiety state is, therefore, but a mild form of agitated depression. In another place Lewis (1934) writes, " One cannot set up the symptom anxiety as an independent type of reaction," and he quotes other authors, e.g. Birnbaum, in support of this statement. In the same paper he also concludes that views on the existence of two varieties of depression (i.e. neurotic and psychotic) are false.

Curran took two groups of cases suffering from anxiety and depression, the one supposedly neurotic, the other psychotic. He compared various features of the two groups, and came to the conclusion that no list of criteria for differential diagnosis could be found. Indeed, his paper clearly demonstrates the futility of what may be termed " diagnosis by category," and the impracticability of drawing up such lists to differentiate between one reaction type and another.

Symonds has summarized the essential features of this viewpoint in the following remarks : " The affective type of mental disorder . . . may be either of the neurotic degree (anxiety neurosis, neurotic depression) or the psychotic degree (manic-depressive psychosis) . . . there is in my view

no essential difference between a neurosis and a psychosis except that of degree."

Such, then, is the essence of the conflict of views—a conflict which is as old as Kraepelin's first formulation of manic-depressive psychosis. This brief résumé of some recent views is intended to do no more than illustrate it. The problem as stated is a twofold one, namely whether it is possible to differentiate between neurosis and psychosis, on the one hand, and between anxiety states and depressions on the other hand. Unless its twofold nature is clearly emphasized confusion is bound to arise, as it has so often in the past.

A few more definitions may be helpful at this point. Ross's definition of an anxiety state already given may be accepted as a good one. Lewis (1938) has defined a depression in the psychological sense as follows: "Any person who is unhappy and ill with his unhappiness may properly be said to be in a state of depression." He proceeds to eliminate from this definition other conditions, psychotic and organic, in which depression may also be a prominent symptom.

With regard to the definition of the term "neurosis," Mapother and Lewis suggest that it is permissible to term a patient "neurotic" if he has insight into his illness, is co-operative, and unlikely to need care in an institution. The first of these three points is sometimes difficult to determine satisfactorily, and has, in fact, been criticized by Lewis himself (1934) in another place. It may perhaps be taken to mean that the patient realizes that he is ill and appreciates the extent of his symptoms. All three points, in fact, depend upon one cardinal factor, namely, that the patient's relationship with reality remains fundamentally intact. This is the point stressed by Ross, who states, "The psychotic lives, in so far as he is a psychotic, in a world of phantasy; the neurotic lives in the real world." This is a point which is implied in Meyer's definition of a neurosis as a "merergasia" or "part reaction." (The same author [1912], in connection with a different type of case, but none the less aptly, speaks of the degree of "deficiency in corrigible foundation and relation to things as they are.")

We have arrived at what is obviously a *clinical* distinction between neurosis and psychosis. We have adduced so far no aetiological and no pathological basis for a differentiation. Is it then of any importance? Can we say, with Mapother and Lewis, that it is "at times convenient but without substance," or should we on the other hand agree with Ross, who "entertains no such view"?

In order to be justified any classification must, as Lewis (1938) points out, be both useful and valid. In the present state of our knowledge, no classification can be devised which shall be universally valid for research worker and clinician alike. It can, however, be valid within certain limits which can be defined, and it can also be useful. The question then is whether this differentiation serves a useful purpose to the clinician. There can be no doubt that

it is a question which is regarded as enormously important by the layman, often in a misguided sense.

The case material of the Cassel Hospital may help to provide an answer. Over a period of nearly 20 years the hospital has admitted for treatment a large number of cases, of which very many have suffered from symptoms of anxiety or depression and have been diagnosed as neuroses before admission. It is, therefore, in the highest degree relevant to refer to this bulk of clinical material for a solution of the problem.

It would be an impossible task to make an abstract of the important features of all these cases; instead it is proposed to present briefly three cases, typical of so many that have passed through the hospital, in which the outstanding symptoms have been depression. Even in these the volume of facts makes it necessary to leave out much that might be relevant if other problems were under consideration, e.g. family history, etc.

CASE 1.—W—, the manager of a steel works, a married man, aged 50, of Welsh extraction, was seen in his eleventh attack of depression. He complained of depression, feeling of worthlessness, lack of concentration and sleeplessness. Each of the previous attacks had lasted for a period of about two months. There had also been three or four mild attacks of elation in the intervening period. The present illness lasted for approximately the same time and cleared up completely without being succeeded by elation. No psychogenic factors to which any importance could be attached were found. Nine of the previous attacks had occurred in the springtime between the months of February and April. There appeared to be no special features of his life which might produce abnormal strain at this time. There was no scope in treatment for psychotherapy of an analytic kind; on the other hand, the patient's response to the daily encouragement of his physician was quite good.

If there were no demonstrable psychogenic factors in the illness there were also no physical ones. It came mysteriously "out of the blue," and one is free either to accept the Kraepelinian theory of an endogenous origin or to suppose that the psychogenic factors remained undiscovered. MacCurdy's work suggests that the latter may be the correct explanation. The history taken may have failed to reveal the true psychogenesis of the condition.

Most clinicians would regard this illness as a mild psychosis. The patient's relationship with reality was undoubtedly disordered by the mood change from which he suffered. This mood change did not bear any immediate relationship to his environmental situation, nor did it appear to be dependent upon his conscious or near-conscious preoccupations. On the contrary, these preoccupations appeared to be the result of the mood change, which had an ebb and flow of its own. Profoundly unconscious factors may have determined the tide of his mood, but there was none of the direct cause and effect relationship with an external situation which accounts for "normal" periods of depression.

It is true that reassurance and sympathy made him feel slightly better for the moment, but that would be likely to happen unless the relationship with the external world had become altogether distorted.

The next case presents a contrast in that certain precipitating factors of a fairly adequate kind could be demonstrated.

CASE 2.—S—, female, unmarried, aged 31, was admitted to hospital with a diagnosis of manic-depressive psychosis. She was depressed and tearful and had considerable sleep disturbance. The present could be said to be the third attack of her illness. She was the youngest of five children and had an unhappy childhood abroad. She came to England at the age of 9, and was educated somewhat unwillingly by relatives. At 17 she took up a career of physical training, which was made more difficult by a series of troubles involving the Head of the College, and her relations who interfered in her affairs. Her physical health was poor, and she feared that she would not be able to hold an independent job when she qualified. She became depressed and sleepless, and was advised to take a rest. After a few weeks she was able to return satisfactorily to work. She remained well for two years, and then, tasting the fruits of independence through the job she held, she became involved with a group of well-to-do and hard-living people. She lived a gay life for a while, got into financial difficulties and became depressed again. On this occasion her illness was complicated by differences of opinion among her relatives as to how she should be treated, and she was ill for several months. She recovered eventually, and having regained her precious freedom began once more to lead a somewhat over-active life with a series of not entirely satisfactory love affairs. After one of these she again became depressed and was later admitted to hospital.

During the first part of her stay in hospital the patient's symptoms bore quite a close resemblance to those of the previous case. It appeared from the history that the mood changes had been produced in the first place by the factors briefly outlined. When the significant factors in the case-history were touched upon a marked emotional reaction was produced in the patient. But it was also observed that, as in the previous case, there was an undercurrent of depression which was fairly constantly present. In other words, the mood change, once produced, pursued a course at least partly independent of the environmental problems. That which started as a mood of depression in response to a difficulty had become to some extent a primary factor in itself.

Cases of this type are often given the most widely varying labels, ranging from "neurosis" to "manic-depressive psychosis." Whether or not such a patient should be called "manic-depressive" is not at the moment relevant, though this label is often used with such a strongly nosological flavour as to hamper a proper understanding of the case. The mood change had, however, become partly dissociated from immediate environmental factors just as in

the previous case. For the same reason, therefore, the patient must be termed psychotic.

The next case to be described is one in which the depression was also the leading symptom. Here, however, the mood change appeared to be almost wholly dependent upon immediate topics of preoccupation of a conscious or co-conscious kind. It had not become groundless, but varied sharply according to these topics of preoccupation.

CASE 3.—G. W—, male, aged 39, complained of intense feelings of depression, faintness, trembling and fear. For five years before admission he had suffered from a pain in his back. Six months before admission he went to a specialist, who found that he was suffering from spondylitis deformans and prescribed a belt for him to wear. Very shortly afterwards he began to suffer from giddy turns and later had a " nervous collapse." He suffered from a wide variety of symptoms at this time, and was referred to a neurologist, who could find no evidence of organic disease except for the mild degree of spondylitis deformans. He was accordingly sent to hospital for psychological treatment.

The previous history was explanatory of the condition. He was an only son, and his father was superintendent of a large cemetery of 800 acres in the middle of which he had a house. Social life, both for the boy and his parents, was therefore very limited. The boy had no companions, but would play solitary games among the gravestones. His mother worried greatly over him, and he was always being kept away from school lest he should " overdo it." Whenever he was ill her anxiety was intensified, and the picture formed in his mind was not made less gloomy by the fact that from his bedroom he could hear the sound of coffins being made.

When he was 14 the family moved away from this house and he trained in secretarial work and later found a job. He was always anxious about his health, though he kept fairly well at this time. He married and got promotion, worrying a good deal, but always being able to carry on his work. When the pain in his back started he at first ignored it, and later got palliative treatment from his doctor. He feared that it might prove to be something terrible and tried to conceal his worry about it. When he overheard the specialist's verdict that he was suffering from spondylitis deformans, and that it was incurable, he became panic-stricken. He would not accept his own doctor's reassurances, which he thought were just to cheer him up. He was convinced that he had a terrible disease, and developed acute symptoms of depression and anxiety. These only added to his worry and so, as is often the case, set up a vicious circle and made him worse.

On admission he presented the symptoms already described. His depression, which was closely associated with anxiety, showed even more marked fluctuation than in the last case. It was much more completely determined by the immediate content of his mind. When something happened which reinforced his worry about himself he felt terribly depressed. When his

thoughts were distracted by occupation or recreation he showed marked improvement. There was none of the spontaneous morning-evening variation shown by the last two cases. When he appeared to be worse in the morning, it was found to be in response to something which had happened since the previous evening.

The case was in fact a psychoneurosis in the sense in which we have defined it. The patient's relationship with reality had undergone no fundamental change. His mood had a corrigible foundation and bore a proper relationship to his preoccupations.

We have thus described three cases in which the outstanding symptom was depression. They all represent well-recognized and quite common syndromes. Two of them appear to be psychotic and one psychoneurotic, using the differentiation discussed. This differentiation is concerned only with the patient's relationship to reality in a broad sense. It has not been made on the basis of "reactivity"; otherwise Cases 2 and 3 would have to be differentiated from Case 1; nor on a basis of mildness or severity, in which Case 1 would have to be picked out as being symptomatically at least milder than Cases 2 and 3. It cannot be made on an exclusive "either-or" basis, since obviously such a criterion as this cannot provide a sharp dividing line between neurosis and psychosis. To attempt to do so would be to fall at once into what Meyer (1928) has called "the arch sin of modern psychiatry—i.e. blinding oneself to the specific facts of the case at hand by asking at once, 'Is it a major psychosis?'" It is of the utmost importance to be clear about what the differentiation does not achieve. One may now inquire whether, within its proper limits, it is valuable and important. The answer is in the affirmative upon three grounds—psychopathology, treatment and prognosis.

To take these in what is medically their logical order means to take the most speculative and difficult problem first. One does not know enough about the state of mind commonly called depression to be able to make dogmatic assertions about its psychopathology. One can only say that it occurs, in normal people, chiefly in circumstances of loss or bereavement. Under these circumstances it persists for a certain length of time and then fades away. It may become abnormal for a variety of reasons. For example, the patient may show an excessive mood reaction to a comparatively trivial situation. This occurred in Case 3. The patient had a reason for his depression. It arose out of his anxiety about his health. But his anxiety about himself was greater than it need have been in the actual situation. It depended upon the lifelong tendency he had developed towards over-concern about his health. Many unconscious associations came into play as soon as this was threatened in any way. They were quite sufficient to account for the depression, which was therefore only *apparently* disproportionate. Moreover, it was directly associated with the conscious and co-conscious preoccupations in his mind, just as would be the case in the normal individual with an adequate cause for

his depression. This is, of course, by definition typical of an illness of this group. The patient may complain of depression for which he cannot find a cause, but preoccupations will always be discoverable, based on reality, which have a cause and effect relationship to the depression. These preoccupations may depend for their intensity and emotional significance upon other, more profound, problems and frustrations, but the rationalizing function of the conscious mind still holds sway between these deeper frustrations and the problems of external reality.

It is otherwise with Cases 1 and 2. One cannot say positively what is the cause of the mood change in these patients. In Case 2 one can point to certain factors which appear to have produced the depression in the first place. But to some extent it has acquired a continuity of its own, it has become a primary factor in the illness. In Case 1 it was not possible to point to any significant aetiological factors of a psychological order. This is not to argue that there was no cause. Perhaps as a result of internal frustrations and difficulties, perhaps as a result of changes best expressed in physiological terms, a mood of depression coloured the content of the patient's mind. But whatever factors were responsible for the depression, it was clearly of a different order to that found in Case 3. The rationalizing function of consciousness no longer held sway. The mood was not related, as in the normal individual, to the problems of external reality. It was not related even to the multitude of associations and derivations which give a personal significance to the factors of external reality, and which in the neurotic can explain an apparent abnormality of mood. It was capable of colouring and distorting the patient's view of these factors, but its roots now lay in other and perhaps deeper levels of the mind.

Having thus amplified the psychopathological differences which lie behind these two groups of cases, it may be appropriate to inquire whether a differential diagnosis can be made by which the clinician can separate them in practice in the majority of instances. If the very limited deductions made are correct it should be possible to do so, but not by means of the criteria so often used. Differences in the type of depression shown by the individual case are useless. Each patient is miserable, but there is no way of differentiating the *quality* of their misery. Mildness or severity affords no clue; an exceedingly depressed patient seen recently at the Cassel Hospital was suffering from a neurosis by the definition used here. He was an ambitious young man of 29, with a complex determined fear of failure in his job which appeared to be about to materialize. Duration varies widely with both conditions. A woman of 38 suffered from symptoms of depression for 15 years, which proved on investigation to be directly related to her home difficulties and to be neurotic in type. The presence of precipitating factors at the outset of the illness, invariable in the neurotic depression, is common also in the psychotic. Our own case material affords conclusive evidence of this. Recurrence is obviously a dangerous guide to adopt; it is not the prerogative of a psychosis. Indeed,

for those who regard neurosis as something to be treated and psychosis as something to be left alone, it may lead to tragic results. Other superficial clinical data are almost equally unreliable, as Curran showed so conclusively. It is true that the psychotic depression tends to run a course more rhythmically variable than the neurotic, with early morning exacerbation, etc., but this is a most unsafe differential guide.

In fact the only method of arriving at the diagnosis is to study the history and day-to-day behaviour of the patient with minute care. It may then be possible to decide whether or not the mood change observed is dependent upon the preoccupations of the patient, themselves related in a proper manner, on the one hand to external reality and on the other to his instinctive strivings. Thus, as in many other medical conditions, diagnosis must still depend upon a careful study of pathology.

Differences in treatment are important, but their importance can be exaggerated. A state of depression is often broadly regarded as a defence mechanism of the individual, leading to a diminution of activity for the time being in the face of intolerable stress. Neurotic depression may best be dealt with by a direct psychotherapeutic attack upon the causal factors. This may not be at all easy, and, indeed, it may be completely unsuccessful if the patient's personality permits of little readjustment. Nevertheless, a direct attack represents the most efficient method of approach in these cases. By this is meant, firstly, an attempt to reach an understanding of the factors, both external and internal, which constitute the patient's problem. For this purpose free association or direct questioning or some other method may be employed. It will be followed by the presentation of the real nature of his problem to the patient in such a way that he can understand and act upon his understanding.

Psychotic depression is not amenable to this approach in quite the same way. Here it might be said that the defence mechanism has come into operation in a far more wholesale manner. To most workers it appears that the time factor assumes an importance in treatment which it does not have to the same extent in the previous group. The direct attack has to be much more limited, especially in the early stages. Principles of rest have to be observed as in many other conditions. The patient has to be placed in a simpler environment in which natural healing forces can come into full play. Only gradually will he be fit to face his problems and learn to deal with them in a healthier way. This is not the place to go extensively into problems of treatment, but it may be said that whereas the principles in the two groups are not really opposite, at certain stages a diametrically different approach is necessary. Rest, in the psychiatric sense, may be unnecessary or actually harmful in the neurotic ; it may be essential for a certain period in the psychotic, for whom a very active therapy at this time may be most deleterious.

Turning lastly to the question of prognosis, one cannot derive much help

from the recovery rate in the individual attack. The majority of cases of psychotic depression, but certainly not all of them, improve or recover. The majority of cases of neurotic depression also improve, but without adequate psychotherapy the degree of improvement is generally less marked than in the psychoses. Relapses occur in both types whether treated or not. Significant information can be obtained from a study of the type of attack shown in these relapses. If the difference between neurotic and psychotic depression were merely one of degree, then it would be likely that mild "neurotic" attacks and more severe "psychotic" attacks would alternate frequently in the same patients. The material of the Cassel Hospital suggests that this is not the case. Ross (1936) found that out of 1,043 patients with a diagnosis of neurosis whose cases were followed up for from 3 to 15 years, about 50 developed psychotic illnesses (i.e. less than 5 per cent.). It is true that Ross included all types of neurosis under this heading, but a considerable proportion of the cases had depression or anxiety as the leading symptom of their illness. Anxiety states and neurotic depressions are, as will be pointed out presently, very closely related. It is also true that, as a result of the methods of follow-up used, the cases had to become quite unequivocally psychotic in order to be classed under this heading. Nevertheless, the figures are impressive. They indicate that in remissions the illness did not differ very greatly, in so far as the fundamental relationship with reality was concerned, from its original form. In this respect *the reaction pattern remained essentially the same.*

All these different observations point to the same conclusion—that in the depressive states a differentiation between neuroses and psychoses is both valid and useful.

If one turns to a consideration of those conditions in which anxiety is the leading symptom of the illness, exactly the same conclusion is reached. This is because the relationship between anxiety and depression is very close. In the earlier discussion it was mentioned that conditions which are essentially depressive are often called anxiety states to emphasize their relationship to the neuroses. Herein lies an error which has produced much of the confusion that surrounds this subject. There is no doubt that anxiety *neuroses* should properly be distinguished from depressive *psychoses*. The grounds for their differentiation should, however, be the distinction between a neurosis and a psychosis, and not between anxiety and depression.

A single case will serve to illustrate this point.

CASE 4.—N. W—, female, aged 42, complained of palpitations, fears of going out and feelings of anxiety. Symptoms had been present for about four years before admission. She was an only child of elderly parents, and had been brought up very much under their eye, so that even in adult life she was afraid of hurting or angering them by independent action. She had not had much opportunity to make friends, but had had two close friendships with women of her own age. Her mother had broken these up quite ruthlessly

because she felt the patient ought to marry a particular young man. She had acquiesced in her mother's actions, but had never been able to bring herself to accept the young man's advances, as she was not in love with him. It was in this setting that the anxiety symptoms developed. During her treatment in hospital, which was lengthy and difficult, she had many severe attacks of anxiety. In every case it was found that these developed in relation to a situation which suggested, consciously or unconsciously, some aspect of her problem.

This case is clearly an anxiety neurosis of a typical, though highly complex variety. The mechanisms involved closely resemble those in Case 3, and the relationship to reality is similar in both. These then are closely allied neuroses, standing apart from Cases 1 and 2. There may be important differences between them, but the criteria used in this paper do not serve to illuminate them, and they would have to be sought in other ways. Attempts to divide a series of such cases, according to the predominance of anxiety or depression, would be a hopeless task. In many of them, now one, now the other stands out.

The close relationship between anxiety and depression becomes even more marked among affective psychoses. If one felt justified in separating anxiety and depressive neuroses, one would be equally justified in distinguishing between anxiety and depressive psychoses. Many of the conditions which are generally termed "agitated depressions" are almost perfect examples of "anxiety psychoses," yet this term is scarcely ever used, and they are grouped with the depressive psychoses without any question. An example here would be superfluous.

Thus a certain order becomes apparent in this confused subject, and one is in a position to sum up the conclusions. Affective states, showing either the predominance of anxiety or depression, fall into two groups, the neuroses and the psychoses. This differentiation is valid and useful when it is made, with due reservations, upon the grounds discussed. The psychoses, whether mainly anxious or depressed, are generally termed depressions. The neuroses, on the other hand, have frequently been termed anxiety states. It would be better perhaps to call them affective neuroses, or, if it proved useful, they might be sub-divided into anxiety and depressive neuroses. In any case the question as to whether anxiety states should be differentiated from depressions now loses much of its meaning, and must be reformulated. If this is done it may properly be said that the affective neuroses can be distinguished from the affective psychoses.

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OBSERVATIONS ON THE AUTONOMIC FUNCTIONS DURING THE HYPOGLYCAEMIC TREATMENT OF SCHIZOPHRENICS.

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THE nature of the action of insulin in producing cure in cases of schizophrenia is still quite obscure. One of the most striking features of insulin hypoglycaemia is the occurrence of phenomena pointing to disturbance of the autonomic nervous system, and many authors on this subject have expressed the belief that insulin produces cure by virtue of its action on the autonomic nervous system. There is, however, extensive contradiction in the literature as to what actually are the changes which take place in autonomic functions during hypoglycaemia. Some authors say that hypoglycaemia produces a generalized sympathetic stimulation, some say a generalized parasympathetic activity and others that there is dissociation of action of the two systems. Sakel (1) appears to believe that hypoglycaemia produces a vagotonia which underlies the curative effects of his treatment; Hadorn (2), that small doses of insulin stimulate the vagus, and large doses cause a primary secretion of adrenaline; Beno (3), that changes on the vegetative system cannot be sufficient to allow a reasonable understanding of the results; Pfister (4), that hypoglycaemia produces beneficial effects in schizophrenia because it damps the sympathetic; Wespi (5), that dissociation appears to prevail in the autonomic regulation; Gellhorn (6), that the treatment is successful because it leads to excitation of the sympathetico-adrenal apparatus through hypoglycaemia of the brain; and lastly, Heilbrunn (7), that his experiments are in favour of a sympatheticotonia.

Owing to the great diversity of opinions which was noticed to exist on the question of the autonomic functions during hypoglycaemia, a special study of this subject was made in the present series of cases, with three objects in view:

(1) If possible, to discover what really were the changes occurring in the autonomic nervous system during hypoglycaemia.

(2) If possible, to account for the diversity of opinions on the subject.

(3) To consider whether autonomic changes had any relation to the improvement which might result in the patients treated.

My investigations consisted of the following observations on patients in

hypoglycaemia, from the time of the injection of insulin to the time of recovery from the hypoglycaemic state :—

(1) Changes of pupil size, and measurements of these.

(2) Pulse-rate behaviour, and its relation to pupil size.

(3) Blood-pressure behaviour, and its relation to pupil size.

(4) The relation of the hypoglycaemic phenomena of perspiration and salivation, to pupil size.

My observations of the pupil size were extensive, and included well over five hundred actual measurements apart from additional repeated observations. These measurements and observations were made in the following manner:

Metal cages were constructed which could be fitted to the head of any of the ward beds. Round these cages dull black cloth was fitted such that an observer inside this cage could watch a patient's pupils with all external light excluded. In order to minimize the effect of the light reflex a constant light was used for all the measurements. This consisted of a 15-watt bulb in an inspection bracket wrapped in several thicknesses of yellow tissue paper. This lamp was fixed on the metal framework at a given point and the patient was always placed so that his observed eye was the same distance from the lamp. This light was just sufficient to permit observation of the pupil and consequently allowed dilatation of the normal pupil to about the mid-size position (6·5–8·0 mm.).

The effect of accommodation was minimized by getting the waking patient to look towards the roof of the cage apparatus. Measurements in coma were taken as far as possible when the eyes were in the same position. Measurements were made at irregular times in order to observe the pupils at all stages of the hypoglycaemia from before the injection to recovery of consciousness.

Before describing these readings and their significance, it is as well to recall that there are two types of hypoglycaemic reaction—the wet and the dry. In the former the patient perspires and salivates freely, while in the latter, perspiration and salivation are slight or absent and the patient is liable to develop either myoclonic muscular contractions which may progress to a fit, or develop a fit without any such warning. Previous authors all tend to draw a hard and fast line between these two types, but, as will be shown later, there are in fact all gradations between the two types.

Changes in the First Stage of Hypoglycaemia.

Soon after commencing these investigations into pupil behaviour a very likely cause for many of the discrepancies in the opinions of different authors was discovered, and this will now be described.

In every patient as hypoglycaemia progresses the pupils become markedly smaller. Measurable difference occurs from 1–1½ hours after injection of the

insulin and then persists until the second stage of the hypoglycaemia described later. This constriction of the pupils however is not at once apparent, for the following reason: The pupils are in a condition of great instability at this stage and the slightest stimulus causes a rapid dilatation of the pupil. This dilatation occurs after a latent period of 1–2 seconds, and then continues slowly for 3–5 seconds after the disturbing stimulus has ceased; it is therefore not a pure nerve reflex. If there is no repetition of the stimulus, the pupils return slowly and progressively to their previously contracted state within 30–60 seconds, and they *remain* in this state so long as the patient is undisturbed and he himself does not move. This state of small pupils is more marked in patients who are perspiring freely, but the dilatation on stimulation is present, though less marked than in the patients who remain dry.

Almost any stimulus causes this dilatation, e.g. touching the patient, speaking to the patient, spontaneous movement of the patient or a noise, even some distance away. In particular it must be noticed that approaching the patient's bed, sitting on the bed, taking the pulse, all cause this rapid dilatation of the pupils.

Analogous changes occur in the pulse rate during this stage. The pupil dilatation is accompanied by a marked increase of pulse rate, from six to fifteen beats per minute. It is obvious therefore that any reading of pupil size or of pulse rate which neglects this fact is entirely erroneous; in order to find their level in a quiet resting state, time must be allowed for the patient to settle. Evidently the effect of a disturbance which would normally produce little change is greatly increased in patients in hypoglycaemia. As will be shown later both the pupil and pulse responses to disturbing stimuli persist during the greater part of the hypoglycaemic process. This is at least one possible reason why sometimes authors have described a fast pulse and sometimes a slow one. Since the patients are for the most part lying quiet and undisturbed, it is the quiet resting pulse and pupil size which represent their true state. If the observer remains with the patient for some time the disturbing effect of his presence soon passes, and it is then seen that the pupils remain small and the pulse slow so long as there is no further disturbance.

In order to get a true pupil reading it is necessary to adopt a special technique. The observer sits beneath the tent formed by the black cloth draped on the metal cage as described earlier; he then rests his hand on the patient's forehead so that with his forefinger he can raise the upper lid and observe the pupil without disturbing the patient. At first the pupil will probably be dilated, but some seconds later it returns to its contracted state, and remains in this condition unless there is extraneous ward disturbance. The question now arises as to what is the cause of the contracted pupils and the mechanism of the dilatation. Sleep is not responsible for the contraction of the pupils for the following reasons:

(1) Although the small pupils are to be seen at this stage when the patient

is drowsy, they are frequently seen at the same stage when the patient is fully awake.

(2) While the pupils are still small, the patient will reply immediately to a question, and if requested he will often keep his eyes open for the observations to be made. The patient may be asked to move himself in order to get his eyes in the right position for observation, dilatation being induced by this disturbance, yet sixty seconds later the pupils are contracted, although the patient is not yet asleep.

(3) Small pupils which dilate in the presence of disturbing stimuli may be found also when the patient can no longer be roused and is in deep coma.

From these facts it is inferred that the contracted pupils at this stage are directly dependent on the hypoglycaemia, and that their dilatation on slight disturbance of the patient is not simply a matter of rousing him from a drowsy condition.

Most probably the dilatation on stimulus is due to the reflex liberation of adrenaline into the blood stream. This appears to be so because—

(1) It is known (Cannon and Britton, *Amer. Journ. Physiol.*, 1927) that hypoglycaemia stimulates the liberation of adrenaline into the blood stream.

(2) The latent period of 1–2 seconds between stimulus and dilatation corresponds with the time it would take for adrenaline to reach the pupil from the suprarenal glands. This latent period is so long as to exclude a purely nervous reflex mechanism (i.e. either direct sympathetic stimulation or parasympathetic inhibition).

(3) The dilatation continues steadily and progressively for some seconds after the cessation of the stimulus and then steadily declines. (This also excludes a purely nervous reflex.)

(4) Successive slight stimuli, such as repeated light taps at about 3-second intervals, cause successive waves of dilatation with a latent period after each stimulus.

(5) The dilatation is accompanied by a rise of pulse rate, often of considerable degree.

(6) A paradoxical reaction to light may frequently be seen at this stage. If a patient is lying quiet with his pupils contracted and a light is shone on the pupil, immediate further contraction occurs, but is followed in 1–2 seconds by dilatation, although the light is kept shining on the pupil. The probable explanation of this is that the immediate nervous reflex due to light contracts the pupil, but the disturbance causes a liberation of adrenaline into the blood and overcomes the effect of light reflex.

It would now appear from the observations of the pupils and of the pulse rate, that at this stage of hypoglycaemia the autonomic nervous system is in the following state: whilst the patient is completely quiet, there is predominant parasympathetic tone (indicated by the small pupils), but at the same time the sympathetico-adrenaline response mechanism is in a state of

hyper-excitability, and the slightest stimulus causes a liberation of adrenaline, which converts the previous parasympathetic tone into a predominant sympathetic tone. It appears that the adrenaline *overcomes* the parasympathetic tone because there is a latent period between stimulus and dilatation, whereas if there was a reflex parasympathetic inhibition the dilatation would be immediate.

The fact that the sympathetic is very active at this stage (in spite of the apparent parasympathetic tone in the pupils) is also suggested by the fact that there is no fall of blood pressure when the patient is lifted *without any exertion on his part* to a sitting position with his legs dependent over the edge of the bed; there is in fact nearly always a rise of pressure. This rise involves both systolic and diastolic pressures, but that of the diastolic is the most marked and constant, The systolic pressure tends to become augmented towards the end of this stage, the diastolic to fall, leading to an increase of pulse pressure.

In considering these blood-pressure readings it should be remembered, from what has been said previously, that disturbance of the patient probably causes these records to be higher than the actual resting values. These blood-pressure readings are always accompanied by pupil dilatation. It may be seen from these remarks that in the experiment mentioned above where the patient is lifted to a sitting position, the initial blood pressure taken with the patient in the horizontal posture is probably already rather high, owing to the disturbance, yet a further rise occurs on sitting the patient up.

It is known (Cannon) that in hypoglycaemia there is early stimulation of at least one part of the sympathetic nervous system, i.e. the supply to the liver, and later adrenaline is secreted from the adrenals. It is curious therefore that in these patients at this stage of hypoglycaemia there appears from pupil observation to be a predominant parasympathetic tone. It has however been shown that at this very time the sympathetico-adrenal mechanism is in a state of hyperexcitability, and the least disturbance of the patient converts the picture of apparent parasympathetic tone with small pupils to one of apparent sympathetic tone with dilatation of the pupils and increased pulse rate; this soon settles and reverts again to the parasympathetic picture as the patient becomes quiet.

It seems probable that at this stage of hypoglycaemia both sides of the autonomic nervous system are in a state of increased excitability and raised above their normal level of tone.

Changes in the Second Stage of Hypoglycaemia.

In the second and next stage of hypoglycaemia, which commences 1½–2 hours after the injection of a dose designed to bring on coma in about 2½–3½ hours, we notice definite changes both in the patient and in the pupil and pulse reactions. At this stage the patient who has previously tended to

drowsiness becomes less so; he first becomes more wakeful, and in almost every case restless to some degree. This restlessness varies from a very slight amount or complete absence to actual furor. At this stage, also, convulsive myoclonic movements of the limbs or epileptiform fits may occur. The myoclonic movements may subside, or may progress in increasing severity until they end in a fit. This would indicate that a study of these myoclonic movements is also a study of the basis of the fit.

During this second stage of the hypoglycaemic process we see different pupil reactions in different patients; each patient tends to react in the same manner each day. (This is contrary to the findings of Hans Wespi (5), which may be explained by the fact that he apparently neglects the tendency of disturbing the patient to cause dilatation of the pupil.) The following are the types of pupil behaviour met with at this stage:

(1) Where the patient perspires freely from early morning, shows no restlessness, but sinks gradually and quietly into coma, soon beginning to salivate. Here, rarely, the pupils remain contracted throughout the whole period, though they still dilate on stimulation. More usually they dilate somewhat (but not always to their normal conscious size) for about half an hour before the onset of coma; they then contract as coma progresses. Throughout this period of dilatation, and more particularly at the beginning and end of it, there may be alternate phases of contraction and dilatation. During this stage the pulse remains slow where the pupils remain contracted; where the pupils widen there may be some pulse acceleration.

(2) The patient may become quite restless for at least half an hour before coma supervenes. This is the most usual occurrence in this second stage of hypoglycaemia. Here the pupils become dilated and dilatation in response to slight stimulus is very active (that is to say, the already dilated pupils dilate still further on slight disturbance of the patient after a latent period of 1–2 seconds). As coma supervenes the pupils contract again and become very small. The pulse follows a similar trend to the pupil size, that is to say, it quickens during the time of pupil dilatation and then slows during coma. The pulse most typically commences to increase before the onset of pupil dilatation and before any obvious change is seen in the patient, and does not slow until after the pupils have been contracted some little time. This restless stage may sometimes persist for as much as an hour.

(3) The patient becomes extremely restless and excited, and may attempt to rush about the room, to sing and to shout. Here, though of course the pupils cannot be measured they are seen to be widely dilated even in the light, and often a state of hippus (alternate dilatation and contraction of the pupil) is seen. Eventually coma occurs and the pupils contract. They still dilate on stimulation of the patient. The pulse is augmented before and during the restless period, and after remaining high for some time following the onset of coma, settles to a lower rate.

(4) The patient, who has previously been drowsy, awakens. The pupils dilate and the pulse increases; soon afterwards myoclonic convulsive movements commence and gradually increase in severity. The pupil changes are as follows:

(*a*) Dilatation (though often not to normal conscious size) of the previously small pupils, before the onset of myoclonus.

(*b*) Myoclonic movements commence and the pupils show—

(i) Fluctuation (hippus) before each separate myoclonic contraction.

(ii) A wave of dilatation follows each myoclonic contraction by a latent period of 1–2 seconds.

(iii) Stimulation of the patient, e.g. by touching him, or by making a noise near him, causes a myoclonic contraction within a fraction of a second, presumably due to a spread nervous reflex similar to that seen in strychnine poisoning. This contraction causes a wave of dilatation of the pupil after a latent period of 1–2 seconds.

(iv) A paradoxical reaction to light may occur, i.e. after initial contraction a wide dilatation occurs.

(v) As myoclonus progresses fluctuation continues but the average size of the pupils increases.

(vi) Temporary lulls in the myoclonus may appear, and during these the pupils may contract to small size.

After the onset of myoclonus two things may happen:

(i) The myoclonus becomes progressively more severe, finally ending in a fit.

(ii) The myoclonus gradually declines and finally settles, the patient becoming comatose. As the myoclonus commences to settle, the patient, who previously was dry, begins to salivate and perspires freely, and the pupils contract. Eventually the patient settles into a typical wet coma with small pupils.

Note.—A stage of myoclonus with wide pupils may persist for over an hour and ultimately settle.

(5) A fifth type of reaction during this second stage of hypoglycaemia is the occurrence of a fit without any warning.

A fit may occur (i) without warning;

(ii) following myoclonus.

In either case the pupil changes are similar. It is not often possible to observe the pupils before the sudden type of fit, but I have chanced at times to have made pupil readings, a fit supervening some minutes later. In all such cases the pupils have been dilated before the fit. In the case of fits following myoclonus the pupils are always dilated before the fit. During the seizure there is invariably pupil dilatation, followed immediately at the cessation of the convulsion by contraction to small size. Previous to the fit the patient is nearly always dry; after the fit there is sweating, salivation and flushing of the

skin. Following the contraction of the pupil, which lasts 1–2 minutes, the pupils become unstable; they dilate on stimulation of the patient after the usual latent period, the stimulus often causing a further convulsive movement; they may show hippus; they may show parodoxical reaction to light.

(6) A further type of reaction may be met with during this second stage. The patient may be restless or have persistent myoclonus. The pupils remain dilated and the pulse rapid. The patient does not perspire or salivate. If on subsequent days the dose of insulin is increased in the hope of producing coma, the patient either develops a fit or, after a protracted restless period, sinks into too deep a coma from which he cannot be roused easily. Such patients can only be got into a normal quiet wet coma with the aid of sedatives such as luminal. If luminal is given the restlessness and myoclonus are of only normal proportions, and a comparatively small dose of insulin is sufficient to produce a coma, and this coma is normal in depth. The pupils become small and remain so.

In all the above six types of reaction the pulse corresponds with the pupil behaviour, that is to say it quickens when the pupils dilate and slows when they contract. Usually however the acceleration precedes the dilatation and the pulse remains increased a little while after the pupils contract, but eventually slows. During myoclonus the pulse increases very considerably and is a fairly exact measure of the severity of the myoclonus. After a fit the pulse is frequently 120–130 per minute. It is an important factor that the pulse accelerates and pupils dilate *some time before* the onset of the myoclonus or fits.

Patients who have little or no restless period or myoclonus perspire and salivate early and profusely. Restless patients may perspire, due presumably to the exertion, but do not salivate until the onset of coma. Myoclonic patients, and particularly patients liable to fits, usually remain fairly dry until the myoclonus settles or the fit occurs.

There is little account in the literature of the effects of drugs acting on the autonomic nervous system on patients in hypoglycaemia. In this series of cases atropine, acetylcholine and pilocarpine were tried on numerous occasions. During the second stage of hypoglycaemia atropine causes—

(i) In patients who are normally fairly quiet at this stage a great increase in restlessness and sometimes myoclonus; the patient is dry (as would be expected) instead of wet as usual; the pulse increases to a greater degree than in patients given atropine without insulin.

(ii) In patients who are inclined to myoclonus atropine invariably causes great increase in the severity of the myoclonus, such that a fit seems imminent. (I have never allowed a fit to develop in these cases, because the pulse normally accelerates greatly in a fit, and it might be unsafe to permit a fit to occur with the inhibiting action of the parasympathetic impeded by atropine.) In considering these effects the central stimulating action of atropine must be borne in mind.

Acetylcholine and pilocarpine, on the other hand, tend to produce quiet wet comas. In the myoclonic type of patient they either abolish, reduce the severity of or considerably delay the onset of myoclonus, and allow it to settle and wet coma to develop. This action did not occur quite so invariably as the atropine reaction; this may be due to the fact that these latter drugs, especially acetylcholine, are rapidly destroyed in the body. There was little doubt, however, that there was a tendency for acetylcholine and pilocarpine to lessen the severity and frequency of myoclonus, and a very definite tendency of atropine to increase the degree and frequency of myoclonus. There was also with atropine a greater acceleration of the pulse in hypoglycaemia than in patients given atropine without insulin.

During this second stage the systolic blood pressure is usually augmented, but the diastolic lowered with resulting increase of pulse pressure. Capillary pulsation may sometimes be seen on examination of the lips or nails.

To summarize the observations made during this second stage we see there is nearly always some relative pupil dilatation and increased pulse rate compared with the first stage of hypoglycaemia. According to Cannon, adrenaline is secreted first at a blood-sugar level of 70 mgm. According to Georgi, no signs of excitement occur until below a blood-sugar level of 60 mgm. If these observations are correct, this stage follows the liberation of adrenaline into the blood stream. The pupil changes as well as those of the pulse rate suggest that adrenaline is being constantly poured into the blood stream at this time, and is overcoming a previous parasympathetic tone, because—

(i) In many cases although the pupils dilate from their earlier small size, they often do not go as wide as their normal conscious size. This is in the quiet type of patient.

(ii) Fluctuation of the pupils between wide and small extremes is very common at this stage and gives the appearance of bursts of adrenaline overcoming a parasympathetic tone in the pupils. This state of hippus is always present during myoclonus between the spasms, and in addition waves of dilatation follow separate clonic movements after a latent period of 1–2 seconds ; this excludes a reflex parasympathetic inhibition or a purely sympathetic nervous reflex.

(iii) As soon as the restless or myoclonic patient of this stage quietens and the stage of coma supervenes, the pupils return to a small size similar to stage I. Also in calm phases between restless or myoclonic bouts, the pupils may revert to a contracted condition.

(iv) The experiments with drugs described above rather support this view.

The observations recorded suggest that this second stage is characterized by sympathetic predominance, but there is some evidence that this overcomes a previous parasympathetic predominance, and consequently, that both systems are acting at a level of increased tone.

It may be mentioned here that if a dose just below a full coma dose is

given the restless and myoclonic stage is much prolonged, and the patient remains with dilated pupils and fast pulse for the majority of the hypoglycaemic process. This effect can be increased in patients who are normally restless, and often induced in patients who are normally quiet, by the administration of atropine (gr. $\frac{1}{60}$). From what has been said previously, it may be inferred that by these means the patient is kept in a state of sympathetic excitation for the majority of the time. Sakel suggests that patients with catatonic stupor should be interrupted in the excitation preceding coma. It seems, however, that it is *not* so much the *interruption* that is important as striving to *keep* the patient in *this condition* for as long as possible. In patients who are excited during the day apart from treatment the reverse is true; in these types the excited stage should be cut as short as possible by large doses of insulin, and production of early coma aided by sedatives such as luminal. Sakel believes that the patient tends to stay in the state in which he is interrupted, but in my experience the length of the excited or the quiet phases is more important than the interruption.

There is wide difference in the degree of restlessness which develops in different patients. This may in part be due to variation of the effects of gradual removal of the cerebral cortical inhibition of lower centres, but it also appears to be due to differences in the store of, and rate of liberation of, sugar from the liver, because—

(i) Restlessness is always greater in the first few coma days of treatment. This suggests that there is gradual reduction of liver glycogen.

(ii) Prolonged restlessness has sometimes occurred in my patients when it has been subsequently found that they were obtaining sweet and cakes surreptitiously during the afternoons.

(iii) After vigorous exercise the previous day (e.g. a game of football) the patients enter coma much more quietly.

Similar factors may be responsible for the occurrence of myoclonus and fits in some patients and not in others.

It was thought that the response of blood-sugar increase on injection of adrenaline might show differences common to the restless types and quiet types respectively. Several blood-sugar curves produced in this way failed to justify my hopes in this respect however. Possibly local vessel constriction at the site of injection varies its absorption on different occasions. The routine blood-sugar tolerance curves also give little help in this respect.

It is a common practice in many hospitals to allay the restless, and more especially the myoclonic, periods with luminal. Experience of this series of cases suggests that patients who, without luminal, have long myoclonic phases, improve well. It would seem that the use of luminal in such cases is often inadvisable.

Changes in the Coma Stage.

During the third and next stage in which the patient enters coma (indicated by extensor plantar reflexes) the following changes may be seen:

(i) The patient salivates and perspires profusely, the pulse slows, often to a very slow rate, the pupils contract below normal size, and often to pin-point, but they still dilate on slight disturbance.

(ii) After severe restlessness or prolonged myoclonus, it is some time before the pupils become very small and the pulse slows, but they eventually do so. In all cases salivation and perspiration increase markedly during this stage.

(iii) Shivering may occur, and is accompanied by pupil dilatation and increased pulse rate.

(iv) Short periods of lighter coma with muscle straining, increased pulse rate, and pupil dilatation.

During this third stage the blood pressure still shows no fall when the patient is lifted against gravity, even though the diastolic pressure is lower than normal.

At this stage the appearances suggest predominance of parasympathetic tone. The pupils are contracted, the pulse slow and often there is bradycardia; there is profuse salivation, perspiration is free (probably due to vessel dilatation in the skin), the diastolic pressure is low and capillary pulsation may be seen.

Certain phenomena, however, suggest there is no depression of sympathetic activity; the pupils still dilate, after a latent period of one to two seconds, on the stimulus of slight disturbance of the patient (e.g. touching the patient, or a noise near him); the blood pressure shows no fall and the pulse increases, when the patient is lifted against gravity; temporary periods of lighter coma occur with pupil dilatation and increased pulse; shivering causes pupil dilatation; these facts indicate that the sympathetic is still active and can at times overcome the predominant parasympathetic tone.

Apparently at this stage there is parasympathetic predominance, but some evidence that both systems are working at a heightened level of activity.

This stage passes gradually to the fourth stage of very deep coma, with absent corneal reflexes and even light reflex. In this stage the pupils are contracted, though often not so markedly as in the first and third stages. The pulse usually shows a slow rate. Salivation and perspiration are extremely profuse. The blood pressure falls on sitting and the pupils no longer dilate on disturbance of the patient. Even at this stage there may be—

(i) Shivering with some pupil dilatation.

(ii) Short periods of lighter coma, possibly due to late adrenaline effects.

At this stage there appears to be definite parasympathetic predominance. This stage is of short duration (half to one hour) relative to the whole of the

hypoglycaemic period of about five hours. By no means every patient is taken to this stage, for example :

(i) Patients who develop fits (which usually occur early).

(ii) Patients who are allowed to continue with long myoclonic periods instead of being precipitated into coma by the aid of luminal.

(iii) Patients who are deliberately interrupted—

(*a*) In the calm phase before coma.

(*b*) In the excited phase before coma.

(iv) A large number of patients who are recovering well with light comas only.

Changes after Recovery from Coma.

When the patient is waking after receiving his glucose, the pupils are unstable, they may show fluctuation, and they dilate on disturbance of the patient.

It has been found here that during the afternoon the pulse rate is usually high, especially before the patients have tea. This seems probably to be due to the fact that there is some degree of hypoglycaemia, as is indicated by the fact that relapses into coma can occur during this time. Evidently this hypoglycaemia plus the simple exercise of sitting up leads to an increased pulse rate. This is not surprising in view of the marked increase of pulse on slight disturbance which occurs during the actual hypoglycaemic treatment.

If adrenaline is injected intravenously into a normal animal there is only a short rise of blood pressure and the pulse is reflexly slowed, owing to vagal action. It seems possible that during hypoglycaemia excess adrenaline is liberated into the blood in an endeavour to increase the output of sugar from the liver. Elsewhere in the body the peripheral adrenaline effects are unwanted (as opposed to when adrenaline is liberated during exercise), and possibly parasympathetic action is called into play to counterbalance these peripheral adrenaline effects. If such a view is correct both sides of the autonomic nervous system are functioning at an increased level of tone.

Summary and Discussion.

(1) The first object of the foregoing observations was, if possible, to discover what really were the changes occurring in the autonomic nervous system during hypoglycaemia.

The observations indicate that there can be no question of predominant tone of one or other of the two sides of the autonomic system throughout the whole of the hypoglycaemic period, but there is in fact oscillation between

these two states. When there is prevalent tone of either system, this seems to be due to increased activity of that system rather than diminished tone of the other. Thus during a typical coma there is first a period of apparent parasympathetic tone, then in the second stage a period of predominant sympathetic tone, followed in the third stage of coma by a further period of parasympathetic tone, lasting until the termination of coma. Throughout this period, except late in coma, the pupils dilate rapidly on slight disturbance of the patient, and this appears to be due to adrenaline, which converts the previous parasympathetic tone into one of sympathetic tone. This indicates that even when there appears to be parasympathetic prevalence the sympathetico-adrenal system is reflexly hyper-excitable. Conversely, during the restless and excited and also in the myoclonic stage, when there appears to be a state of sympathetic excitement, there is a constant tendency for the pupil to return to a contracted state ; the fluctuation (hippus) which is common, and in the case of myoclonus always present, in this stage, suggests an oscillation between sympathetic and parasympathetic action. This is also supported by the fact that where alternate restless or myoclonic and quiet phases happen, the pupils, which are dilated in the excited phases, often contract to small size in the periods of calm. When the restlessness or myoclonus eventually settles and coma supervenes, the pupils are small, there is profuse salivation and ultimately slow pulse, all indicating that the parasympathetic tone is due to increased activity of that system rather than inhibited sympathetic action. This is especially so since the pupils usually still dilate on disturbance of the patient, showing there is no exhaustion of the sympathetic.

(2) The second object of these observations was, if possible, to account for the diversity of opinions on this subject.

The diversity of views seems fairly easy to understand in the light of these observations, because both the pictures of sympatheticotonia and of parasympatheticotonia may occur during the hypoglycaemic state. In addition, slight disturbance of the patient may change the picture and cause the fundamental quiet state of the patient to be overlooked. A further point is that where the hospital ward is very quiet the parasympathetic picture will tend to be more frequently observed, but so sensitive are these patients' sympathetico-adrenaline systems to noise, that if the ward is not completely free from either inside or outside disturbance the sympathetic picture will be more often seen. This may explain why some workers have found a rapid pulse the rule, and some a slow pulse most common.

(3) The third object was to consider whether the autonomic changes in hypoglycaemia had any relation to improvement of the patients treated.

In this connection it is interesting to note that recovery has occurred both in cases whose hypoglycaemic reaction appears to have been chiefly of the sympathetic type, and in those whose reaction has appeared to be chiefly of the parasympathetic type. Some cases have repeatedly had quiet wet comas,

some have had long myoclonic spells with dilated pupils and rapid pulse, some have had repeated fits, others have been deliberately and constantly interrupted in the excited stage, and others in the calm stage before coma; in all types of cases there have been some recoveries. From these facts we must conclude either—

(*a*) That autonomic functions play no part in the cure of these cases. This is difficult to believe when one considers that the cardinal symptom of schizophrenia is apathy. There seems to be a diminution of the emotional response mechanism, a body function with which the autonomic nervous system is intimately concerned. Furthermore one of the most striking phenomena of insulin hypoglycaemia is the occurrence of emotional disturbance just before and on recovering from coma; this disturbance may be weeping or anxiety, but most commonly is euphoria. In addition some authors, such as Pfister (9) and Singer (10), have shown that in schizophrenia there is dysfunction of the autonomic system.

(*b*) *Or*, we must conclude that in schizophrenia one side of the autonomic nervous system is depressed, and insulin, since it stimulates both systems, increases the activity of the depressed system.

(*c*) *Or*, we must conclude that in schizophrenia there is impaired function of the autonomic system as a whole, and insulin by stimulating both sides of this system restores its normal balance. If autonomic changes do play a part in the beneficial effects of this treatment, it is this last-mentioned view which is likely to be the correct one.

It has been mentioned that a patient who is in the stage of apparent sympathetic excitement is liable to myoclonus and fits, and that at this stage slight disturbance is liable to cause immediate myoclonic contractions, and often a fit, apparently due to a spread-over reflex. This apparent ease of reflex spread at such times is interesting. because in schizophrenia there so often seems to be behaviour suggesting that the introverted thought processes of the patient are partially blocked from, and do not readily associate with, his other nervous pathways. Does an increased ease of association, produced during this stage of apparent sympathetic excitement, extend also to cerebral processes and persist when the hypoglycaemic state is recovered from? Is this why catatonic and stuporose patients sometimes improve when interrupted in this stage of hypoglycaemia, or after myoclonus or fits (however produced)?

Finally it must be mentioned that the autonomic nervous system is intimately bound up with the functions of the endocrine system and also the hypothalamic region. The autonomic changes in hypoglycaemia may merely be significant of disturbance of hypothalamic and endocrine functions.

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CONVULSION THERAPY BY AMMONIUM CHLORIDE.

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IT is generally agreed that there are many objections to the use of cardiazol and azoman (triazol) as convulsants. The treatment is generally disliked and the injections are attended by much apprehension. There is frequently amnesia, though usually of a temporary nature. There may be some actual damage to the brain, fractures are not infrequent, and other complications sometimes occur. Old tuberculous lesions have been reactivated and deaths have occurred in *status epilepticus* from the use of azoman.

For these reasons much interest is attached to the description by Bertolani (1938) of the production of epileptiform convulsions by the intravenous injection of a solution of ammonium chloride. He believes that the irritant effect of the solution on the walls of the blood vessels causes an acute vaso-motor action. Good clinical results are stated to have been obtained in cases of schizophrenia by the use of this drug.

Mazza (1938) treated 27 acute cases of schizophrenia in this way. 22 per cent. showed a complete remission, 15 per cent. a marked improvement, and 63 per cent. were unaffected. The number of convulsions given varied from 4 to 19.

It was hoped that in ammonium chloride a drug had been found which would avoid some of the ill-effects associated with the other convulsants and give comparable clinical results. Although the drug fulfils neither of these wishes completely, it appears that it may still be considered as a useful accessory in this form of treatment.

The following investigations were nearly all made on female patients. No sedatives are given in the previous twelve hours, the bowels are opened on the morning of treatment and breakfast is withheld.

The same procedure for avoiding fractures and dislocations is used as in other convulsions, except that the jaw need not be held and no gag is necessary. The patient wears nothing but knickers. The bedclothes are completely removed in the period of hyperpnoea and only replaced after the convulsions cease. A hard pillow is used and the patient lies flat on her back before the

injection is given. No one touches her during the convulsions, and if there is any likelihood of her falling from the bed, all that is done is to raise the edge of the sheet. The writer is in agreement with Good (1940) in believing that certain of the recorded dislocations and fractures of the limbs are due to restraint of the patient and not to the convulsions.

Ten c.c. of a 5 per cent. solution of pure ammonium chloride are given through a large needle as rapidly as possible. A No. 10 needle has been used on the easier and a No. 12 on the more difficult veins, with little difference in the results. If a vein in the ante-cubital fossa be used, the forearm must be rapidly flexed and extended a number of times directly following the injection to avoid thrombosis. If the vein is lost there is pain of a smarting or burning character. Occasionally the patient complains of cramp or a feeling of uselessness in the arm, which disappears on further movement. The blood does not coagulate and may be aspirated into the syringe.

The Fit.

There are four stages to the fit, which may be termed (1) preliminary, (2) hyperpnoeic, (3) convulsive, (4) recovery.

(1) In about five seconds after the injection the patient sometimes complains that she is "going off," and may become rather red about the face. She is in a state of apprehension, often screws her eyes up or clutches at the bedclothes. There is no cough. One patient complained of a bitter taste before she lost consciousness.

(2) Ten to 20 seconds after the injection there is hyperpnoea and a simultaneous dilatation of the pupils with a deviation of the head and eyes. The pupils do not react to light and they are often oval and eccentric. The corneal reflex is lost. There may be a lace-like blotching about the neck and upper chest, as is seen with cardiazol. The face may be slightly congested, sometimes with circum-oral pallor. The rather objectionable odour noticed with the other convulsive drugs is absent. This stage lasts from 10 to 20 seconds.

(3) The hyperpnoea and head deviation are suddenly replaced by convulsive movements, varying largely in degree, but never approaching the severity of those seen with cardiazol or azoman. In the mildest form there has been a twitching of the muscles about the lower jaw, but there may be choreiform movements of the hands and forearms. Usually there is abduction of the arms, movement of the forearms and hands, and an accompanying flexion and extension or twitching of the legs. In the severest form the body has been thrown into the position of stretching with extension of the legs and spine, and abduction of the arms with flexion of the forearms. In some cases this has been followed by relaxation and repetition of the contractions, ending with a localized clonus of the legs. The pupils return to normal at the beginning

of this stage, and the eyes are no longer deviated. There is no cyanosis, but sometimes pallor. Incontinence of the urine or faeces has not occurred. In the male there is no seminal emission. This stage lasts 10 to 20 seconds, then consciousness is regained before the muscular movements have ceased.

(4) The position in which the convulsion ends is maintained for two or three seconds; the conduct is then variable. In many cases there is an attempt to sit up or to get out of bed, and usually there is bewilderment. The patient asks such questions as "Where am I?" "What are you doing?" or "What is the matter?" Two used to regain consciousness with a beatific smile, and in several an erotic phase followed the convulsions. Mild confusion is not infrequent, but some patients become quite rational for perhaps half a minute before gradually fading into their abnormal mental state. Sometimes there is uncontrolled weeping, which is often amenable to suggestion. Increased suggestibility is one of the characteristics of this stage and many patients may even be persuaded to agree that they have never felt better.

The patients' descriptions of the fits are interesting. Many describe something going up their arms and a sensation of blackness or emptiness. The following are typical accounts: "It went along my arm to my head and down my legs"; "It goes to my chest and up to my throat"; "When I said 'Where am I?' I was seeing stars as if atoms were splitting." After a mild convulsion another said, "I didn't go off; it made my legs shiver, but it felt like peace on earth." Two or three have had the sensation of seeing colours as they lost consciousness.

In five or ten minutes they are well enough to sit up and have lunch and many can get up soon afterwards. Nausea is rare, there has been no vomiting and headaches are infrequent. The patients who had previously had cardiazol or azoman without exception preferred the ammonium chloride.

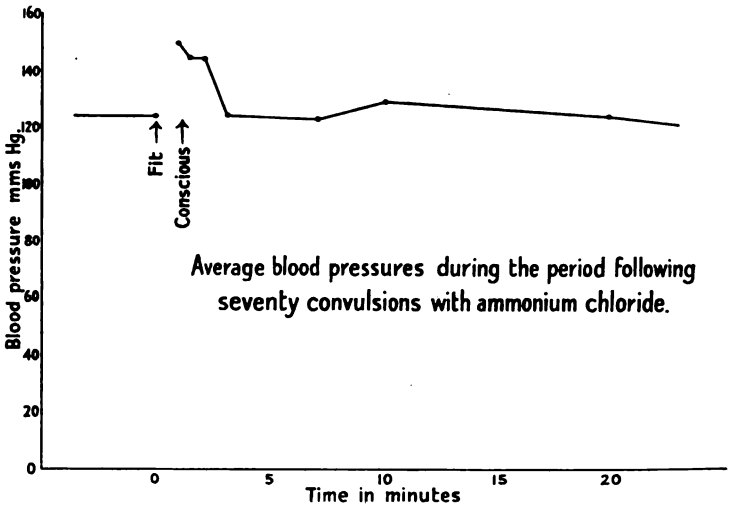
Observations.

Blood pressure.—The blood pressure is raised following the convulsions, but usually falls again within three minutes. An hour later it is often less than it was 20 to 30 minutes before the injection, but the state of expectation may make this latter reading higher than normal. The curve shows the compounded readings for a series of 70 observations on the systolic blood pressure. The diastolic pressure rarely rises by more than 10–15 mm. Hg and is sometimes unchanged.

The rise in systolic blood pressure is not more than half that usually observed with azoman or cardiazol, but since a corresponding number of readings have not been made on the same patients no curves are drawn for comparison. The temporary fall which often occurs immediately after the clonic contractions of the cardiazol (Guttmann and Reitmann, 1939) and azoman fits was never observed with ammonium chloride. With cardiazol the pressure an hour

after the convulsion was sometimes observed to be higher than the initial reading, but with azoman it fell as with ammonium chloride. In electrically induced convulsions there is a rise of systolic blood pressure immediately after the fit by 50–60 mm. Hg, and a fall to normal within 30 minutes; in this case also, the diastolic pressure does not rise by more than 10–15 mm. Hg (Kalinowsky, 1940).

Pulse rate.—The pulse rate may increase to as much as 180 during the fit, but it usually settles within three minutes after the convulsions have ended. Irregularity has not been observed.



Average blood pressures during the period following seventy convulsions with ammonium chloride.

Pupillary reactions.—The pupillary dilatation is often oval and eccentric, which is the type of reaction obtained in a positive Loewi's eye sign. For this reason adrenaline was dropped into one eye before, during or after the fit on a number of occasions. The pupil on this side was sometimes observed to be more sluggish in its reaction to light, or to remain dilated longer than the other; on several occasions its oval dilatation and eccentricity has been maintained for more than an hour.

Reflexes.—The reflexes are brisk directly after the fit. There is usually a flexor plantar response; once or twice there has been a dubious extensor reaction.

The urine.—Several 30-gr. doses of ammonium chloride are usually given by the mouth to acidify the urine. The single intravenous dose is only about $7\frac{3}{4}$ gr., and thus little change in urinary reaction would be expected. The muscular exercise and hyperpnoea are probably the main factors in influencing the reaction of the urine passed after the fit.

The average pH values before and after 102 fits were 6·86 and 6·83; for 16 azoman convulsions the values were 7·2 and 6·25 respectively.

The average total acidity values in the urine excreted before and after 40 fits were 16·5 and 15·4 c.c. $\frac{N}{10}$ NaOH/100 c.c., and the average amount of ammonia excreted was ·061 and ·058 gm./100 c.c. respectively.

Thus the ammonium chloride injections make a negligible difference to the acidity of the urine and the ammonia nitrogen excreted.

No albumen or sugar has been found in the urine following the fits.

Modified convulsions.—(1) If the convulsant dose of cardiazol is known and an equal volume of the ammonium chloride is mixed with it and injected, the effect is that of the ammonium chloride alone with perhaps slight prolongation of the twitching and confusion.

(2) If a convulsant dose of azoman is mixed with about 8 c.c. of the ammonium chloride solution and injected intravenously, the usual effects of the ammonium chloride are observed. The fourth stage of the fit is, however, replaced by one corresponding to the pre-convulsive period after azoman has been given intramuscularly. The usual azoman convulsion occurs after perhaps ten minutes instead of within a few seconds of the injection.

(3) If three or four c.c. of sodium amytal solution are given intravenously and followed by a convulsant dose of cardiazol or azoman no fit results, though there may be twitching and restlessness. If this is followed by ammonium chloride the first and second stages occur as usual, but the twitching is very slight.

(4) An intravenous injection of 10 c.c. of 5 per cent. sodium chloride has no comparable effect to that of ammonium chloride, but ammonium bromide has an identical effect.

Ammonium chloride thus appears to inhibit the action of cardiazol or azoman when mixed with them, without losing its own effect.

Perhaps the inhibitory action of sodium amytal on the convulsions due to azoman is not well enough known. When 5 c.c. are given intramuscularly the fits stop so promptly that it seems doubtful if deaths in *status epilepticus* will occur if it is used. It appears from the third of the observations that the ammonium chloride convulsions may have a similar cerebral mechanism to those due to cardiazol or azoman, but that the second stage of the ammonium chloride fit is peculiar to this drug.

From the fourth observation it appears that the effect of the drug is due to the ammonium radical.

The stages of the fit are very definite and the above observations appear to assist in their interpretation.

The pain caused by leakage into the surrounding tissues is probably due to an irritant action. The thrombosis which can occur and the sensations apparently accompanying the passage of the drug through the vessels suggest

that they, too, are irritated, thus accounting for the unpleasant preliminary stage.

The time taken for the hyperpnoea to develop and the sensations described suggest that there is a direct action of the drug on the lower brain centres. The results of the injection of sodium chloride and ammonium bromide indicate that the effect is due to the ammonia present.

Further support to this theory is given by the simultaneous deviation of the head and eyes and the rise in the pulse rate and blood pressure.

The muscular movements of the third stage may be compared, it seems, with those produced by the other convulsants.

Results.

The injections were given twice weekly to 24 patients. (*a*) 16 had received no previous treatment. (*b*) Four had completed a course with cardiazol or azoman without success. (*c*) Four received injections during a course which had been commenced with cardiazol or azoman.

(*a*) Ten of these 16 were patients with schizophrenia, of which one was acute, one had had a remission for two years and the present illness for six months, three had a history of from one to two years, and five had been ill from two to ten years.

Of the other six patients, one was an involutional melancholic, two were cases of mania who showed no signs of recovery, one was confused and not improving, and the other two were depressed.

The acute case of schizophrenia had 13 injections of ammonium chloride with some improvement, though she remained impulsive in her actions, hallucinated for hearing and uncertain in conduct. After nine injections of cardiazol she recovered and has been discharged. The girl with the previous remission recovered and was discharged after nine ammonium chloride convulsions. Of the remaining eight patients with schizophrenia four showed improvement, one had heart failure after five convulsions though making good progress, three were no better and were given other convulsants.

The involutional melancholic had 20 fits with improvement and now appears to be recovering. The confused patient had ten injections with little change, but is now awaiting discharge after having three cardiazol convulsions. One of the cases of melancholia had 20 ammonium chloride fits with only moderate improvement. One injection of cardiazol was given, but she complained of pain following the fit and a small crack was found in one of her dorsal vertebrae. The other melancholic had 13 fits with ammonium chloride, resulting in only a slight improvement, but after four injections of cardiazol she recovered. One case of mania showed little improvement with ammonium chloride, but has not cleared up with the other convulsants. The other maniacal patient had ten ammonium chloride convulsions and became a little less restless;

these were followed by one injection of cardiazol, another of azoman and three more of ammonium chloride; she then recovered.

(*b*) The four cases who had previously been treated by convulsion therapy were all schizophrenics. Two had fifteen ammonium chloride convulsions without effect. The others have both shown considerable improvement and have not had injections for the past two months. They have been home for week-ends, and application is being made for discharge in each case. Neither is quite well, but they can live in the convalescent villa without upsetting the other patients. Both have been ill for more than three years. The one had previously received 17 injections of cardiazol and 5 of azoman with a little improvement. She has had 28 ammonium chloride fits. The other had been given 14 cardiazol injections in the past and improved a little. She has had 16 ammonium chloride convulsions.

(*c*) The only case of note in this group is one of schizophrenia. She had been in one of the hospital wards for restless patients for a year. She improved considerably after eleven cardiazol injections, and was discharged as a recovery when a further ten convulsions with ammonium chloride had been given.

Discussion.

Although patients much prefer ammonium chloride injections to those of azoman and cardiazol they do not like them, and there is a good deal of apprehension beforehand. This preliminary fear is naturally attendant on all such treatment.

The muscular movements are so slight, in comparison with the convulsions produced in other ways, that the risks of fracture or dislocation appear to be negligible providing the staff do not interfere during the fit.

There appears to be a danger of heart failure. In the case where this occurred the lesion was unnoticed, although it appears that there was probably mitral disease and possibly some decompensation. The patient has since had dyspnoea on exercise, tachycardia, palpitations and precordial, pain. She is improving slowly, but has been in bed for two months.

Although the patients look well during the treatment, they often lose several pounds in weight. It is regained after the injections are stopped.

From these few investigations it does not appear that the results given by ammonium chloride convulsions are nearly so good as when cardiazol or azoman are used. It is, however, less unpleasant in use, the risk of fractures is negligible, and the elevation of blood pressure after the fit is comparatively small. It is believed that it may be found to fulfil a useful purpose in completing courses of treatment after an improvement has been obtained with the other drugs. It seems to be well worth trying on chosen cases where cardiazol or azoman have failed, and it may prove to be of use in the older, more feeble or bedridden cases.

SUMMARY.

Ammonium chloride has been used as a convulsant on 24 psychotics, 16 of whom were cases of schizophrenia.

The fits are described and the action of the drug is discussed.

The results do not appear to be so satisfactory as those given by cardiazol or azoman. The risk of fractures or dislocations appears to be negligible, but there was one case of heart failure.

It appears, nevertheless, that ammonium chloride may be usefully employed in the treatment of certain cases of mental illness.

I should like to express my thanks for the kind help and encouragement Dr. L. M. Webber, the Medical Superintendent, has given to me.

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A PSYCHOTHERAPEUTIC APPROACH IN SCHIZOPHRENIA.*

By M. GWENDOLINE ERNST, M.R.C.S., L.R.C.P.

I AM presenting to you in this paper my own views and experience in a practical psychotherapeutic approach to psychotics. I am aware—acutely aware—that I am speaking, with only two or three years' experience behind me, to distinguished psychiatrists. I cannot bring myself to apologize for having definite views on so short an experience; they are views that struck me before I had been employed in a mental hospital for a week, and I have had no occasion to change them since. I am not even sufficiently well up in the subject to know if they are peculiar to me.

The first point that I want to make is, that of all the patients in a mental hospital, those who seem to me to be the most accessible to psychotherapeutic approach are the advanced schizophrenics. Not the borderline cases, nor the so-called fleeting schizophrenias who, however acute and severe their symptoms, still give one the impression that they will eventually find their feet again. Both the above types are very tempting to the psychotherapist because one feels that psychotherapy ought to be able to do something to tip the mental balance in the right direction for them, but nevertheless, I feel that, as a psychotherapist, certainly as an analytic psychotherapist, I should keep my hands off those cases. The advanced case is a different matter—I mean the patient who has set a psychotic course and kept to it five, ten, twenty years, with little change except progressive dementia. It is this approach to such cases that I find encouraging.

The second point concerns this dementia. It is constant in the advanced schizophrenic, but I am convinced that it is more apparent than real. The obvious evidence of this is the occurrence, described in all textbooks, of spontaneous remissions in old-standing cases, and the temporary remissions under the influence of severe illness that are often observed. However short the remission, the patient's real personality emerges on these occasions—they are not just improvements in behaviour. So the personality cannot be disintegrated; it must be *there*. I am more interested in the psychotherapeutic evidence of this point, and my best story here concerns a patient who presented the perefect picture of dementia. She was completely withdrawn—chattered

* Read at the Spring Meeting of the South-Western Division of the Royal Medico-Psychological Association held at the Warneford Hospital, Oxford, April 25, 1940.

unintelligibly, was dirty and helpless, and just played with her fingers all day, and had done it for about twenty years. I made contact with her on my own lines, and after about a month decided, on what evidence I cannot remember, that there was opportunity to make her take a step out into reality. I conveyed this to her and the immediate result was very striking. She stopped playing and chattering, and looked terrified, then showed all the signs of a severe mental struggle: she sweated, went pale, and her breath came in gasps and she did not speak a word. I have never seen such a severe mental struggle, and complete with physical signs, and she kept it up for an hour and a half while I just watched and put in an occasional word of encouragement. At the end she lay back and looked me full in the face and said, "I can't; I shall lose too much," and went back to her psychotic behaviour as if she had clicked a switch. To be able to face a problem dead square like that in a way that I have never known even an intelligent neurotic to do, that, to my mind, is inconsistent with true dementia.

The Approach.

The difficulty in speaking intelligently about this approach lies in its simplicity. When I have done more work on it I might be able to complicate it sufficiently to make it acceptable to the intellectual mind, but that has not been achieved up to date. For the sake of clarity I want to outline the principle of the method as a whole before attempting any details of technique.

Please think of the schizophrenic as if it were a child at an age when a child creates definite fears for itself which then hold sway over it for a period. Fears of the kind I mean are fairly general at a certain stage. I mean that stage in one's childhood when one knows that, at a certain turn on the stairs or bush in the garden, something will jump out on one. Or that when the bedroom door is shut at night, a man will jump out of the cupboard. It is not a generalized fearfulness—the fear is definite and remains the same with perhaps embellishments for days or even weeks. If you know anything about the sort of fear I mean, you will know that one does not talk about it; one wouldn't—couldn't—except perhaps impersonally to frighten other children, and that is not the same as telling one's fear. You will know too the characteristic intensity of the fear—one lies and sweats with it. I often wonder how much night-sweats in children, attributed to rickets, etc., really come under this heading; I think quite a lot. Usually the child ultimately deals satisfactorily with these fears and they disappear. But suppose the fear gains in intensity so as to become really intolerable; the child will then, as a last resort, and against its intuitive judgment, make a desperate effort to tell someone about it. Suppose everything is in its favour and mother is the most understanding person in the world, she will still probably rely on reassurance and proof that there *is* no man in the cupboard. The child is now in a really

desperate plight. For the first time she is utterly alone with her fear. Mother doesn't know about the man in the cupboard—the child *can't* make her know. The fear was intolerable before; now, shut up alone with it and made aware that she lacks the ability to convey it to the outside world, i.e. mother, the situation is sufficiently hideous to warrant the most drastic measures being taken by the child to bring itself relief. For instance, a plunge into wild unlimited fantasy or the cutting of all ability to feel down to *nil* may be justified.

In a recent number of the *Journal of Mental Science*, Sawle Thomas quotes Skottowe on schizophrenia, and it reads to this effect, that Skottowe considers the hall-mark of true schizophrenia to be a symptom which he calls dys-symbole, and defines as "a state of mind which manifests itself by the inability of the patient to formulate his conceptual thoughts upon personal topics or to discriminate the gradations of his emotions in language which is intelligible to others." I differ only from Skottowe in that I consider dys-symbole to be not only the hall-mark, but the basis of schizophrenia, and this I have tried to convey in the above picture. I do not wish to convey that I think schizophrenia has a purely psychological basis; I believe it *has* a physical basis, but it is the psychological disturbance irrespective of the nature of its physical basis that I am concerned with in this paper.

To return to the picture of the schizophrenic that I drew, and thinking still in terms of the child, there is only one way in which it occurs to me to approach the situation. I *watch* the child, behaving to her in the meantime as an ordinary friendly person, and avoiding interference with the line of conduct she has taken up. I avoid questioning her or any attitude of "trying to find out" about her, but I watch, and there will be straws to show which way the wind blows. I shall notice, for instance, that the fear is directed towards the cupboard, and with Freud behind me shall realize that it is probably a man that she is afraid of, and shall wait for evidence confirming this, and so on until I have mapped out the fear as much as I think I am going to be able to. I then play the first active move by saying simply as I tuck the child up in bed at night, "I'll just see to the man in the cupboard before I go." "So she knows about the man in the cupboard!"—there is a sharp response—fear and then relief that is unmistakable to the psychotherapist.

I now keep out of the patient's way for about a fortnight—and this is important. I see her in passing and do meet her a good deal, but not on the footing of her fear situation. You see, if I put the child to bed the next night, I shall have, in order to be consistent, to deal with the man in the cupboard again—and repetition of this will fix him as a reality, and this I have no intention of doing. So an assistant who knows what is required of her who can take over at this point is a necessity.

Towards the end of the fortnight, maybe longer, the relief of tension associated with this first move begins to wear off and the fear itself predominates.

The next move must come from the child, and I wait for it; it will probably be some plan on her part for escaping from or mastering the fear produced to me in such terms as: "I was silly; I thought there was a man, etc." The child is just being disloyal to herself; the fear is as potent as ever, and she is attempting intellectually to gain mastery over it by deprecating it, and she seeks my support in this. My answer—a dead serious "I know" is a refusal to give this support and conveys—"I'm not going to pretend that it is silly; you can do as you like about it." A patient here played this move a week or two ago, saying "I'm going off my head. I had a baby last night." I answered, "I understand about that." She turned almost fiercely on me and said, "Yes, I know you do—I can't make you out." That, incidentally, is a patient who has been ill nine years and was mute. A period of antagonism to me probably follows this second move, but the patient *is* better, and in due course this phase passes and she goes on to *her* first active move—which will be in this case an open interest in essentially feminine things in relation to herself—very tentative, but with quick response to encouragement. She is now on solid ground for the first time, and although obviously mentally ill, has a normality about her, something quiet and sure, that is very satisfactory. My assistant now takes over again and I just see the patient in passing though she can always see me if she asks for an interview. These periods when the psychotherapist gets out of the patient's way and yet remains available to her are important. The patient is encouraged in feminine activity. Also a piece of slow satisfactory constructive work is started—tapestry or weaving—the sort of work that grows so slowly that the end is scarcely in sight so that the doing of it is the whole point, not the finishing, and from this point the process is just one of building up. From the time that the first active move is played by me I put the patient on suicide caution observation and keep it up well into the last constructive phase. A strong positive transference to me is usual; it runs a full course and dies a natural death. It is important that the Staff should understand the handling of a patient showing a strong transference.

The outward and visible signs, as these stages are passed, are quite definite. When the first corner is turned, i.e. response to the active move, the patient gives me a good working contact with her and this lasts. Coincidentally with this, and presumably because the fact that she can communicate with me gives her some faith in her ability to communicate with the outside world, she responds to her relatives in a way that they never fail to notice even if they do not know she is under treatment; and thirdly there is a marked improvement in her appearance, not only in health, but in looks generally; the rather revolting facial changes largely disappear.

On turning the second corner there is an awakening of interest, but the internal problem still occupies most of the mental energy, and the patient cannot concentrate sufficiently to be occupiable. Here, at the moment, I have got two patients round the first corner and one round the second.

The detailed technique amounts just to the *language* in which these conversations are held. I find that once one has accepted dys-symbole as *absolute* for the schizophrenic and has put ordinary language right away as a means of communication, one is free to discover what forms of expression are in actual use by any one patient. I find the schizophrenic range of language surprisingly wide, even for a katatonic stupor, so that one can select out of the range at least one method of expression in which one has scope for replying—because it is a *conversation* and both must speak the same language. I find, too, that once patients realize that one is listening to *their* language, they often vary it and elaborate it until they have made one understand. It is the listening more than the accurate understanding that is important. In fact, one can answer a patient's question without grasping more than just the gist of it. For instance, there is a gesture that I frankly do not understand, and yet every patient I have treated has handed it to me in exactly the same way and at the same point, i.e. somewhere in relation to the second move in the approach—I have never got a patient round that second corner, whether they have been hebephrenic or katatonic, without receiving this gesture—the patient out of the blue asks to be allowed to wash her clothes. Now what does she mean? Washings are certainly prominent in age-old rites, and this gesture is probably rooted deep in the archaic levels of the mind. But I am concerned with the immediate meaning. Observing the patient I know that that gesture is one of "finishing with something satisfactorily." I have noticed, too, that patients tend to shrink from completing the washing—it is as if this act of "putting paid to something" is courageously undertaken, but they "get cold feet about"—and I always stand by and help them to see it through. But I still do not understand it.

The schizophrenic language of expression includes:

1. *Drawing.*—Volumes have been written on the interpretation of schizophrenic drawings, and I have nothing to add except that I myself do not value interpretations made on the drawings alone by some fixed code of symbols, but find it necessary to be with the patient and observe her while the drawing is being "spoken."

2. *Posture.*—Katatonics seem to rely a great deal on posture for their expression. Literature is very limited on this subject, and one knows very little about its meaning. One patient here managed to convey meaning to me by posturing because it happened that I had seen exactly the same posturing in two cases before. She always held herself rigid, yet the rigidity was mixed with extreme flaccidity; it is difficult to describe—the limbs are at once stiff and yet flail-like. This, together with her insistence on maintaining the erect posture so that one had a struggle to make her sit down, obviously had a definite meaning for her; anyhow she abandoned it after I had conveyed to her what I felt to be the answer.

3. *Creative ability.*—Working with earth and growth is one avenue here.

Clay modelling is another, and an extremely instructive one. Apart from the symbolic value of the models created, it gives one the opportunity of watching patients construct and destroy—of seeing what they preserve and discard—what they handle tenderly and what cruelly. I have watched a patient model a breast and stroke it tenderly and love it—the wet surface of clay makes it a very satisfactory medium for love play of any sort—and go on loving it more and more until, in an ecstasy of loving, the breast was completely destroyed, and then the patient mourned the loss of it in utter depression. Watching this, one may be able to see the patient enact the complete phantasy that lies behind the characteristic schizophrenic mouth movements—and handed to one in that form, one can deal with it.

4. *Behaviour associated with taking of food, defaecation, urination.*—This form of expression is so full as to need a paper to itself. It is common knowledge that urination is frequently associated with phallic phantasies, and defaecation with ideas of pregnancy. An infantile love desire to give out of itself can be expressed here too. It suffices to say that observation of patient's habits rarely fails to give some clue as to what the patient is trying to say.

5. *Lastly, there is communication in words.*—It is necessary to differentiate sharply between utterances that matter to the patient and what I call "mental froth." This is not as difficult as it sounds, but does need experience. I first hit on it by something in the timing of the answer. I must emphasize that the patient is dys-symbolic so that the meaning of the utterance will not be what the words appear to convey. If I say "I am cold," I mean that the temperature of my environment is low. If the schizophrenic says "I am cold," you can take it that she does *not* mean that—she may mean "something that matters to me is cold, deathly, and still, inside me," or alternatively, something like "I am utterly alone." The background here reads like this: "At my birth when separate and alone for the first time, I also experienced first the sensation of cold." You will reject the latter if you do not believe in analysis of birth separation—it does not matter. I just happen to believe in it and deal with that remark by cuddling the patient up close to me to convey that, although she could not have the intra-uterine warmth back, she could have close physical contact, which, as life goes on, more than replaces the loss. If I felt that the first meaning was the true one, I should make the patient strike matches and light a fire, adding a verbal promise to keep the fire in, backed up by a demonstration on succeeding days that the fire was still alight. I do believe that schizophrenic utterances always concern the big, deep, simple things of life—birth, death, life, love, hate, destruction—and that the meaning has to be looked for on this level.

In spite of the fact that I have tried to explain it intelligently, in practice, one's intellectual reasoning power has no part in this therapy. I believe it is possible to ask one's intellect to stand aside and not interfere, and one can then speak the schizophrenic language fluently because one is thinking in

that language. I say this because I believe that the schizophrenic's difficulty is not so much her inability to express to the *outside world* concepts and emotions that matter to her, but that, primarily, within herself, an inability exists on the part of the simpler instinctive levels of the mind to communicate with and obtain the co-operation of the higher intellectual levels. At this point, of course, I am back to the old conception of a schizophrenic split.

I am grateful to Dr. McInnes for the rare and invaluable help of really open-minded support.

VITAMIN C IN SENILE PSYCHOSES. (A PRELIMINARY REPORT.)*

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THE senile psychoses are in regard to their origin an unsolved problem. Much valid work has been done in the field of anatomy and histology in approaching this problem, but as the mental diseases of old age cannot be separated from the growing old of body and mind generally, this problem is more or less a biological one. The borderline between old age and senile dementia is not a sharp one. In brains of old people without clinical symptoms of dementia there have been found histological changes, such as are usually found in cases of senile dementia. This makes it probable that the extent of degeneration of brain cells alone is not decisive for the appearance of senile psychoses. The finding of the characteristic plaques in the brain of senile psychoses may give evidence of the extent of the process and the severity of clinical symptoms, but it does not tell us anything about their nature and origin. Whether a constitutional factor is decisive or whether the histological changes are a reaction to an unknown noxa is undecided. Heredity may have its share too.

Two considerations aroused our special interest in the problem of origin of senile psychoses. Some authors have discovered the plaques which are always found in senile psychoses in brains of persons who had suffered from alcoholism. That gave us the idea that some toxic factors or disturbances in general metabolism might have their share in the origin of the pathological changes in brains of old people. A further consideration was the fact that in one case of senile dementia it seemed probable from the past history that a sudden incident had precipitated the syndrome of a senile psychosis, or at least had led to a great deterioration. When inspecting the literature we found a series of cases which supported this assumption. We bore in mind that humoral factors might have played their part in the production of senile changes in the brain.

The investigations of biochemists into the nature of the vitamins, especially of the B complex and vitamin C, have taught us that they are important for the maintenance of a regulated and ordered change of energies and metabolism. Their close connections with hormones, especially of the suprarenal gland, is well known. The suprarenal gland contains more vitamin C than

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any other organ of the body. This suggests biological relationship between these two substances. Ascorbic acid with its reducing quality probably protects the cortical hormone from oxidative disintegration. Furthermore the suprarenal cortex is an important factor for the maintenance and increase of the resistance of the body against infections. Especially in acute infections there is a lack of vitamin C, and this has been proved in our own experience. In this connection it may be mentioned that the intracerebral injection of the virus of poliomyelitis in the monkey is stated to be non-infectious when small quantities of vitamin C have been added. The task of the vitamins as catalysts is to prevent the appearance of toxic intermediate products. The removal of creatinuria by vitamin C in progressive muscular dystrophy has been followed by considerations, which lead into the field of psychiatry. According to Jahn the occurrence of creatinuria is characteristic of the metabolism of asthenics. The same author has found creatinuria in schizophrenias of the asthenic type. On the other hand, a low content of vitamin C in the spinal fluid of schizophrenias with catatonic and depressive features has been said to be typical.

Plaut and Bülow have examined the content of vitamin C in different parts of the human brain and at different ages. Normally the brain has a high content of vitamin C. The cortex of old people has only 12% of the content of the cortex of the foetus, whereas the diminution of the content of the cerebellum and the brain-stem is much less in old age. A comparison of different parts of the brain in adults shows a higher content of vitamin C in the cerebellum than in the cerebrum, in the grey matter more than in the white substance. According to Plaut and Bülow the degree of saturation of vitamin C in the body is reflected in the spinal fluid. According to Monauni the vitamin C content of the spinal fluid is dependent on age, the vitamin C content of food and physical diseases. Melka and Klimo have found that the average amount of vitamin C in the spinal fluid depends, too, on the season; the minimum was found in April and May, the maximum in autumn. This fluctuation may be connected with the content of vitamin C in food. Simons has found low values in the spinal fluid of schizophrenias and patients suffering from general paralysis, especially in progressive cases. He considers the reason to be insufficient nutrition or increased consumption.

This paper, being a preliminary communication, contains a full report of our results as to the content of vitamin C in the urine of senile psychoses. Our investigations of vitamin C in the blood and spinal fluid and its relations to metabolism are still in the beginning.

The conditions for estimation of the content of vitamin C in blood are much more complicated than those in the spinal fluid and urine. Zilva and Kellie have found that there exists a competition for the ascorbic acid of the blood between the absorptive tendency of the tissues, which varies with the degree of saturation and the excretory function of the kidneys. In this respect there

are important individual differences, and as far as it concerns our own investigations in senile psychoses no definite relations between blood and urine content of vitamin C have so far been found.

As a valid and reliable procedure the saturation test of the urine, which has been introduced by Harris, Roy and Ward, has proved useful and sufficient for clinical purposes. Though the method is not exact enough for the estimation of the daily need of vitamin C, it is sufficient and reliable for the calculation of the degree of saturation. For this purpose 300 mgm. of ascorbic acid are given daily by mouth until bodily saturation is reached, that is to say, until a distinct increase of the excretion follows. The number of the days is counted until about 50% of this quantity is recovered in a 24 hours' specimen of urine. We titrated with dichlorphenolindophenol as suggested by Tillmans. The objection which has been made to this test that it is not specific enough can be broadly met by observing rules considering the chemical characteristics of the ascorbic acid. This is the more important as critical reviews of biochemists consider the results obtained as being for the most part faulty, the protection from oxidation having not been sufficient.

Before describing our procedure, the cases which had to undergo the test may now be shortly described. Among the seven patients, aged from 72 to 82, were six women and one man. They displayed more or less deterioration of the mind and had no obvious physical diseases. For a control we took one epileptic and two normal persons.

From each patient the 24 hours' urine was collected. Bedridden patients were given the bed-pan every two hours. To each specimen $\frac{1}{10}$ of the volume glacial acetic acid was immediately added. The next day the same procedure was carried out, but instead of glacial-acetic-acid 22% sulphosalicylic acid plus glutathione were added. The latter is an albuminous by-product, and also has a protective function in the body, as it inhibits to a certain extent the efficiency of ferments which cause oxidation of ascorbic acid. When added to the urine, glutathione forms a relatively stable compound with heavy metals, nearly always found in traces in the urine, and which otherwise would oxidize ascorbic acid. At a pH of 2–3, the speed of oxidation of other reducing substances slows down and estimation of ascorbic acid can be carried out without interference, if titration ensues within 2–3 minutes. The result was several times a relevant loss of vitamin C in those cases where acid alone had been added as protection from oxidation. This fact caused us to divide the freshly passed specimens of the patients and control persons into four parts. The first portion was examined immediately, the second without any protection several hours later, and the third and fourth with the reagents just mentioned also after several hours. We got nearly identical results from the examination of freshly passed and immediately examined urines and those portions containing acid plus glutathione. The patients were all on normal diet. From the third day onwards the patients and control persons got each

day 300 mgm. ascorbic acid, until saturation was reached. Every case of senile psychosis showed a significant delay until the required excretion of about half the intake had been obtained. Of the controls, two of them on the same diet as the patients showed a saturation after two to five days, whereas in senile psychoses saturation was reached only after eight to eleven days. Thus we got a deficit of about 2,400 to 3,300 mgm. of vitamin C. A deficit of 1,000 mgm., or at the most 1,500 mgm., may be regarded as pathological. In one case there was a sudden drop of vitamin C content after a completed saturation, although the daily intake of 300 mgm. of ascorbic acid had been continued. First we had no explanation for it, and investigation showed that a failure in the method could be excluded. Next day there was a rise of temperature, and a fortnight later the patient died from pneumonia. The increased consumption of vitamin C had been doubtlessly caused by the infection. In another case we gave cortin plus 300 mgm. ascorbic acid at the same time in order to see whether a shortening of time until saturation occurred. No such result followed.

As we had to counter the question whether there was a delayed resorption in aged people we gave in two cases 200 mgm. vitamin C by injection, when saturation had not been reached after five days. In both cases no increase of excretion resulted. The other question whether there is an increased need of vitamin C in aged people has to be left open. An increased need would be in contradiction to rules in general metabolism of ageing cells.

As to our investigations of spinal fluids we have no definite results yet; the number of cases in which lumbar punctures could be made is still too small. A high content of vitamin C was present in the spinal fluid in two cases—one aged person and one control—after saturation in the urine had been reached. The quantity was greater than that which is usually found in the spinal fluid of non-saturated persons. Immediate titration of the spinal fluid is essential.

The delay of saturation in aged people shows the existence of a hypovitaminosis. We do not venture to state whether the tendency to infections, the delayed healing of fractures in old age, belonging as well to the picture of a hypovitaminosis, are due to the deficiencies of vitamin C in old age, and we certainly cannot assume at this stage that the vitamin C deficiency is important for the aetiology of the senile psychoses. But I think further investigations along these lines are worth while, especially if we consider the manifold relationships of vitamin C to vital functions. It may yet be that tracing of normal and pathological activity of vitamins and hormones may be of value in psychiatry.

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MIRROR WRITING IN NORMAL ADULTS.

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This subject has a moderately extensive literature and examples have been recorded by various authors for some years. Most of the cases, however, have been the subjects of some pathological lesion, either congenital or acquired. Perhaps the earliest authentic case is the one originally described by Rosinius Lentilius in 1698, and quoted by Critchley, of a female, presumably young, epileptic sinistrad. The sex is not as important as the other factors, but it is a pity that there is no reference to the intellectual capacity. It is, if nothing else, a pointer to the usual type of case studied. In the adults, hemiplegics seem to have proved the most fruitful source for those collecting examples of this phenomenon, although a full list of causes is well known.

There would, then, seem to be some excuse for examining instances of mirror-writing in normal adults if only to have some "yardstick," as it were, by which the frequencies and variants in the normal can be known. To this end 50 male and 50 female specimens have been obtained under conditions described more fully below.

Material.

The people who gave the specimens were mainly members of the staff of a hospital, holding varied positions from maids on the one hand to medical officers on the other. Each was asked for nine signatures as follows:

1. (*a*) Right hand. As in ordinary writing, i.e. on the upper surface of a piece of paper.

(*b*) Left hand. As in 1 (*a*).

(*c*) Both hands together. As in 1 (*a*).

2. A repetition of 1 except that this time it is done with the eyes shut.

3. A further repetition of the original, but this time the under surface of a piece of paper is used. It is obvious that under these circumstances the script is hidden from the writer's view, as in 2.

1 and 2 present no difficulties when the specimens are obtained, but there is a point that it is wise to observe when the last test is undertaken. Much trouble will be avoided when the writing is examined at leisure if the paper is labelled so that the edge nearest the performer is marked "bottom" and those

on his right and left also noted. It will be seen that these are opposite from the examiner's. Unless this is done reversals either in the lateral or more probably in the vertical may be missed.

RESULTS.

The classification of these is best done under the headings (*a*) frequency and (*b*) types of variants from normal writing. The former of these is shown in Table I, which is set out in two parts so that not only are the male and female results separated, but it also divides those obtained on the upper surface of the paper from those on the under surface and conveniently leaves apart the examples that were made with and without the visual aid. Table II deals only with the more unusual and, as a rule, minor variants of normal writing other than the common complete reversal.

TABLE I.

	Upper surface.					
	Eyes open.		Eyes shut.		Under surface.	
	Male.	Female.	Male.	Female.	Male.	Female.
Right hand	0	0	0	0	42	47
Left hand	0	0	0	1	41	45
Both together	0	0	0	0	40	46
Right only (both used)	0	0	0	0	1	1
Left only (both used)	1	0	1	1	0	1

The figures in this and the next table note the occurrence or absence of abnormal script.

In the whole series there will be 600 right- and 600 left-hand signatures, of which 100 are normal ordinary writing examples as practised daily. 800 are made on the upper and 400 on the under surface of the paper.

Firstly let the results on the upper surface be considered. Only on one occasion was mirror writing found when the eyes were open, and this in the left hand when both were used. When, however, the eyes are closed it occurred on three occasions, once in the left hand alone and twice in the left hand when both were used. Although such figures are not very great, yet it is rather extraordinary that such writing occurs three times more frequently with the eyes shut than when they are open and always in the left hand.

Let us now pay attention to the under surface of the paper. Of the 100 right-hand signatures 89 per cent. are written mirror-wise. 86 per cent. of left-hand signatures follow this rule and the same figure holds good when both hands were used together. Only 2 per cent. show it in the right hand alone if both were used, and only 1 per cent. of people in the left hand alone under the same circumstances. Roughly speaking, then, mirror writing is as usual

on the under surface as ordinary left to right script is on the upper. Throughout it will be noted that females show a slightly higher reading than males.

Discussion.

Before going into the theories that have been advanced to explain this phenomenon it is perhaps as well to realize on what these results are founded. In each instance the subject was writing his or her name—one of the first things we are taught to write from childhood, if not the first, and, if we exclude the articles "the" and "a," the words that have been written most frequently by each of us. The result of this continued repetition is that one no longer, in adult life, spells one's name when putting it on paper, but draws a pattern in which particular letters may be quite indiscernible and the whole a mere shape, undecipherable and defying analysis except by those of the signatory's friends and acquaintances who are already aware of its peculiarities. These remarks are particularly true of the right hand, since this is the one mostly used, though not always for writing. When, however, a more unusual method of autographing is adopted the tendency to reproduce the usual right-hand pattern still persists, but there is also introduced an effort to spell the word, i.e. form a number of joined letters, where each is written as a separate entity, and in Table II this may account for the misspelling noted there.

It may be convenient at this stage to consider some of the theories that have been put forward to account for mirror writing. The following summary of causes is a modification of that given by Critchley :

(1) Dulling of the highest mental faculties.

(2) Post-hemiplegic cases, usually in left-sided cerebral lesions and associated with aphasia and apraxia.

(3) Normal left-handed children.

(4) Congenitally word-blind.

(5) Eyedness as well as handedness.

(1) *Dulling of the Highest Mental Faculties.*

Mirror writing has been observed on many occasions when the highest mental faculties are in abeyance, as in states of hypnosis and the cases described by Porot, Abély and Raircoule. This type can have no direct bearing on the present inquiry as, rather than a dulling of mental faculties, the attention of each subject was focused on the signatures he was making.

(2) *Post-hemiplegic Cases.*

This group leads at once to the relation between speech and writing, since a certain degree of aphasia and apraxia is usually present. In considering the laryngeal movements during speech Drennan has pointed out that those on one side of the body are a mirror image of those on the other. This is also

true of movements of the hands and arms, as is readily seen in the clinical test for dysdiadokokinesia. Drennan further states that, in spite of the bilateral innervation of the larynx, one half of the brain is dominant and the side controlling the dominant hand also controls the larynx, i.e. the left hemisphere in right-handed persons. The movement predominant in the act of writing is abduction. When for any reason a right-sided hemiplegia occurs, the controlling half of the brain is removed functionally and the left hand, free from this influence, no longer writes from left to right, but reverts to the " natural " movement of abduction, thus producing mirror script. Does this unilateral cerebral dominance play any part in the first group of causes noted above? There is no proof, but it is at least feasible to imagine that when the higher faculties are dulled the main stress falls on the dominant hemisphere.

(3) *Normal Left-handed Children.*

It has been shown that mirror writing is commoner in left-handed children than it is in the right-handed. From what has been said before this might be expected, since the left-handed child is usually taught to write with the right hand and consequently uses the subdominant cerebral hemisphere. The reversal is made with the left hand following the natural action of abduction which has already been learnt with the right. As Critchley has noted, such writing may be neater than the right-handed efforts and the child is often unconscious that he is writing mirror-wise with his left hand. Such writing, too, is read by such children quite easily.

(4) *and* (5) *Congenital Word-blindness and Eyedness.*

Critchley has suggested that the condition of word-blindness is not so rare as has been formerly supposed. He also says that when writing is first learnt kinaesthetic memory is more important than visual, the latter replacing the former as the child grows up. Presumably in these subjects there is no visual memory to replace the kinaesthetic, which will again be formed by the movement of abduction. The physiology of sight deserves some consideration at this point. In his interesting paper, Drennan points out that the images on the two retinae are identical, whereas those on the visual cortex are mirrors of each other. He does not, however, hold the usual view that these fuse, his reason being that it has been shown that people are as consistently right- or left-eyed as they are right- or left-handed. His explanation of mirror writing lies in the suppression of the normal or dominant image and the ascendency of the lesser images or " ghosts," through the association fibres to the auditory and motor paths. But it must, in fairness to him, be noted that dominance in one eye cannot be considered indicative of which hemisphere is dominant, since correlation between handedness and eyedness is not absolute. Hogben and Drennan have endeavoured to show that sinistrads are more often left- than

right-eyed, and quote Elliot Smith's ape fissure in the left occipital cortex of dextrads as an anatomical support. There is an anatomical reason for the fact that handedness and eyedness do not correspond absolutely, namely, the simple one that both retinae are represented on both sides of the brain. Perhaps future research will show that it would be more correct to speak of people being right or left "retina-ed" than right or left-eyed.

From these various explanations it will be seen that certain facts stand out and may be summarized under the following heads:

(*a*) Normal movement of writing is abduction.

(*b*) Unilateral cerebral dominance including eyedness and handedness.

(*c*) Primary kinaesthetic and secondary visual memory.

It must now be seen what relation these hold to the results here obtained.

Firstly, let us take the results from the under surface of the paper. When the right hand alone is used no less than 89 per cent. of the subjects wrote mirror-wise, 86 per cent. with the left hand alone and 86 per cent. with both hands together. When both hands are used together we note that only 2 per cent. showed mirror writing in the right hand alone and only 1 per cent. in the left hand alone. It would thus seem that this form of script is the common result on the under surface of the paper. It will likewise be obvious that to produce it the person is using the normal movement of abduction. During this they experience the usual kinaesthetic sensations that accompany this action, and although they will say that it feels strange to write in this way when further questioned, they will also say that in order to make their signature they form a mental picture of what they are writing. Another point is that they rarely know that they are not writing in the usual way because of the strength of the kinaesthetic impressions experienced. In other words they actually try to sign their names in the usual way. What then accounts for those occasions when mirror writing was not shown? As has been noted, when a person tries to re-orientate himself to write on the under surface he forms a visual image of his effort, and it is here suggested that this is in excess of or overrules the abnormal kinaesthetic sensation of adduction that must accompany such an effort. It is difficult to interpret this by any other means with the data that are known to influence this phenomenon.

Now for the signatures on the upper surface of the paper. It will at once be observed that here mirror writing is a rarity; in fact it is only found four times in 800 autographs. Of these four times, no less than three occur when the eyes are closed. This fact alone must indicate the importance of visual aid in signing. The next fact is that in all these four the left hand was at fault and never the right. But it can also be seen that three of these four are to be found only when both hands are used together. Can these figures be explained in the same way as were the under-surface ones? The increase of mirror-writing when sight is removed leaves the person with only a visual memory or image and the kinaesthetic memory of his previous effort. It can

be fairly argued that since the kinaesthetic element is the same if the eyes are closed or open, it is not surprising that we occasionally find the left hand reverts to its original abduction pattern and so produces mirror script, especially as it is so much commoner when both hands are used together. A further point of interest here is that the one female case showing this example in the left hand with the eyes shut, although a dextrad herself, said that she came from a left-handed family.

Since these results are, however, the exception rather than the rule, it must be assumed that in most circumstances the visual memory is in itself sufficient to produce normal left to right caligraphy, and takes precedence over the kinaesthetic memory.

So far the results have been interpreted mainly from the consideration of kinaesthetic and visual memories and their relation to the normal abductive movement in writing, but what of the question of unilateral cerebral dominance? With the figures at our disposal here it is best considered by studying the effects of one hand on the other. It does not greatly matter if this be on the upper or under side of the paper.

It will be noted at once that when both hands are used together, on the upper surface, mirroring occurred only on the three occasions referred to above. On the under surface of the paper the occasions when the two hands differed number only three again. So that in three hundred occasions when both hands were used together we find only six examples of one hand not following the other. It is also shown that this difference is distributed equally between the upper and under surfaces of the paper. Surely this must mean that the factor causing it is independent of either sight or visual imagery. Why is it, also, that almost consistently the two hands follow each other so happily? It would seem that the dominant hand has a strong guiding influence on the other. To put it another way, the right hand acting as an aid to the left overrides the original tendency for them both to abduct, and this in spite of the adductive kinaesthetic impulses that must be received from the left in this act. The fact that the divergence from the usual remains the same even when visual help is removed is also important. As has been said, the kinaesthetic imagery is in abeyance, and so one can only attribute this to the dominance that one half of the brain is able to exert over the other side since visual aid made no difference.

TABLE II.

	Male.	Female.
Fragmentary reversals (parts of letters)	1	0
Individual letters only	1	2
Misspelling	1	2
Vertical transposition :		
(*a*) Incomplete	1	0
(*b*) Complete	4	2

The results in this table are of more interest from the point of view of the clinician, and show some of the rarer variations in calligraphy that can occur.

The solitary case in which a fragmentary reversal of part of a letter occurred is that of a male who, although he describes himself as being right-handed, is actually ambidextrous, for when playing cricket he bats left-handed. The fault was to make the convexity of the curve of a capital R go to the left instead of the right in a left-handed signature with the eyes shut.

The next column deals with three cases in which individual letters alone were reversed, two of these being female cases. In the case of the man one of the initials of his signature was mirrored when the left hand alone was used on the upper surface of the paper, and again when both hands were used and the eyes shut. On the under surface of the paper a different initial was mirrored by the right hand. In the female cases one mirrored a capital P at the beginning of her name when both hands were used with eyes both shut and open in the left-hand signature. In the last case it was the final letter of the name that was at fault, an "h," when both hands were used together with the eyes shut. This case also showed vertical transposition with each hand used separately on the under surface of the paper.

The third heading deals with misspellings, once in a man and twice in women. The man was the case of a fragmentary reversal already noted, and he reduplicated an "e" at the end of his name when the right hand was used and the eyes shut. One of the female cases is somewhat similar, a "b" erroneously being repeated in the middle of the name when both eyes were shut, but the last case differs from the others in that a letter was omitted when both hands were used on the under surface.

The last item is the incidence of vertical as opposed to lateral transposition. It is as common as all the other variants in this table put together and is twice as common in men as in women. It is usually complete, only one incomplete specimen happening. In no less than four of these six cases it replaced lateral transposition.

Nearly all the points noted in this table can be explained in the same way as those in the first table.

So far we have considered the occurrence of this phenomenon in bulk as it were and have not applied the theories noted above to any individual case. The figures in the tables denote only the presence or absence of transposed script and do not show what may happen in any particular instance. It may be said at once that no case necessarily shows a complete consistency in performance. Let us illustrate this. A male mirror-wrote on the following occasions during his test: with the left hand when both were used together on the upper surface of the paper with the eyes shut and open, and also with the right hand only when both were used together on the under surface Or the case of a woman whose only lateral transposition occurred when both hands

were used together on the under surface, but each hand separately, underneath the paper, gave vertical alteration; and finally the case of a woman whose mirror writing followed the usual course except that in the right hand under the paper part of a letter, i.e. the tail of a final "y," was not mirrored.

Can such apparent inconsistencies be explained by the factors put forward above, namely, the balance between the visual and kinaesthetic elements, whilst bearing in mind that there is a dominant or controlling hemisphere exerting a guiding influence on both hands? These factors would appear to be sufficient if it is admitted that they do not act with unvarying force continuously, i.e. if visual imagery is the main factor in any given case moments may occur when it fails, and then a temporary reversion to the primitive movement of abduction may result, giving the fragmentary and minor alterations in the writing that have been seen to occur at times; or if the kinaesthetic influence is the greater it can, for a longer or shorter period, be replaced by a visual dominance.

There is still one final point to be considered. We have no satisfactory explanation for the disorientation that produces vertical transposition. That it occurs with or replaces the more usual form of mirror writing is clear. The six names actually so written were the following: Hamilton, Higgins, Ridpath, Winter, Smith and Stark. All these have in the written script a fair sprinkling of vertical as opposed to round letters, and consequently in forming their visual images the vertical rather than the horizontal becomes relatively important, as may the to-and-fro kinaesthetic sense experienced in writing them, but such an explanation is not entirely satisfactory, as many others with similar spellings do not show this abnormality.

Summary and Conclusions.

From the above the following points of interest emerge:

(1) 100 normal adults have been examined for mirror-writing.

(2) The frequency of this type of writing has been shown, under stated conditions, in both males and females, together with the minor variants.

(3) The causation has been discussed and in the light of present knowledge accounted for by the balance between visual and kinaesthetic elements under the guiding influence of the dominant cerebral hemisphere, although there are still some points not fully explained.

Finally I should like to thank Dr. Wootton for letting me get specimens from the members of his staff, and also those who so kindly gave me samples of their writing.

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BLOOD-SUGAR CHANGES FOLLOWING CARDIAZOL TREATMENT.

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(Received December 15, 1939.)

MEDUNA and Rohny (1939) have recently commented on the rise of sugar and lactic acid in the blood of schizophrenic patients following therapeutic cardiazol fits. Insulin causes a lowering of the blood sugar, but later the resting level becomes higher than before treatment. Hence they suggest that the alteration of carbohydrate metabolism in the direction of diabetes may be the common mechanism underlying both forms of treatment, and this hypothesis is supported by Nyiro's observation (quoted by Meduna and Rohny) that diabetes is rare amongst patients with schizophrenia.

In view of these findings it was decided to treat a diabetic schizophrenic with cardiazol, and determine the alterations in his blood sugar.

Mr. M—, now aged 56, was admitted in October, 1911. There is no relevant family history. He was backward at school and then worked in several offices, finally becoming a bank clerk. In March, 1910, he had a breakdown, but recovered in two months. The following year he had another attack, from which he recovered, but soon began to behave in a peculiar manner, writing incomprehensible and indecent letters. On admission he was rambling and often incoherent in speech and restless in his movements. Since then he has been mostly quiet and unoccupied, but obeying when told to do things. He has shown periodic outbursts during which he is restless and talkative. On one occasion he tried to commit suicide by keeping his head in a basin of water, and another time he thrust his fist through a pane of glass. At present he remains in the same position all day if left alone. He often replies to simple questions in a rational manner, but then will continue by talking about some other apparently unrelated subject. Sometimes he shows simple association of ideas, as when asked why he came here he replied, " Oh yes, cent, American, British Columbia—that's it, Christopher Columbus."

In January, 1939, sugar was found in his urine on routine examination. A glucose tolerance test confirmed the diagnosis of mild diabetes. Clinically he showed excessive appetite and thirst, passed large quantities of urine and was generally obese. B.P. 180/90. No other abnormalities were noted.

The diabetes was controlled by dietetic treatment and insulin, but later the insulin was omitted without the occurrence of glycosuria.

July 13, 1939: At 12.35 p.m., after having had his usual breakfast, 4 c.c. of 10 per cent. cardiazol were given intravenously. No fit occurred so 5 c.c. were given at 12.42. A normal fit followed. Blood sugar: Before fit, 135 mgm. per cent.; immediately at end of clonic phase, 132 mgm. per cent.; ¼ hour after fit, 125 mgm. per cent.; ½ hour after fit, 190 mgm. per cent.; ¾ hour after fit, 185 mgm. per cent.; 1¼ hour after fit, 190 mgm. per cent. He had no lunch

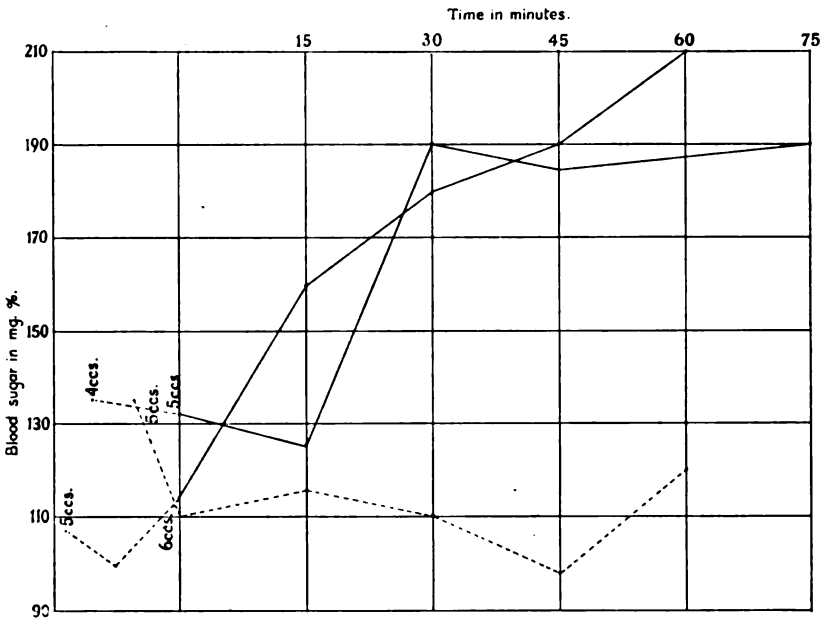

FIG. 1.—The effect of cardiazol on the blood sugar of a diabetic patient. The continuous lines indicate the changes following a convulsion. On one occasion no fit occurred.

and very little food for the rest of the day. A specimen of urine passed at 6 p.m. contained 2 per cent. of sugar.

July 16, 1939: At 10.25 a.m., following his usual breakfast, 5 c.c. of cardiazol were given. He sat up, breathed more deeply, had a few clonic spasms and then became quiet again. As he did not show any discomfort, it was decided not to give him a further injection so as to determine the effect of a sub-convulsive dose. Blood sugar: Before injection, 135 mgm. per cent.; 5 minutes after injection, 110 mgm. per cent.; 20 minutes after injection, 115 mgm. per cent.; 35 minutes after injection, 110 mgm. per cent.; 50 minutes after injection, 98 mgm. per cent.; 65 minutes after injection, 120 mgm. per cent. The 6 p.m. specimen of urine contained 1·4 per cent. of sugar.

July 18, 1939: At 12·5 p.m., having had his usual breakfast, 5 c.c. of cardiazol were given. He sat up and gave a few clonic spasms. At 12.17 p.m. 6 c.c. of cardiazol were injected and a normal fit followed. Blood sugar, before first injection, 107 mgm. per cent. Immediately following first injection, 100 mgm. per cent.; immediately at end of clonic phase, 114 mgm. per cent.; ¼ hour after fit, 160 mgm. per cent.; ½ hour after fit, 180 mgm. per cent.; ¾ hour after fit, 190 mgm. per cent.; 1 hour after fit, 210 mgm. per cent. There was no sugar present in the 6 p.m. specimen of urine. The patient was unduly cyanosed during the fit and later he became restless. One hour after the fit the apical heart rate was 170/minute with an irregularity occurring every 7th to 10th beat. The patient was sweating and cold. Numerous small petechiae were seen around the base of his neck and over the upper part of the chest. Digitalin gr. 1/100 was given subcutaneously. His pulse gradually became normal during the course of the afternoon, and at 11.30 p.m. was perfectly regular and beating at 105/minute.

Comments.

It was hoped that these observations would be the preliminary to further investigations, but the occurrence of auricular fibrillation in a fat diabetic contra-indicated further treatment. No change was noted in his mental condition, and his appetite was poor for a few days after the last fit.

The effect of giving cardiazol was to produce a preliminary lowering of the blood-sugar level followed by a slow rise, which had not begun to fall by the end of an hour. Meduna and Rohny found, in non-diabetic patients, a rise which reached its peak about half an hour after the fit and was not preceded by a fall.

I wish to thank Dr. T. E. Harper, Superintendent of Holloway Sanatorium, for permission to publish this paper.

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Part II.—Reviews.

A Text-Book of Psychiatry. By D. K. HENDERSON, M.D., and R. D. GILLESPIE, M.D. Fifth edition. London: Oxford University Press; Humphrey Milford, 1940. Pp. xii + 659. Price 20s.

The fifth edition of this ever popular textbook has succeeded in presenting us with an up-to-date account of psychiatry regarded rather from the Adolf Meyerian point of view. At the same time the authors have preserved a very even balance between the new and the old. A well considered account is given of shock therapy, but the authors are careful not to express too definite an opinion as to the ultimate value of this form of treatment.

The chapter on psychopathic states which follows the lines of Prof. Henderson's Salmon Memorial Lectures is very well done and we welcome it as an advance.

We are glad to read that the word "amentia" is "best avoided altogether."

The suggestion that vitamin deficiency plays an important part in the alcoholic psychoses is beginning to receive more attention. Better results we think are obtained by combining vitamin C with vitamin B.

The book remains the best textbook in psychiatry that we possess.

G. W. T. H. FLEMING.

Neurology. By S. A. KINNIER WILSON, M.D., F.R.C.P. 2 vols. London: Edward Arnold & Co., 1940. Pp. xxxvi + 1,838. Price four guineas.

This large work on Neurology has been long expected both by those of us who had the privilege of being taught by the author and by the British Neurological School.

Fortunately when Dr. Kinnier Wilson died the work was sufficiently far advanced so that in its present form it represents what he would have wished to appear.

The book represents Kinnier Wilson at his very best. He had an extraordinary knowledge of Neurology and all its "confinia." As editor of the *Journal of Neurology and Psychopathology* he came in contact with a great deal of the world's literature on neurology.

Volume One is devoted to toxic-infective diseases of the nervous system, special forms of toxi-infection of the nervous system, and special forms of toxicosis of the nervous system. Volume Two deals with degeneration or toxidegenerative disorders, diseases of vascular origin, tumours of the nervous system, metabolic and deficiency disease states, congenital anomalies and disease states, disease conditions of uncertain nature and the neuroses.

It is almost impossible to find fault with anything; there is an air of quiet efficiency which was so characteristic of the author's personality.

The chapter on the epilepsies is very well done indeed. His views represent the experience of many years on hundreds of epileptics. He wisely stresses the small part played by heredity. While appearing to favour the neural

theory of the epilepsies the author says: "When the problem is surveyed from every angle, it seems illogical to expect a single and unique common factor for the totality of epileptic symptoms. Their immense diversity precludes the likelihood of an identical basis for all; . . . much of the controversy over theories of discharge seems rather academic and can well await physiological advance."

One hundred and fourteen pages are devoted to neurosyphilis and this is probably the best chapter in volume one. It is very well done.

Neurologists in this country have long wanted a real masterpiece on Neurology which could be favourably compared with the best American and Continental textbooks and now it has appeared. The book is extremely well produced.

G. W. T. H. FLEMING.

Mythology of the Soul. By H. G. BAYNES, M.B., B.C. London: Baillière, Tindall & Cox, 1940. Pp. x + 939. Price 32*s.* 6*d.*

This important contribution to the psychology of schizophrenia is from the viewpoint of the analytical psychologist. The work is devoted to an analysis of the artistic productions of two schizoid subjects. It should be stated right away that the two series of drawings and paintings are of exceptional psychological interest, and that the productions of the second subject are not without artistic merit. The book is well worth obtaining for the illustrations alone.

Regarding the first subject, the sceptically minded may be struck by two facts. The early drawings followed an intensive reading of Freud; they are redolent with sexual symbols. Gradually as analysis proceeded, these are replaced by the dragon, demon, symbols of the anima and persona and all the paraphernalia of analytical psychology. Incontinently one is reminded of the patient who complained to his psychiatrist that there was a demon in his belly and, when pressed further, explained that his analytical psychologist had put it there.

Whatever views may be held on the individual interpretation of these drawings, those readers with a scientific training may find the collective and prophetic interpretations hard to swallow. Regarding a picture in the second series, we are told that its prophetic meaning is supported by astrological calculation. "The present," we learn, "is a transitional period, corresponding to a point in the Zodiac between the constellations of the Fishes and Aquarius." It appears that this picture and astrology agree in predicting the appearance of anti-Christ at the end of the second millennium.

Psycho-analysis attempts a direct drive towards fundamental issues. Analytical psychology is constantly struggling towards a wider meaning and ultimate issues. The author assures us that there is some deeper meaning in unreason, known alone to the mystical East. In this book there are constant references to the deities of the Veda, Babylonia, China and Egypt. With Jurgen the reviewer is inclined to retort that the trouble with these gods is "they have no conversation. They merely bellow—or twitter or bleat or jibber or purr, according to their respective incarnations—about unspeakable mysteries and monstrous pleasures until I am driven to the verge of virtue by their imbecility."

For those with plenty of leisure, and a taste for mythology in general and dereistic thinking in particular, the present work can be confidently recommended.

S. M. COLEMAN.

Part III.—Bibliography and Epitome.

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VOL. CXII. RÜDIN COMMEMORATION NUMBER. 1939.

VOL. CXIII. 1939.

AMER. J. PSYCHIAT.

VOL. XCVI. JANUARY, 1940.

Evaluation of the Electroencephalograms of Schizophrenic Patients.

From a study of 132 schizophrenic patients at the Metropolitan State Hospital and McLean Hospital the author comes to the following conclusions:

The EEG's of schizophrenics fall into three groups:

Group I: Essentially normal.

Group II: Dysrhythmic type, which is indistinguishable from EEG's of individuals known to have convulsive disorders.

Group III: "Choppy" type, which suggests the possibility of a pathological condition in the brain.

Patients in Group II frequently present in their histories the same syndrome as found in epileptics. These patients are either diagnosed as "catatonic schizophrenia" or give a history on the hospital ward of catatonic stupors and excitements. (Author's abstr.)

Electroencephalography in the Psychoses.

The bilateral distribution of the amount of alpha-wave activity (per cent. time alpha) from the cerebrum of 14 schizophrenics, two manic-depressives and one case of traumatic psychosis was determined.

From differences in the distribution of per cent. time alpha over the two cerebral hemispheres, it was found possible to localize cerebral atrophy. The electroencephalographic diagnoses were confirmed pneumoencephalographically in eight of the nine schizophrenics and in both manic-depressive patients. Air injections have not yet been done on the other five schizophrenics.

In two of the schizophrenics with cerebral atrophy delta-wave discharges were occasionally observed. Epileptiform discharges were recorded from the forehead of one of the manic-depressive patients. The patient with traumatic psychosis had no detectable alpha rhythm, so that it was not possible to localize the extensive, marked cerebral atrophy, both deep and superficial, which was subsequently found pneumoencephalographically. However, potential changes typical of normal sleep were obtained while this patient was asleep. (Author's abstr.)

A Five to Ten Year Follow-up Study of 641 Schizophrenic Cases.

1. Of 641 clinically diagnosed cases of schizophrenia, admitted to the Rhode Island State Hospital for Mental Diseases between 1929 and 1934, and followed for five to ten years, 27·5 per cent. were found to be at present in the community, 53·5 per cent. were in mental hospitals, 13·9 per cent. were dead, and for 5·1 per cent. no adequate follow-up information could be obtained.

2. Adequate follow-up data were available for 608 patients; of these 6·6 per cent. were much improved, 15·3 per cent. improved, 63·5 per cent. unimproved and 14·6 per cent. dead.

3. Classification on the basis of diagnostic subtype showed that 35 per cent. of the simple, 16·4 per cent. of the hebephrenic, 30 per cent. of the catatonic, 16 per cent. of the paranoid and 36·4 per cent. of the "other" group were much improved or improved. Many of the cases in the latter category were of the so-called schizo-affective type.

4. The age of onset of psychotic symptoms had little bearing on the outcome, except that those cases having an onset at the age of 45 or later tended to do less well than those having the onset at a younger age.

5. Of those cases with symptoms of less than six months' duration prior to hospitalization 34·5 per cent. were much improved or improved. For those with symptoms of six to eleven months, 29·4 per cent. were benefited; for those with symptoms of 12 to 23 months 27·8 per cent. benefited; while for those with symptoms of two years or longer only 16 per cent. were benefited.

6. 75·3 per cent. of the patients requiring a hospital stay of six months or less were improved, while only 4·2 per cent. of those remaining in the hospital for five years or longer improved. Patients requiring hospital care for more than two years showed little tendency to improve.

7. Disregarding the dead and untraced cases, 259 or approximately 50 per cent. of 519 patients left the hospital at some time or other for more than one month; of these 129 have continued to remain outside the hospital, while 47 returned temporarily and 83 permanently. The much improved and improved groups show a higher percentage of cases remaining out of the hospital continuously and a smaller percentage of returns than the unimproved group.

8. Pulmonary tuberculosis was the most common cause of death, being responsible for 43 or 48·2 per cent. of 89 deaths. Ten (11·2 per cent.) cases committed suicide. (Authors' abstr.)

The Effect of Treatment of Depression in the Menopause with Estrogenic Hormone.

In the group of menopausal and post-menopausal depressions studied, the beneficial effect of estrogenic hormone was confined to the relief of vasomotor symptoms with associated improvement in feelings of well-being. There was no evidence that the depressive illness as such was influenced specifically or its course shortened. (Authors' abstr.)

Detoxication of Sodium Benzoate in Neuropsychiatric Disorders. The Excretion of Hippuric Acid after the Ingestion of Sodium Benzoate.

The rate of detoxication of benzoic acid was determined in patients with various neuropsychiatric diseases. About one half of the patients with catatonia showed a defect in hippuric acid synthesis. This may be due to the state of muscular rigidity and immobility of these patients. Deteriorated patients with epilepsy showed a defect in the synthesis of hippuric acid, whereas extramural patients with epilepsy showed a normal excretion of the equivalent benzoic acid. This may indicate a defect in glycine synthesis in deteriorated patients with epilepsy. Normal average values were found in post-encephalitic Parkinsonism and multiple sclerosis. A patient with progressive muscular dystrophy was able to synthesize glycine at a normal rate. (Authors' abstr.)

An Observation on the Treatment of Mental Cases with Sub-shock Doses of Insulin.

1. The authors have observed in the past year and a half, among a mixed population of over 2,400 patients, that a course of sub-shock doses of insulin is effective in controlling most of the problems of management of unco-operative mental patients.

2. The necessity of sedation by drugs can be limited to epileptics and emergency nocturnal disturbances.

3. Difficult feeding cases can be largely corrected by the use of sub-shock doses of insulin.

4. Sub-shock doses of insulin are effective in all types of cases where there are no physical contraindications.

5. No special equipment or personnel is necessary to carry out this form of therapy.

6. Sub-shock insulin therapy is effective in aborting furuncles, carbuncles and acne simplex, as well as in producing more rapid healing in the well-developed lesion.

7. Sub-shock insulin therapy is in no sense considered a curative therapy, although many favourable remissions occur.

8. There is need for further controlled study of this type of therapy.

(Author's abstr.)

MARCH, 1940.

Further Experiences with the Use of Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders.

In 227 of 267 patients previously refractory to other forms of therapy, sodium diphenyl hydantoinate was found to be an effective, non-sedative and relatively non-toxic means of controlling or reducing convulsive seizures over periods varying from two months to two years. A more prolonged study on a larger series of cases is necessary to establish its place in the treatment of patients with convulsive seizures. (Authors' abstr.)

A Comparative Study of the Effectiveness of Dilantin Sodium and Phenobarbital in a Group of Epileptics.

1. A comparative study of the effectiveness of phenobarbital and dilantin-sodium on a group of chronic epileptics whose average duration of illness has been 15·6 years was undertaken. While phenobarbital has proven beneficial in most cases, the best results were obtained by using dilantin-sodium, as on the latter

drug 40 per cent. showed a complete cessation of seizures for a period of three to six months and 13·3 per cent. showed a marked diminution in the number of convulsive responses, or a total of 53·3 per cent. of improvement.

2. Complications ranging from slight myoclonic tremors to frank psychotic episodes occurred. However, most of them cleared upon withdrawal of the drug or diminution of the dosage.

3. In the treatment of epileptics, the therapy of choice varies with the individual. In our series of cases, dilantin-sodium has been the medication of choice despite its complications and has proven its worth as a valuable adjunct in the treatment of epileptics. (Authors' abstr.)

Dementia Paralytica Accompanied by Manic-depressive and Schizophrenic Psychoses.

In five clinically and serologically typical cases of dementia paralytica, there developed features strongly suggestive of manic-depressive or schizophrenic psychoses.

Long-section studies of the cases pointed to the conclusion that these features were not merely a part of the neurosyphilitic disease, but were manifestations of true manic-depressive and schizophrenic psychoses which pursued their own lines of development independent of the organic disease. Anatomical observations available in one case supported this view.

It is believed that manic-depressive or schizophrenic psychoses accompany dementia paralytica too frequently to be regarded as accidental concomitants of the latter. Apparently they are directly provoked by the organic brain disease. (Author's abstr.)

A Case of Partial Bilateral Frontal Lobectomy.

A case is presented in which the anterior-inferior portions of both frontal lobes were removed in 1934. The present (1939) functional activity of the remaining frontal structures is not definitely known, but the nutrition of the tissue seemed not to be grossly impaired at the time of operation. There is no evidence from encephalography of local or general pressure. As nearly as can be determined from the surgeons' maps the ablation involves all of Brodmann's areas 11 and 47, the lower three-quarters of area 10, and the inferior quarters of areas 45 and 46. This patient's present I.Q. is approximately 120. Nevertheless his behaviour is far from normal. He lacks initiative, and tends to become stereotyped in his routine. A careful psychological study was made, using a number of standard and special tests, from which we draw the following conclusions:

1. The Babcock test indicates a loss in his efficiency.

2. Bender's visual-motor gestalt test gave no evidence of deficit.

3. Two of Goldstein's tests, namely, his adaptation of the Kohs-Block test and his adaptation of the Holmgren wool test, uncovered no defect, but the Vigotsky test brought out a rigidity in his categorical attitude and a failure to appreciate the total situation.

4. On the Knox-Cube test his performance approximated the median for children of seven and eight years. On our adaptation of this test, he could reproduce only lines of four taps. Following instruction to group them he reproduced lines of six taps. Interspersing a delay reduced his performance slightly, but not sufficiently to demonstrate that Jacobsen's findings concerning the deficit in temporal integration in monkeys with frontal lobectomies can be extended to this man.

5. With Hunt's arithmetic progressions and narrative containing absurdities, his performance was similar to that of paretics. He failed with the progressions but noted most of the absurdities at the first reading.

6. Increased motivation did not improve his performance with the arithmetic progression, but suggestions concerning procedure led to considerable improvement. His failure with more complicated progressions consisted in an inability to keep more than two series of numbers separated.

7. On the Ishihara test of colour vision he failed to see any figures until told to look for them.

8. These performances led the writers to formulate this patient's deficit into four aspects: Failure to supply spontaneously fresh modes of attack on a problem apparently resulting from an inability to abstract that aspect of the situation causing the difficulty, a rigidity of the "categorical attitude," a sharp limitation in the number of lines of endeavour that he can successfully keep separated simultaneously, and inability to integrate several aspects of a situation. We were inclined to regard the deficit as a defect of abstract behaviour at a relatively high level.

9. The encouraging response of our patient to instruction gives hope of considerable rehabilitation.

10. We wish to emphasize that the frontal lobes cannot be considered as silent areas, and that in psychosurgery it must be remembered that one disease is substituted for another. (Authors' abstr.)

The Control of Normal and "Convulsive" Brain Potentials.

Brain potentials can be used within limits as an index of the action of cerebral neurones. The recorded waves are the envelope of the beats of many single neurones, and their profile depends on the shape of the unit potential and the temporal relation of the many units.

The isolated frog brain, with relatively few and similar neurones which can be subjected to a wide variety of experimental conditions, is especially favourable for studying the control of potentials. Mammalian brain in situ, so far as similar experiments have been made, shows like behaviour.

The olfactory bulb of the isolated brain gives an electrical beat, at six per second, larger and more regular than before removal from the frog. Under varied conditions, the frequency, still regular, may be shifted from one to 50 per second and the single wave from a sine to many highly skewed forms constantly repeated. Such patterns indicate strong unison of the many cells and so reproduce the potential profile of the unit.

The unit beat is controlled by the metabolism of the cell, oxidative or glycolytic energy supplying the driving force. It is also controlled by a trip mechanism, presumably the cell membrane, which determines the frequency of oscillation at constant drive. Amplitude and frequency vary inversely as the trip mechanism is altered, together as metabolism is changed.

Control of cell potentials mainly through metabolism is considered in the cases of oxygen lack, narcosis, cyanide, glucose lack, insulin, B_1 avitaminosis, iodoacetate, and nicotine poisoning. The action and interaction of these and subsequent agents is presented.

Control mainly through the trip mechanism is considered from altered osmotic pressure, sodium, potassium, calcium, magnesium, and hydrogen ions; for neural stimulation and, in more detail, for polarization by constant currents.

Unification of the beats of the many units into synchronous or simultaneous patterns must depend on the propagation of nerve impulses or on electric fields and currents. The mechanism of unification is analysed and tests for its effectiveness are described. The following conditions favour unison: high temperature and calcium, low potassium and sodium, diminution in afferent nerve impulses (in patterns), increased polarization (or injury potentials), the drugs nicotine and caffeine.

Further analysis is made with caffeine, which leads to large repeated waves which may travel along the hemisphere. These are described in detail; and also the control of their size, shape, frequency, speed, and direction of travel by temperature and polarization.

The spreading caffeine waves are not stopped by nicotine, which blocks synaptic conduction; they cross a complete transection of the hemisphere when the two

halves are in good apposition, and so in electrical mechanism can regulate nerve-cell beats and cause a spreading activation. This may prove of considerable importance in the interpretation of normal activity, electronarcosis, and of the massed " convulsive " action of the cortex in epilepsy.

A theoretical explanation of the mechanism of spread is presented. It demands the existence in brain of maintained polarization gradients in certain directions. These have been found present as predicted. (Authors' abstr.)

Insulin Shock Treatment of Schizophrenia.

The method used and general observations made during insulin shock treatment of schizophrenia are discussed.

From November, 1936, to March, 1939, 76 cases of schizophrenia were treated: 56 of them finished the complete course of therapy; the remaining 20 are either still taking the treatment or the treatment was interrupted for various reasons.

A higher percentage of patients in China compared with those in western countries proved to be unfit for insulin shock treatment. Observations point more to climatic than to racial differences.

From this study, the prospect for remission appears to be dependent on the duration of the disease, the type and course of schizophrenia as well as the form of the onset, cases with an acute onset showing more inclination for remission than those with a gradually progressive course.

The duration of the treatment until remission is not dependent on the duration of the disease.

Remissions in certain cases with protracted treatment or late remissions after shock therapy cannot be positively considered as the result of the shock therapy.

The shock usually decreases during the course of treatment.

In one particular case the shock dose fluctuated in accordance with the mental condition of the patient.

Relapses occurred in 5 of the 20 cases with full remission after the shock therapy. (Author's abstr.)

Clinical Observations in the Insulin Treatment of Schizophrenia.

1. Observations of symptoms of 6,587 insulin treatments recorded on special charts with regard to quality and time of appearance showed that the symptoms succeed each other in a definite and constant order.

2. The progression of symptoms is determined phylogenetically and moves in an order inverse to the phylogenetic age of the layers. At first the activity of the cortex becomes suppressed, releasing the syndromes of the basal ganglia. As time progresses activity of the basal ganglia ceases, giving way to a release of the mid-brain. Finally centres in the medulla oblongata are released.

3. If the signs of release of the medulla oblongata have lasted beyond the time in which pin-point pupils were observed and corneal reflex disappeared, a protracted shock may be expected. Release of medulla oblongata has, therefore, to be considered as the biological border of the therapeutic application of the insulin effect.

4. The time of appearance and disappearance of symptoms depends upon the size of the dose. Increase of the dose speeds up, decrease of the dose slows the rate of progression. Sensitization is another factor affecting the time of appearance of the symptoms. The dose does not influence the sequence of the symptoms.

5. In order to adapt the insulin effect on the brain to the therapeutic purposes, the writer proposed a standard time of five hours.

6. The pharmacological shock has to be managed in this way, that medullary symptoms (tonic extensor spasms, parasympathetic syndrome) are to be expected in the last half of the fifth hour.

7. The shock seems to be therapeutically sufficient if the tonic phase has lasted no less than one hour. (Author's abstr.)

AM. J. PSYCHOL.

VOL. LIII. APRIL, 1940.

ANAL. DEL INSTIT. DE NEUROL. URUGUAY.

VOL. II. 1939.

Two Cases of Brachial Palsy due to Injections of Antitetanic Serum.

Two cases of paralysis accompanying intense serum reaction in the form of oedema and urticaria. One case had had a previous serum injection nine years before; the other case was having his first injection of antitetanic serum. With the appearance of these symptoms the patients noted pain and loss of power in the arm.

The type of paralysis was that of the L'Hermitte syndromes with no disturbance of sensation. Both cases recovered rapidly.

The Value of the Electro-encephalogram Compared with that of Ventriculography in the Localization of Cerebral Hydatids.

It is claimed that the electro-encephalogram permits the differential diagnosis of hydatid cysts from tumours in that the zone of high-frequency waves of high potential surrounding cerebral tumours is absent in the case of hydatids.

ANN. MÉD. PSYCHOL.

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VOL. XCVIII. JANUARY, 1940.

FEBRUARY.

MARCH.

ARCH. ARGENTINOS DE NEUROLOGIA.

VOL. XXI. NOS. 5–6. 1939.

Subdural Chronic Haematoma.

The formation of a subdural haematoma predicates the absolute integrity of the subdural space. This explains the fact that a subdural haematoma can never arise as a sequel of operative interference when the walls of the space must necessarily be breached. In the diagnosis ventriculography is a necessary and decisive step.

Suppurative Epiduritis.

Suppurative epiduritis signifies an acute infection of the fatty tissue of the epidural space and corresponds to the acute perimeningitis of Albers. This paper gives a review of our present knowledge of the symptomatology, pathology and treatment of this condition, together with a complete bibliography.

ARCH. NEUROL. PSYCHIAT.
VOL. XLIII. MARCH, 1940.

Spread of the Epileptic Discharge: An Experimental Study of the After-discharge Induced by Electrical Stimulation of the Cerebral Cortex.

The spread of the epileptic after-discharge induced in monkeys by electrical stimulation of the cerebral cortex was studied, using several indexes of epileptic activity. These indexes are, first, the spread of clonic movements; second, the local changes of blood flow in the cerebral cortex during epileptic activity. These changes, which in themselves cast light on the nature of the epileptic discharge, cast additional light on the nature of the epileptic discharge by helping to reveal the manner in which the epileptic discharge spreads. Two types of procedures altering the spread of this discharge have been carried out, namely, section of the corpus callosum and transcortical section at right angles to the central sulcus of Rolando.

This study has concerned mainly the motor regions, so as to correlate the motor manifestations of the fit with the other concomitant phenomena of the epileptic discharge. Some observations have been made on other areas of the cerebral cortex. The following conclusions have been reached :

1. The after-discharge induced by electrical stimulation of the cortex is a faithful experimental counterpart of clinical types of epilepsy. Various motor variants have been observed which appear to be identical in their characteristics with those seen in certain clinical forms of epilepsy. The changes in blood flow in these animals during fits are the same as those seen in man during epileptic fits. The changes in electrical potential during and after epileptiform fits are the same in monkeys as they are in man during epileptic seizures.

2. A constant type of fit is easily reproducible in monkeys by electrical stimulation of the cortex. A study of the various factors which influence it renders the mechanism of these epileptiform fits accessible to experimental analysis.

3. The corpus callosum plays a definite role in the spread of the epileptic discharge from one hemisphere to the other, and this is demonstrable by all the indexes of epileptic discharge, although it is best recorded and illustrated graphically by the electrical activity.

4. Epileptic discharge from one hemisphere, if widespread over that cortex and prevented from spreading to the other hemisphere by section of the corpus callosum, gives rise to contralateral clonic movements and ipsilateral slow tonic movements, the latter being due, at least in part, to epileptic discharge from an area in the premotor region governing ipsilateral movements.

5. Epileptic discharge of the neurons of the ipsilateral areas of the cerebral cortex gives rise to a large part of the tonic element of the convulsion.

6. Transcortical section at right angles to the central sulcus, if it is of sufficient extent in a sagittal direction and of sufficient depth, alters the pathway for the spread of the epileptic discharge. This appears to be due to interruption of certain corticocortical association pathways. A significant characteristic circuitous pathway involving the corpus callosum and contralateral motor cortex is then evident in the spread of the epileptic discharge.

7. With the cerebral cortex intact, subcortical centres play a secondary role in the spread of the epileptic discharge.

8. The spread of the epileptic discharge takes place by neuronal pathways.

(Author's abstr.)

Heat-regulatory Mechanisms in Normal and in Schizophrenic Subjects; Under Basal Conditions and after the Administration of Dinitrophenol.

A study was made of the skin and rectal temperature, the oxygen consumption rate and the rate of evaporation of insensible perspiration under controlled environmental conditions of 30° C. and 20 per cent. relative humidity in 20 normal controls and 20 otherwise healthy schizophrenic patients in a chronic stage of the psychosis. The investigation was carried on under identical conditions on two days, on the first of which no medicament was given, and on the second of which 300 mgm. of dinitrophenol was administered by mouth to each subject.

Under basal conditions the normal subjects showed a distinct elevation of skin temperature, a rise in the rate of oxygen consumption and a slight fall in the rate of evaporation. The patients showed little increase in temperature, no change in the rate of oxygen consumption and a more rapid fall in the rate of evaporation.

After the administration of dinitrophenol, the normal subjects showed an increase in skin temperature up to 2·2° C. (3·96° F.), an elevation in the oxygen consumption rate of 31 per cent. and an augmentation in the evaporation rate of 51 per cent. The patients showed less reactivity to the drug, the corresponding changes being 1·3° C. (2·34° F.), 25 per cent. and 28 per cent. respectively.

In the chronic stage of the psychosis, schizophrenic patients show less reactivity to metabolic stimulation than do normal subjects. (Author's abstr.)

Mineral Content of the Brain: Changes in Experimental Animals Following Injection of Insulin and Metrazol.

Microincinerated sections of the brains of rabbits treated with either insulin or metrazol or a combination of the two, by a technique similar to that employed in the treatment of patients with psychoses, showed marked changes in the mineral content of the cerebral neurons. These changes consisted of dust formation, hypomineralization, vacuolation or complete demineralization of the ganglion cells. The changes were prominent in the cornu ammonis, but were also observed in other parts of the brain and appeared to correspond with those in sections stained with cresyl violet. Dust formation and complete demineralization indicated severe damage to the protoplasm, and could be observed as long as 117 days after completion of treatment.

Brains of normal and hypoglycaemic rabbits and guinea-pigs did not present any significant difference in total water content.

Since comparative studies of the brains of normal and of treated guinea-pigs did not show any significant difference in the total amount of minerals present, it was thought that there was no actual loss of total ash in the central nervous system.

Experiments in which material was obtained for biopsy during the individual insulin shock and during and at certain intervals shortly after a metrazol seizure showed that changes were present immediately after a convulsive seizure, but that these changes were completely reversible after a certain time.

(Authors' abstr.)

The Electroencephalogram in Cases of Neoplasms of the Posterior Fossa.

Electroencephalographic findings in seven cases of neoplasms of the posterior fossa and one case of neoplasm of the third ventricle with secondary involvement of the posterior fossa have been presented. In all cases pathologic foci of delta waves were shown posteriorly, primarily over the occipital lobes. Of three cases in which examination was made before and after operation, post-operative improvement was clear-cut in two and partial in one. Delta waves were present in a fourth case after partial removal of a cerebellar tumour. This patient was examined only a few days prior to recurrence of symptoms. It is suggested that the recorded delta waves were the result of secondary damage to the occipital lobes produced by pressure exerted by the lesions upward through the tentorium.

(Authors' abstr.)

Dissociation of Deep Sensibility at Different Levels of the Central Nervous System.

1. Dissociated loss of postural and vibratory sensation was found to be not uncommon with lesions of the cerebrum, brain-stem and spinal cord.

2. In seven patients with cerebral lesions causing disturbance of deep sensibility, position sense, stereognosis and two-point discrimination were lost or markedly diminished, while the appreciation of vibration was spared or slightly affected. There were no instances in which the converse was true.

3. With lesions at the thoracic and lumbar levels of the cord the opposite type of dissociation was found. Vibratory sense in the lower extremities was affected earlier and more severely than was the sense of position.

4. In three patients with compression of the cervical region of the cord and medulla, with dissociated loss of deep sensation involving the upper extremities, sense of position was more affected than that of vibration, again with astereognosis.

(Authors' abstr.)

Colloid Cysts of the Third Ventricle.

1. The most reasonable explanation of the origin of these cysts is that they arise from the paraphysis, which is an embryonic structure derived from the foetal ependyma of the anterior portion of the roof of the third ventricle. The histologic structure of the cysts seems to substantiate this view, as tubules are frequently observed in their walls and suggest origin from a glandular structure.

2. The symptoms are usually suggestive, and when combined with evidence of blockage of one or both foramens of Monro, as shown in a ventriculogram and with other neurologic findings indicating increased intra-cranial pressure and pressure on adjacent parts, make possible a preoperative diagnosis with a fair degree of certainty.

3. Surgical treatment of these cysts is remarkably successful. Both patients in this series who underwent operation recovered with cessation of all symptoms referable to the tumour. (Author's abstr.)

Myoclonus Epilepsy.

Three cases of myoclonus epilepsy are reported. A familial history of the disorder was found only in Case 2. In Cases 1 and 2 the myoclonus was associated with mental symptoms and generalized convulsions. In addition to extrapyramidal symptoms and signs present in all three cases, cerebellar signs were noted in Case 2.

In Case 1 the central nervous system was studied histopathologically. Inclusion bodies, consisting of amyloid and argentophilic substances, with amitotic division in some, were observed throughout the nerve and glia cells of the central nervous system, except the spinal cord. The substantia nigra and the dentate nuclei were the main sites of these bodies. In correlating the clinical picture with the pathologic changes we are inclined to attribute the mental symptoms to involvement of the cerebral convolutions, especially the frontal, and the so-called extrapyramidal symptoms to lesions in the substantia nigra. The myoclonus may possibly be due to the changes in the dentate mechanism, as in the palatal myoclonus.

(Authors' abstr.)

Electrical Activity of the Exposed Human Brain: Description of Technique and Report of Observations.

A method is described whereby action potentials may be recorded from the exposed human brain under the aseptic conditions of the operating room.

The records obtained in a mixed series of 22 cases are briefly discussed.

Records from the frontal cortex of four patients with " normal " brains in which no space-occupying lesion was present are characterized by activity of the beta type. Reduction of potential was observed when electrodes were inserted in the deeper layers of the cortex.

Large potentials were not observed in six cases of increased intracranial pressure without primary cerebral tumour. In one case of hydrocephalus high potentials were noted only after release of ventricular fluid.

In ten cases of cerebral tumour characteristic waves of high amplitude and slow frequency were observed in tissue overlying or adjacent to the tumour. Tumour tissue itself is not electrically active, but apparently exerts an effect only through functional change in the surrounding brain.

A comparison is made of activity from tissue overlying a cerebellar tumour and that from a similar area in a case of Menière's disease.

The aforementioned observations suggest as possibilities for further investigation: (1) More precise localization of potentials in the layers of the cortex; (2) the association of large potentials with normal activity observed elsewhere in the brain; and (3) the relation of the abnormal waves to the response to sensory stimulation. (Authors' abstr.)

VOL. XLIII. APRIL, 1940.

New York Neurological Society.

Philadelphia Psychiatric Society.

Michigan Society of Neurology and Psychiatry.

Temporary Arrest of the Circulation to the Central Nervous System.

The circulation to the entire body can be stopped abruptly and completely by clamping the pulmonary artery. When the pulmonary artery is released, the moment at which the circulation returns to the cerebrum can be determined accurately by observation of the retinal vessels. With this method it is possible to produce severe neurologic disability and still keep an animal alive for long periods. Twenty-four animals were subjected to periods of circulatory arrest, ranging from two minutes to ten minutes and fifteen seconds. Arrest of the circulation for three minutes and ten seconds, or less, was tolerated without any obvious neurologic disturbances. Permanent alterations in behaviour and psychic

function occurred in animals subjected to three minutes and twenty-five seconds or more of circulatory arrest. After six minutes of circulatory arrest vision and sensation suffered some degree of permanent injury. After seven minutes and thirty-six seconds of circulatory arrest there were permanent and practically complete dementia, blindness, serious sensory and auditory defects, motor and postural defects and reflex abnormalities. When the circulation was interrupted for eight minutes and forty-five seconds or longer, life could not be restored for more than a few hours. In a subsequent paper the pathologic studies on this material will be presented. (Authors' abstr.)

Tuberculoma of the Brain.

Tuberculomas of the brain occur at all ages and in a variety of types. With a few exceptions, they arise by haematogenous metastasis from a tuberculous focus elsewhere in the body, usually in the lungs or related lymph nodes. Clinical and pathologic studies indicate that tuberculomas producing the symptoms of tumour of the brain develop most frequently in adolescents and young adults with a single extracranial tuberculous focus. Tuberculomas associated with tuberculous meningitis tend to occur chiefly in children and in the presence of generalized tuberculosis. The pathologic characteristics of tuberculomas are not different from those of tuberculosis elsewhere. Tuberculomas may be positively identified by finding acid-fast bacilli in them.

Tuberculomas constitute only a small and declining percentage of verified tumours of the brain. The clinical syndromes which they produce are not significantly different from those produced by other varieties of cerebral tumour. A correct aetiologic diagnosis is made only when the patient has active tuberculosis in another organ or in the presence of a positive tuberculin reaction in a child. A history of tuberculous disease in the past is suggestive but not conclusive. Laboratory studies do not aid in the differential diagnosis. Calcified tuberculoma must be considered in the differential diagnosis of calcified intracranial masses noted in the roentgenogram.

The treatment of tuberculomas of the brain must be directed against tuberculosis as a disease, as well as toward the removal of the local lesion if possible. Experience has shown that attempts at removal of cerebellar tuberculomas almost always end in disaster, owing to the development of tuberculous meningitis. Decompressive operations may afford relief until healing can take place. Fibrocaseous tuberculomas of the cerebrum and arachnoid tuberculomas, particularly those in the Rolandic region, form the best subjects for surgical extirpation. They produce symptoms permitting early diagnosis and are accessible to removal in one piece. Good results will follow in a gratifying percentage of cases.

(Authors' abstr.)

Metrazol Convulsions.

Changes in the oxygen, carbon dioxide and sugar contents of blood from the basilic vein, the internal jugular vein and the brachial artery were followed in a group of subjects with dementia praecox in whom convulsions were induced with metrazol. The following observations were made:

A. Changes in basilic venous blood:

1. The oxygen content becomes lowered as the convulsion progresses, reaching its lowest levels near the end of the seizure and quickly returning to basal or higher than basal levels soon after the convulsion.

2. Sugar gradually increases as the convulsion progresses, usually reaching its highest levels some time after the convulsion.

B. Changes in arterial and internal jugular venous blood:

1. A gradual fall in oxygen with a rise in carbon dioxide occurs in the arterial blood during the convulsion, these changes being most marked at the end or soon after the end of the seizure. The oxygen quickly returns to original levels within

a few minutes after the convulsion, at which time the carbon dioxide gradually diminishes during the stage of hyperpnea.

2. Blood collected from the internal jugular vein immediately before or at the very beginning of the convulsion is unchanged in oxygen and carbon dioxide content. As the convulsion progresses the oxygen content gradually diminishes, so that at the end of the seizure it is at its lowest level. At this time the carbon dioxide content is increased. During the stage of hyperpnea the oxygen quickly returns to original or higher than original levels, while the carbon dioxide gradually falls.

3. An increase in sugar usually occurs as the convulsion progresses, with little change in the difference between arterial and internal jugular venous blood.

These data support the following comments: Although local cerebral vasoconstriction may immediately precede a metrazol convulsion, there is no evidence from these studies that cerebral anaemia initiates the seizure. As the convulsion progresses, however, a change occurs in cerebral blood flow, dependent on the altered relationship of blood gases and changes in blood pressure. Any change in cerebral blood flow following the convulsion is temporary, as indicated by the return of blood gases to original levels within a short time after the convulsion. There is no similarity between insulin hypoglycaemia and a metrazol convulsion as regards changes in the relationship of dextrose and oxygen. The cerebral hypoxia occurring in the former condition has only a superficial resemblance to the cerebral hypoxia of the latter condition. So far as these data are concerned, changes in mental states following metrazol convulsions and insulin hypoglycaemia cannot be explained on the basis of any common alteration in either cerebral chemistry or cerebral blood flow. (Authors' abstr.)

Action Potentials of Muscles in Rigidity and Tremor.

Electrical records were taken by means of single or multiple surface or coaxial leads from the muscles in a variety of cases of tremor and rigidity.

In paralysis agitans voluntary movements produce electrical records characterized by abnormal synchronization of the motor units innervated. A similar synchronization is reported in cases of spasticity.

The state of parkinsonian rigidity is characterized by a continuous slight innervation of the rigid muscles, even when the limb is placed in its most relaxed position. No such constant innervation is observed in cases of spasticity.

Stretching of a rigid muscle, by means of either active or passive movement, produces a marked increase in this innervation. In this respect, rigidity resembles spasticity. Deep reflexes in cases of rigidity may or may not take a " spastic " form, but they do not spread to other muscles, as in true spasticity.

A characteristic parkinsonian tremor consists of bursts of innervation affecting alternately protagonists and antagonists, at an average rate of 5·5 per second. The rate is surprisingly constant over long periods and in all the muscles affected. No such constancy is seen in " cerebellar " and in " essential " tremors.

The bursts of innervation of tremor affect all activated motor units synchronously. There is usually quiescence of antagonists during them.

The electrical activity characteristic of tremor is abolished temporarily by injection of curare under favourable circumstances. It is greatly diminished, apparently permanently, by section of the pyramidal tract in the lateral column of the spinal cord and by resection of the cortical area 6a. (Authors' abstr.)

Influence of Insulin and of Stimulation of the Sympathetic Nervous System on the Blood.

When insulin leads to a fall of the blood sugar below 50 mgm. per hundred cubic centimetres this is accompanied by a fall in the carbon dioxide tension of the alveolar air. Restoration of the blood-sugar level leads to a rise in the carbon dioxide tension (experiments on schizophrenic patients).

In deep coma the carbon dioxide tension of the alveolar air at a given level of the blood sugar is higher than at similar levels before coma occurs.

The carbon dioxide tension of the arterial blood is lowered during insulin hypoglycaemia, and restored to control levels in unanaesthetized dogs on injection of dextrose.

General excitement induced by painful stimuli and struggle leads to rise of the blood sugar and lowering of the carbon dioxide tension of the arterial blood in unanaesthetized dogs.

Injection of metrazol or epinephrine has effects on the carbon dioxide tension and the sugar of arterial blood similar to those of general excitement. All effects are reversible and are not accompanied by a change in the pH of the arterial blood.

It is assumed that excitation of the sympathetic nerve centres is responsible for the decrease in carbon dioxide tension of the arterial blood and of the alveolar air.

(Authors' abstr.)

Paraplegia in Flexion.

The frequent involuntary movements of the lower limbs characteristic of spastic paraplegia in flexion are identical with the flexor reflex or withdrawal reaction, which is greatly exaggerated in the condition. These movements result from various stimuli to which parts below the level of the lesion are unavoidably exposed. Although the patellar and Achilles reflexes, particularly the former, may be sluggish or unobtainable, the hamstring reflexes remain active.

Extramedullary tumour and caries of the spine are perhaps the most frequent causes of paraplegia in flexion. The condition has been seen, however, in a number of cases of intramedullary tumour, multiple sclerosis, acute myelitis, acute encephalomyelitis and subacute combined degeneration. It may be associated with any lesion of the cord which leaves the reflex pathways of the lumbosacral segments functionally intact, and isolates these segments to a considerable degree from the influence of higher levels.

Although always the result in cases of lesions of the cord of extensive interference with spinal conduction, paraplegia in flexion is not necessarily indicative of an irreversible lesion. Though generally coming on some time after the lower limbs are entirely paralysed, it may appear relatively early when the paraplegia has an abrupt onset or is rapidly progressive.

When reflexes return to the lower limbs after complete transection of the cord, they behave in a manner more or less characteristic of paraplegia in flexion ; if a spastic contracture develops it is generally one in flexion. When the cord is gradually compressed to a degree amounting to total section, however, the extensor muscles may remain in a spastic state over long periods.

Paraplegia in flexion resulting from supraspinal lesions appears to be most frequent in cases of diffuse cerebral degeneration with progressive dementia and pseudobulbar palsy.

Development of a spastic contracture in flexion is due primarily to exaggeration of the flexor reflex. As the lower limbs are brought into the flexed position, a fixation reflex, or shortening reaction, is induced in the flexor muscles. This reflex tends to hold the limbs in a flexed position for longer and longer intervals until the stretch reflex becomes augmented to the degree that the limbs can no longer be passively extended.

There is ample evidence, both clinical and experimental, to support the view that for any great release of flexor reflexes not only the pyramidal tracts but other descending pathways must be involved.

Decubitus ulcers and other sources of painful stimuli are a potent factor in the exaggeration of the flexor reflex. A poor general condition, which is believed to have a depressing effect on the extensor reflexes, may also contribute to the development of a flexion contracture. There is reason to suspect that, on occasion, these two factors have the effect of a more extensive anatomic lesion in the central nervous system. (Author's abstr.)

BUL. SOC. PSIHOL. MED. SIBIU.

VOL. VI. 1939.

BRAIN.

VOL. LXIII. MARCH, 1940.

The Forms of Growth in Gliomas and their Practical Significance.

The mode of growth of 120 necropsy cases of glioma was studied by means of large celloidin sections including the whole tumour with surrounding tissues from one end of the glioma to the other (incomplete serial section study). This method is indispensable because the true limits and extent of most gliomas are not macroscopically visible. The great majority of gliomas are more extensive than their macroscopic aspect might lead us to suppose.

Only one rare kind of glioma shows a purely expansive mode of growth, the ependymoma. However, even in rare cases of ependymoma, a circumscribed infiltrative form of growth has been observed.

All the other gliomas, without exception, show an infiltrative type of growth, although in widely differing degrees. This degree by no means corresponds to the more or less " malignant " aspect of the glioma cells. On the contrary, cerebral astrocytomas are the most invasive of all cerebral tumours, while glioblastomas include a considerable percentage of fairly well-defined neoplasms with a narrow zone of growth. The cytological tumour entities include gliomas of quite different types of growth ; thus proving yet again that cytology and histogenesis are insufficient to characterize the biological behaviour of a given glioma.

Only about 30 per cent. of all gliomas are relatively circumscribed tumours the real extent of which exceeds but moderately their macroscopically visible limits. This group includes oligodendrogliomas, about 20 per cent. of glioblastomas, many cerebellar astrocytomas and certain medulloblastomas. Factors underlying this surgically rather favourable mode of growth are : (1) A narrow, compact zone of growth ; (2) a halting of the tumour at certain pre-existing structures, especially the cortex ; (3) degenerative processes at the edge of the glioma. Tumours of the hippocampal region and the septum lucidum grow frequently in the form of round, expansive masses in the ventricular cavity.

About 60 per cent. of all gliomas have a more diffuse character with a widespread zone of growth considerably exceeding the macroscopically visible " tumour," and involving more than one lobe. Nearly 35 per cent. show what is probably a secondary diffuse growth (especially in the form of " secondary structures "),

while 25 per cent. must be considered as primarily diffuse neoplastic processes forming no circumscribed tumour. All cerebral astrocytomas, without exception, belong to this group. In the common case of malignant dedifferentiation of an astrocytoma into a glioblastoma, often the glioblastoma alone is visible as a macroscopic "tumour," surrounded by a large astrocytoma zone the true character of which is discovered by microscopic examination only.

About 10 per cent. of all gliomas—most of them belonging to the glioblastoma group—show a primarily multicentric type of growth; in half of the cases this multicentricity is only visible on complete microscopic study, the macroscopic examination showing only one main tumour.

Infiltration and destruction by growth are by no means necessarily associated in gliomas. Long-continued preservation of nerve cells and nerve fibres in the midst of tumour tissue is not specific for astrocytomas (although most constant in this group), but occurs also in glioblastomas.

The practical importance of these various findings is discussed.

(Author's abstr.)

Pyramidal Lesion in the Monkey.

Reinterpreting the results of pyramidal lesion, the functions of the pyramidal tract are characteristically organized both in space and in time. The spatial organization derives from a relatively stable topographical relationship between loci in the cortical field of origin of the tract and loci in the motor mechanism of the spinal cord. The fineness of this topographical organization underlies the unique feature of corticospinal function: the ability to bring into action any portion of the skeletal musculature, and in all combinations. This detailed control of the skeletal musculature enables the discrete usage of the musculature, especially of the digits, and the modulation of extrapyramidal activity, which are outstanding pyramidal functions. Furthermore, by increasing the excitation in specific portions of the segmental mechanism, it may enable fragments of the stereotyped patterns of extrapyramidal activity to be brought to threshold as part reactions, detached from the frame which usually gives them usefulness. The pyramidal tract operates in a crossed relationship on the extremities, but bilaterally on the axial musculature other than abdominal.

The functions of the pyramidal tract are not, however, covered by description, no matter how detailed, of results of stimulation in its field of origin because the organization in time is not in this manner brought out. In time, the pyramidal tract operates in two phases. On the one hand is a continuous, or tonic action in effect at all times in the waking state. On the other hand is a specially timed increase of discharge, or phasic action, which is evoked in relation to particular situations. The tonic function contributes to the excitatory state throughout the spinal cord, supporting muscle tone, keeping thresholds low, facilitating, reinforcing, steadying and moderating whatever tonic or phasic activity may be set in train at segmental or suprasegmental levels. The delivery of this excitation is not to all parts equally, but is influenced by original preponderance, and by postural and other immediate factors. Its volume is a function of the temper of the individual and of extraneous factors of great variety, reaching its lowest level short of sleep when the animal verges on sleep either from exhaustion or from boredom.

The phasic or episodic function initiates movement or speeds initiation. It enters into all somatic motor activity or any complexity, to confer on the stereotyped extrapyramidal performances: adjustability in space, modifiability in the course of execution, and all the modulations of pattern which make for aim, accuracy, economy, lability and finish. More than this in the primate, this function enables the discrete usage of the musculature, and especially of the digits, which is characteristic of the order.

Together, the tonic function provides for smooth, continuous, efficient action while the phasic function contributes, outstandingly, precision and lability to total

performance. In the realm of somatic motor function both of these are unquestionably motor or excitor functions. Of inhibitory function as such there is no evidence.

On the vascular system, the corticospinal system likewise exercises a continuous influence in the waking state which supports dilator tone and facilitates, reinforces and moderates reflex action. Whether this influence is excitatory of dilatation or inhibitory of constriction is uncertain. Also whether or not there is a further phasic action has not been determined.

Function of the pyramidal tract is thus co-extensive in time at least with the waking state, and determined in intensity by both general and specific demands of that condition. It is distributed to the entire somatic motor mechanism of the body, and to parts of the autonomic mechanism, the survey of the autonomic relationship being as yet incomplete. It is organized in complexity to match virtually the full range of activity, from simple tonic functions wherein it merely assists, to complicated performances which are primarily its responsibility. Although traditionally the pyramidal system has been considered "the voluntary motor pathway," this is too sweeping. An impressive capacity for voluntary movement survives pyramid section, especially if the lesion be bilateral, forcing the issue. Conversely, some activities eliminated by pyramidal lesion, for example the contact replacing reactions, must be considered, if not involuntary, at least highly automatic. By virtue of its tonic action on the spinal cord, pyramidal function must assist all somatic motor activity, if not, indeed, all motor activity of the waking animal, at whatever level initiated, even the spinal reflex level, without regard for the voluntary or automatic quality of particular acts. As the agent of lability, however, the pyramidal tract makes a unique contribution to total performance. Together, the all-pervading, and the discrimination qualities of cortico-spinal action afford the cerebral cortex that influence in virtually all realms of final motor action, and that minuteness of control which determines its effectiveness as an agent of choice. In this service of choice the pyramidal tract is unquestionably the outstanding, though not the exclusive voluntary motor pathway.

(Author's abstr.)

BRIT. J. PSYCHOL.

VOL. XXX. APRIL, 1940.

CERVELLO.

VOL. XIX. MARCH, 1940.

Variations in Sodium and Magnesium in the Blood during Convulsion Treatment with Acetylcholine in Schizophrenia.

The author found an hour after intravenous injection of acetylcholine in convulsive doses that there was an increase in the amount of sodium in the blood and a decrease in the amount of magnesium. G. W. T. H. FLEMING.

L'ENCÉPHALE.

VOL. XXXIV. JUNE, 1939.

Investigations on 100 Patients Admitted to the Special Service for Alcoholic Insanity in the Department of the Seine.

A detailed report and statistical analysis of 100 consecutive admissions. The main factors considered are the family, personal and social background, the drinking habits and the physical and mental symptoms. The series is divided into three groups, heavy (36), moderate (31) and non-drinkers (33).

The first group was characterized by a prolonged history of steady, heavy drinking, a late onset of psychotic symptoms and well-marked somatic evidence of alcoholism. There was frequently an alcoholic heredity and the onset of the psychosis was often associated with behaviour disorders, which had brought the subject into conflict with the police. For this group, alcohol was considered the essential aetiological factor and the immediate prognosis was good.

In the second group there was only moderate or periodic excess and a poor tolerance for alcohol. The psychosis occurred earlier and was preceded by evidence of mental instability. Somatic signs of chronic alcoholism were absent. Many showed a psychotic or epileptic heredity. The confusional onset usually evolved towards chronic mental illness. In this group alcohol was regarded as only an associated cause. In the third group alcohol intake was absent or considered to be without significance for the psychosis. S. M. COLEMAN.

INT. J. PSYCHOANAL.

VOL. XXI. JANUARY, 1940.

An Outline of Psycho-analysis.

This work, commenced in 1938, was left unfinished. The first part deals with the nature of mind ; its division into id, super-ego and ego ; the theory of instincts ; the development of the sexual function and the hypothesis of the unconscious. The second part is concerned with the technique of psycho-analysis and with the male and female reactions to the oedipus situation. In the third part, left incomplete, the value of the practical application is reviewed. S. M. COLEMAN.

APRIL.

J. COMP. NEUR.

VOL. LXXII. APRIL, 1940.

J. COMP. PSYCHOL.

VOL. XXIX. APRIL, 1940.

The Effect of Testosterone on the Sex Behaviour of Female Rats.

Ten normal young adult female rats were given injections of testosterone and testosterone propionate over a period of two months. Sex behaviour was tested, and vaginal smears were made throughout this time and for several weeks before and after it.

Vaginal cycles and high degrees of heat behaviour were repressed, but eight of the ten rats continued to accept aggressive males throughout the injection period in spite of diestrous smears.

Masculine sex behaviour was considerably increased during the injection period and disappeared rather rapidly thereafter.

The ovaries made a prompt recovery also, as shown by resumption of normal cycles and sex behaviour and by subsequent reproductive performance about equal to that of the untreated females of the colony. But the clitorides, which had hypertrophied under the influence of the injections, were not noticeably smaller in the animals autopsied twelve months after the last injection than in those sacrificed immediately after the cessation of injections.

The existence of the male copulatory behaviour pattern in the untreated female and certain stimuli which are especially effective in bringing it out are discussed. The failure to lower its threshold by permitting only female companions during pubescence and early adult life is also mentioned.

It is concluded that the male copulatory pattern in more or less rudimentary form is part of the equipment of the normal female rat. The threshold of this behaviour pattern is very high normally, but it can be lowered by testosterone administration which, however, although suppressing vaginal cycles, does not completely eliminate female sex behaviour. (Author's abstr.)

J. CRIM. PSYCHOPATHOL.

VOL. I. APRIL, 1940.

J. EDUC. PSYCHOL.

VOL. XXX. 1939.

J. EXP. PSYCHOL.

VOL. XXV. 1939.

VOL. XXVI. 1940.

J. GEN. PSYCHOL.

VOL. XXII. APRIL, 1940.

J. GENET. PSYCHOL.

VOL. LVI. MARCH, 1940.

J. NERV. MENT. DIS.

VOL. XCI. FEBRUARY, 1940.

A Comparison of Treatment in Hypertension.

This report is based on a study of 92 consecutive cases. It is concluded that most instances of hypertension are central in origin and that psychotherapy is the most important factor in treatment; it should be supported by dietary, rest and medicinal treatment. The wide use of operation, splanchnic resection, adrenalectomy, etc., is not to be encouraged. S. M. COLEMAN.

Shock Therapy in Korsakoff's Psychosis.

Report of a case of Korsakoff's psychosis successfully treated by insulin shock. It is concluded that this form of therapy is particularly suited for the more chronic types of alcoholic psychosis. S. M. COLEMAN.

J. NEUROL. PSYCHIAT.

VOL. III (N.S.). APRIL, 1940.

Antibodies to Brain and Their Relation to Demyelinization.

It was found impossible to produce lesions in the brain of rats who had received injections of rabbit serum containing brain antibodies. The rabbits had received intraperitoneal injections of brain emulsion for three months, the technique corresponding to that employed by Masugi and others to produce experimental glomerulonephritis in animals. The result suggests that the demyelinization found in animals is probably not to be explained as due to the development of autogenous antibodies to brain or to some " cerebrotoxin " developed in the presence of brain lipoids. (Authors' abstr.)

Atrophy of the Thalamus in a Case of Acquired Hemiplegia Associated with Diffuse Porencephaly and Sclerosis of the Left Cerebral Hemisphere.

Clinical and pathological details are given of a case in which a hemiplegia, acquired in childhood, is associated with diffuse atrophy of the corresponding cerebral hemisphere and conspicuous atrophy of the optic thalamus.

With the exception of a few specified areas the cortex is replaced by spongy

glial tissue from which almost all the neurones have disappeared. The result is practically equivalent to an experimental hemidecortication.

Thalamic atrophy is practically complete on the affected side with the exception of the centre median nucleus, the lateral geniculate body, and a narrow subependymal zone of small cells. From this it is concluded that all other parts of the thalamus are concerned with the projection of impulses on to some part of the cerebral cortex. The connections of the centre median nucleus remain obscure.

(Author's abstr.)

J. PARAPSYCHOL.

VOL. III. 1939.

J. PHYSIOL. U.S.S.R.

VOL. XXVI. NO. 6. 1939.

Micro- and Ultra-Elements in the Brain.

In the investigation of the elementary constituents of living organism the composition of nerve tissue and especially of the brain of vertebrates has not received due consideration. The object of the present work was a study of the elementary composition of the various parts of the brain in the cat (*Felis domestica*). The distribution of the elements Si, Cu, Zn, Mn, Al, Pb, Mo, Ti is of special interest.

The copper content of the white and grey substance and of the cerebellum is equal in the cat, while there is a definite accumulation of copper in the medulla. Zinc is entirely absent from the medulla, in the cerebellum there is but a faint indication of Zn lines, in the grey substance they are somewhat more clearly marked, while a concentration of Zn takes place in the white substance of the brain.

The partition of molybdenum is of particular interest.

In the cat's brain molybdenum is present in noticeable amount in the white substance: there are traces of Mo in the cerebellum, while none are detectable in the other parts of the brain. (Authors' abstr.)

VOL. XXVII. NO. 7.

On the Conditioned Cortical Bonds Established upon Morphine Administration.

1. The conditioned morphine vomiting reflex is completely identical, with regard to functional structure and sequence of phases, with the complex act of vomiting in response to direct morphine administration. The conditioned reflex is acquired fairly rapidly provided that the isolated conditioned stimulus is regularly applied prior to the moment of morphine administration. The reflex is of the delayed type with a lag time of 8–10 minutes, corresponding to the time interval required for the full development of the act of vomiting with all its phasic phenomena.

2. The conditioned morphine reflex (vomiting and hypnotic) displays the character of a generalized response to the entire pattern of experimental surroundings. Its specialization without the counteraction of an inhibitory stimulus is rather difficult, though quite possible in principle.

3. The stability of the conditioned vomiting reflex and the intensity of its experimental manifestation depend upon the excitational condition of the nervous centres controlling the act of vomiting.

4. Supraliminar inhibition called forth by chronic over-excitement of the central regulatory apparatus of the act of vomiting results in a more or less marked depression of the conditioned morphine response. (Author's abstr.)

Conditioned Dyspnoea of Toxic Origin.

1. The conditioned morphine response, manifesting itself in combined disturbances of the activity of various physiological systems (circulation, secretion, respiration) represents a peculiar conditioned cortical bond established upon definite alterations of bodily function.

2. Alteration of respiratory function is the most sensitive index of the disturbances arising through the effect of morphine, or of the conditioned stimulus acting as a substitute for the drug.

3. Conditioned reflex dyspnoea is less subject to external or internal inhibition than is the basic vomitory conditioned reflex. Upon partial inhibition of the vomitory reflex owing to supraliminar inhibition of the parabiotic condition of the centre the respiratory phenomenon exhibits no decrease, persisting as a sensitive reagent to conditioned and non-conditioned stimulation.

4. This viewpoint supplies a basis for the understanding of the importance of functional polypnoea and dyspnoea in various nervous diseases where they play the part of prodromal phenomena preceding disturbances of wider extension arising from obstacles to nervous function. (Authors' abstr.)

NO. 9.

Solution of the Ukhtomsky Problem.

A method has been developed for the stimulation of nerve with varying sinusoidal potentials at different frequencies. The curve of thresholds of the frog's nerve-muscle preparations has been investigated in relation to the frequency of applied potentials (from 10 to 14,000 Hz). The conditions have been determined for the existence of Ukhtomsky's area and its shape has been established. The

curve of onset of maximal tetani has been explored in relation to frequency (from 10 to 14,000 Hz). A determination has been made of the curve of Wedensky's optima at varying frequencies. (Author's abstr.)

Measurement of Motor Chronaxie as a Method for the Investigation of Sleep Inhibition in Man.

The alterations of motor chronaxie during sleep, established by Bourguignon and Haldane, are fully corroborated by the author's experiments. The values of motor chronaxie undergo a gradual rise as the sleep grows deeper, attaining a maximum level at the stage of profound sleep and rapidly decreasing in the stage of awaking, the original level being restored at wakefulness.

The relation between these changes of chronaxie (and also of rheobase) and the development of sleep is evidently a direct one. It is suggested that peripheral chronaxie reflects the functional state of the centres, undergoing alterations that depend upon the intensity of sleep inhibition which arises, according to the concepts of the Pavlov school, in the cerebral cortex and gradually spreads to the subcortical ganglia, including the red nuclei.

The application of the chronaximetric method to the investigation of the physiology of human sleep is very promising, and will doubtless be of considerable theoretical and practical importance. The authors are happy to state that the present work is a reply to the challenge of Prof. Lapicque, in his report to the XVth Physiological Congress, to attempt a synthesis of the theory of chronaxie and Pavlov's theory of conditioned reflexes. (Authors' abstr.)

The Phenomenon of Equalization of the Chronaxies of Antagonists During Sleep in Man.

The authors have demonstrated for the first time a phenomenon consisting in the equalization of the chronaxies of antagonists during normal sleep in human subjects. In two experiments (without the use of hypnotic drugs) they observed a distinct tendency to equalization of chronaxie in antagonists : as the sleep grows deeper, the increase of the flexor's chronaxie is several times superior to the increase of the extensor's chronaxie. In other experiments made with the administration of hypnotics, the authors observed complete equalization of the chronaxies of the antagonists in 10 cases. Equalization is attained at a high level, coincides with the objective symptoms of maximal sleep and occurs simultaneously with the moment of equalization of the chronaxies of the antagonists. On this basis, the authors believe that the phenomenon of equalization can be utilized as an objective quantitative index of the maximum depth of sleep, possibly the limit of depth of sleep. From the viewpoints of Lapicque's and Pavlov's teachings, a hypothetical explanation of these data is suggested : sleep inhibition, arising in the cerebral cortex and gradually descending to the subcortical region and lower, reaches the system of the red nuclei and abolishes their function of subordination. Such might be the mechanism of the phenomenon of equalization of maximal depth of sleep.

(Authors' abstr.)

Alterations of Motor Chronaxie in the Course of Natural Sleep in Healthy Human Subjects.

On the basis of their experimental investigations the authors arrive at the following conclusions :

1. The development of sleep is associated with corresponding alterations of motor chronaxie, namely, increase of chronaxie with deepening of sleep and decrease of chronaxie as the sleep becomes less deep. A regular relation exists between the variations of the level of chronaxie and the dynamics of sleep inhibition.

2. At the stage of profound sleep a phenomenon of equalization of the chronaxies of antagonists is observed, coinciding with complete relaxation of the muscles.

3. At maximal depth of sleep a reversal of the ratio of chronaxies of the antagonists takes place, the level of the flexor's chronaxie being superior to the level of

the extensor's chronaxie. This phase of reversal is always attained at a higher level than the phase of equalization.

4. The data obtained justify the application of chronaximetry as a new method for the investigation of sleep and hypnotic states in human subjects.

(Authors' abstr.)

NO. 10.

Chronaxie during Exercise as Related to the Dynamics of Nervous Processes.

The author made an investigation of the alterations of the chronaxie in the biceps muscle of the right arm, resulting from the influence of work performed by different muscles of the upper extremities.

It has been shown that exercise affects the chronaxie not only of the working, but likewise of the resting muscles; the character of the alterations of chronaxie in the muscle not involved in exercise depends upon which muscles perform the exercise.

Work of the extensors of the right arm mostly results in increase of the chronaxie of the homolateral biceps during the exercise and in its decrease after the exercise.

Work of the extensors of the contralateral arm usually leads to decrease of the chronaxie of the biceps during the exercise and to an increase after the exercise.

During exercise of the flexors of the opposite arm the chronaxie of the right biceps is increased in most cases. A decrease of chronaxie after the exercise is of considerably less frequent occurrence.

It is likely that the phenomena here reported are related to the processes of successive and simultaneous induction in the central nervous system and to the reciprocal division of impulses in the muscles of the upper extermities.

(Author's abstr.)

NO. 11.

J. PSIHOTEH.

VOL. III. 1930.

J. PSYCHOL.

VOL. IX. APRIL, 1940.

J. SOC. PSYCHOL.

VOL. X. NOVEMBER, 1939.

VOL. XI. FEBRUARY, 1940.

J. SPEECH DISORDERS.

VOL. IV. 1939.

MIND.

VOL. XLIX. APRIL, 1940.

NEUROBIOLOGIA.

VOL. II. NO. 2. JUNE, 1939.

Biotypological Studies on Cases of Schizophrenia Treated by the Meduna Method.

Observations on a small number of cases showing complete or partial remission after shock therapy gave no evidence of the efficacy of the therapy being related to the biological type of the patient.

NO. 4. DECEMBER, 1939.

The Neuroses of the Parents of Neurotic Children.

The fact that neurotic patients frequently have neurotic parents is not considered to be necessarily a proof that neuroses are hereditary, since the symptomatology of the child's neurosis may differ entirely from that of the parent. The author considers that all neuroses arise from conflicts in childhood and that the likelihood of such conflicts occurring is greatest with neurotic parents.

A Statistical Study on the Age of Insane Patients.

During the years 1931–1937, 5,055 first admissions were made to the psychiatric hospital of Recife Pernambuco. Males and females suffering from constitutional psychosis enter between ages of 16 and 35. Organic psychoses are more frequent among females of 16 to 30 years and men of 16 to 40. The toxic and infectious psychoses occur more frequently among males between 21 to 40 and females 16 to 40.

NEVRASSE.

VOL. I. JANUARY–FEBRUARY, 1940.

OCCUP. THER. AND REHABIL.

VOL. XIX. FEBRUARY, 1940.

Organizing an Occupational Therapy Department.

For the successful planning of an occupational department at a mental hospital a number of factors must be taken into consideration. The following points should be taken into account: The type of hospital (private or rate-aided); the number of patients; the situation of the institution; its financial resources and the average age, social status and environmental background of the majority of patients.

S. M. COLEMAN.

PROC. AMER. ASSOC. STUD. MENT. DEF.

VOL. XLIV. 1939.

Further Clinical and Pathologic Studies in Mongolism.

True mongoloid deficiency represents a growth disorder in which the absence of proliferative growth of cartilaginous and fibrous tissue is an essential factor. This seems to be related to some disorder of the anterior pituitary. Skull measurements of 125 mongoloid children were graphed, and comparison is made between

these growth curves and the normal one. Marked differences in circumference and length are apparent. Histologic study of the skull basis is reported upon briefly. X-ray study showed that skull features are essentially foetal in shape and proportion. The author found that any disease of the foetus producing growth disorder (such as anaemias, infectious diseases including syphilis, and certain congenital heart conditions) is able to exhibit some mongoloid traces. These are temporary arrests in growth. M. W. KUENZEL (Psychol. Abstr.).

Biochemical Studies in Mongolism.

Opposing the hypothesis that mongolism is due to a racial regression, the author publishes a distribution of the blood groups of 125 American mongoloid defectives. This is seen to be practically identical with that of the general American population and unlike that of people of the Mongolian races. Basal metabolic rates of 25 mongoloids aged 6 to 29 years are reported, and the results rule out hyperthyroidism as a condition of mongolism after the sixth year. Fasting serum cholesterols of 50 mongoloids aged 2 to 29 years were found to be within normal limits. Indications are that hypothyroidism is not present in mongolism at least after two years of age. Fasting blood sugars, glucose tolerances, serum calcium, inorganic phosphorus and phosphatase findings are also reported. Apparently a hypofunction of the pituitary accounts for the disorder. A bibliography of 19 titles is appended. M. W. KUENZEL (Psychol. Abstr.).

A Study of the Frequency of Mongolianism in Negro Children in the United States.

A questionnaire was sent to both state and private institutions for the feeble-minded and to public school systems in over 100 large cities concerning the number of mongolians in their populations. No school system reported any mongolian of the coloured race. Returns from southern schools as well as from southern institutions failed to reveal any mongolians of the coloured race. Of 1,777 mongolians in 45 institutions 21 were coloured. Of 139 cases of the mixed type with mongolian tendencies only one was coloured. Comparisons among age, sex and mental level of coloured and whites are made. M. W. KUENZEL (Psychol. Abstr.).

Mental Deficiency from Paranatal Asphyxia.

"Examination of the paranatal records of mentally defective infants and children (for whom there was no history of inherited defect, infection, or trauma unassociated with birth) has disclosed a definite relationship between foetal oxygen want and the later neurological defect." In a group of 252 children whose mental deficiency was thought due to conditions at birth, 176 (70 per cent.) were found to have a history of asphyxia. The commonest presenting symptom of cerebral cell disintegration as a result of destructive anoxia is described as a deterioration of intellect, evidenced mainly by character change and memory defect. Several figures show sections of cortex from infants delivered after long labour, illustrating degenerative cellular changes. The inter-relationship between different type mechanisms by which infant brain tissue may be deprived of oxygen with resultant cell necrosis and later evidence of mental deficiency are described. Classification of these types of anoxia follow: anoxic, anaemic, stagnant, and histotoxic. The author urges a re-evaluation of the controllable factors inducing asphyxia, among which are the optional drug and anaesthetic agents used to produce analgesia and amnesia in the mother. A bibliography of 18 titles completes the article.
M. W. KUENZEL (Psychol. Abstr.).

A Critical Analysis of Five Years' Work with Cases of Cerebral Palsy.

Of the 48 cases of cerebral palsy given treatment in one of the New York State institutions for the feeble-minded slightly more than one-third have shown improvement. The Binet IQ range of these patients was 29 to 71. Improvement occurred

in walking, feeding, and dressing. IQ's following treatment ranged from 30 to 72. However, in treatment by physical therapy it is not the degree of the child's intelligence but his degree of co-operation and initiative that counts.

M. W. KUENZEL (Psychol. Abstr.).

A Study of the Effects of Differential Stimulation on Mentally Retarded Children.

Study was made of the effect on mental growth of young children of a radical shift from one institutional environment to another providing superior stimulation. "The experimental group included 13 mentally retarded orphanage children (mean IQ 64, Kuhlmann) from one to two years of age, placed singly or by twos on wards with brighter older girls in a school for the feeble-minded. This environment was stimulating, with many adult contacts provided. As a contrast group, 12 average and dull normal children (mean IQ 87, Kuhlmann) of similar ages in an orphanage nursery were studied. Few adult contacts were afforded, with limited opportunities for play and development. Retests of both groups after two years showed marked gains in intelligence (mean IQ 60·5) for the contrast group." The author points out that "the possibility of increasing the mental capacity of 'functionally' feeble-minded children should be considered as an essential objective in setting up an individualized treatment and educational programme in a school for feeble-minded."

M. W. KUENZEL (Psychol. Abstr.).

The Effect of a Highly Specialized Programme upon the IQ in High-grade Mentally Deficient Boys.

Departing from customary methods of training, where external productivity is more important than internal changes which might take place, this specialized programme aimed at the individuals' own development of means towards ends. Constructive activity was stimulated and social approval directed toward recognition of productions, both concrete and abstract, which showed ingenuity, initiative, and original planning. In social relations individuals were required to work out their own problems. Where help was required suggestion and discussion were preferred. During informal settings abstract problems were presented for solution in order to provide experience in recognition of absurd and illogical statements. This cottage group consisted of 16 boys, aged 15 to 18 years, whose IQ's ranged from 48 to 80. An average gain in IQ of 10 points was made within a year. 81 per cent. of the cases showed a gain of 5 or more points. The gain is shown to be specific to the experimental group and does not hold in other institutional groups or control cases.

M. W. KUENZEL (Psychol. Abstr.).

PSYCHOANAL. REV.

VOL. XXVII. APRIL, 1940.

PSYCHIAT. QUART.

VOL. XIV. APRIL, 1940.

Testosterone in Psychotic Male Homosexuals.

1. Seven psychotic male homosexual patients were treated with testosterone propionate.

2. All showed some stimulation of secondary sex characteristics, as well as an increase in libido.

3. There was no change in the direction of the libido, the result being an increase in homosexual activities.

4. There was little or no change in the mental condition.

5. These results would seem to favour the view that homosexuality is of psychic origin. (Author's abstr.)

The Force Required to Crush Vertebrae : Its Probable Mechanical Relation to the Postmetrazol Fracture.

1. Several related factors probably explain the high incidence of postmetrazol vertebral fractures.

2. The relation of mechanical factors to the production of the fracture is confirmed.

3. The peculiar anatomical nature of the thoracic spine with its limitation in extension may explain in part the mechanical advantage of the spinal flexor muscles.

4. The postmetrazol fracture of the thoracic vertebral body is probably as frequent as that following epileptic convulsions.

5. It is found by direct measurement that the fifth thoracic vertebra, when longitudinally compressed, will be crushed at the periphery of its superior and inferior ventral margins by a force approximately one-third of that required to crush the body.

6. The unique construction of its trabeculae may predispose the vertebral body to a wedge-shaped deformity.

7. The compression load placed upon a vertebra seems of less importance than the recurrent impacts of the clonic-tonic-clonic convulsion.

8. Compression of the intervertebral discs following fracture of the thoracic vertebral body may occur in about 86 per cent. of cases. Invasion of the prolapsed

nucleus pulposus of the disc into the spongiosa of the vertebral body, resulting in the formation of a Schmorl's node, has been demonstrated.

9. The necessity for maintaining spinal hyperextension in preventing post-metrazol vertebral fractures and intervertebral disc complications is emphasized. Its use may result in a reduction of fractures from 50 to 8 per cent.

(Author's abstr.)

PSYCHOL. BULL.

VOL. XXXVII. MARCH, 1940.

APRIL.

PSYCHOL. REV.

VOL. XLVII. MARCH, 1940.

REV. PSIHOL.

VOL. II. 1939.

REV. DE NEURO-PSIQUIAT.

VOL. II. NO. 3. 1939.

The Latent Period in the Development of Cardiazol Fits in the Epileptic and Non-epileptic.

Contrary to expectation the latent period from the injection of cardiazol to the development of a fit is longer in epileptics than in non-epileptic schizophrenics and luminal shortens the latent period in epileptics. The length of the latent period in cases of idiopathic epilepsy is greater than in cases of symptomatic epilepsy.

A Study of the Schizophrenic Thought Processes during Treatment by Cardiazol.

This study is devoted to a critical examination of the paper by Zucker and Hubert on the changes in function found in schizophrenic thought disorder and particularly of their subjective nature.

NO. 4.

The Zig-Zag Test in Neuro-psychiatry.

It is claimed that examination of zigzag patterns drawn under standard conditions permits certain conclusions as to the mental reactions of psychotic subjects. The paper is illustrated by reproductions of actual graphs, but it is by no means clear on what evidence the conclusions are arrived at.

Complications Arising in the Treatment of Schizophrenia by Insulin Shock.

Ninety-six cases of schizophrenia treated by insulin exhibited some form of complication in 80 per cent. of their number. The complications were distributed as follows: Pulmonary and circulatory 14 per cent., spasm of glottis 6·25 per cent., prolonged coma 21 per cent., gastric and gastro-intestinal 22 per cent.

REV. DI NEUR. E PSYCHIAT. S. PAOLO.

VOL. V. NO. 3. SEPTEMBER, 1939.

The Diagnosis of Epilepsy.

Thirteen epileptics, seventeen schizophrenics, five patients suffering from general paralysis and other psychoses were given cardiazol convulsions. It was found that the threshold value of cardiazol for producing fits in cases of epilepsy was ·50 gm. In the non-epileptics the threshold was a little above this.

Urea in the Cerebro-spinal Fluid.

Urea estimations are made on 1·5 c.c. of cerebro-spinal fluid by the hypobromite method and the nitrogen extracted by using a van Slyke apparatus for alkali reserve estimations. From 500 determinations it was seen that the urea varies in normal subjects between ·15 and ·35 mgm. per thousand.

NO. 4. OCTOBER-DECEMBER, 1939.

Psychiatric Nosology.

The author protests against the description of such ill-defined conditions as schizophrenia as morbid entities. He considers that we can now usefully talk of a schizophrenic syndrome, a paraphrenic syndrome, a confusion syndrome, etc., thus recognizing about ten mental syndromes. He divides mental diseases into two groups—organic and functional.

Considerations on a Case of Facial Diplegia Probably Due to Scarlet Fever.

In studying the physiopathology of this case the author arrives at the conclusion that the lesion could not have been either extracranial or nuclear. From the fact that taste was affected in the anterior two-thirds of the tongue he considers that it must have been localized either in the meninges or the petrous bone.

SEGUNDA REUNION DE LAS JORNADAS NEURO-PSIQUIAT. PAN-AMERICANAS.

VOL. I. MARCH 20–25, 1939.

NEUROLOGY.

SOV. PSICHONEUROL.

VOL. XV. NOS. 4–5. 1939.

NO. 6.

TOHOKU PSYCHOL. FOLIA.

VOL. VII. 1939.

On the Fundamental Problem of the Spontaneous Fluctuations of the Brain Current.

Electroencephalographic studies were made on many Japanese, and from the results the authors conclude that the time from the sense stimulation to the beginning of the suppression of the alpha waves is dependent upon the intensity of the stimulus, and therefore that the sensation time, threshold, or sensitivity, etc., is measurable objectively from this time relation of the suppression of alpha waves.

T. FUJITA (Psychol. Abstr.).

The Electroencephalographic Study of Taste Sensitivity.

The sensitivity of the tongue-tip to taste stimuli was determined by measuring the time from the moment of stimulation to the beginning of suppression of alpha waves and the duration of the suppression to the reappearance of alpha waves. Distilled water of 38° C. in a volume of 0·1 c.c. dropped on the tip of the tongue evoked no sensation and no suppression of alpha waves. This indifferent tem-

perature and volume were taken as the standard for the investigation of several influences on the latent time and duration, such as the temperature, volume, or concentration of the solution of taste substances. The larger the volume and the more intense the concentration, the earlier the suppression of alpha waves took place and the longer it continued. The threshold concentration which evoked just visible suppression was determined for substances representing four taste qualities. For the solution of NaCl the latent time was shortest and the duration longest at moderate temperatures, i.e. it was most active at these temperatures. The time of the suppression of alpha waves to sense stimulation was shorter than the usual reaction time. The acuity of the tongue surface for the taste sensation measured by the suppression of alpha waves corresponded with the result obtained by the usual subjective method. T. FUJITA (Psychol. Abstr.).

Z. GES. NEUROL. PSYCHIAT.

VOL. CLXIV. NO. 4. 1939.

NO. 5.

VOL. CLXV. 1939.

THE FOURTH ANNUAL MEETING OF THE SOCIETY OF GERMAN NEUROLOGISTS AND PSYCHIATRISTS.

A. PSYCHIATRY.

B. NEUROLOGY.

C. COMMON SESSION OF THE NEUROLOGICAL AND PSYCHIATRICAL DIVISIONS.

VOL. CLXVI. NO. 1. 1939.

NO. 2.

NO. 3.

NO. 4.

Z. PSYCHOL.

VOL. CXLV. 1939.

VOL. CXLVI. 1939.

1. Biochemistry, Pathology and Physiology.*

Arsenical Encephalopathy. I. Clinical Study. Tzanck, A., and Lewi, S. [*Ann. dermatol. syphil.*, **10**, 752–70 (1939.)]

Arsenical encephalopathy is produced by trivalent arsenicals of the arsenobenzene type and by quinquevalent arsenicals derived from 3-amino-4-hydroxybenzenearsonic acid, e.g. stovarsol, treparsol, acetylarsan. It is never produced by mineral arsenicals (arsenic anhydride, arseniates, cacodylates, etc.) nor by quinquevalent organic arsenicals derived from p-aminobenzenearsonic acid, e.g. atoxyl or tryparsamide, despite the fact that these compounds may exert toxic action on the peripheral nervous system. Intravenous, intramuscular, subcutaneous, oral and vaginal administration of arsenicals have all led to encephalopathy. According to Budlowsky (*Deut. derm. Ges. in der Tschech. Rep.* (December 3, 1933)) patients with encephalopathy give negative skin tests to arsenicals. However, Kapuscincki (*Ceska Dermatol. Samberger Festschr.*, **148** (1931)) claims to have induced passive sensitization to neoarsphenamine by injection of serum from a patient showing intolerance to this drug. Five cases are presented of encephalopathy due to neoarsphenamine; two of the patients were pregnant women, who seem, as a group, to be especially susceptible to this disorder.

MARION HORN (Chem. Abstr.).

Golgi Apparatus and Vitamin C. I. Review. Miwa, Atunobu. [*Oriental J. Diseases Infants*, **25**, 38–9 (1939) (*in English*).]

Vitamin C probably plays a part in the fixation of Golgi apparatus by the reduction of $AgNo_3$ and osmic acid.

II. Experimental Studies. I. [*Ibid.*, **25**, 40.]

An aqueous solution of vitamin C, 1 : 50,000, reduces 10 per cent. $AgNO_3$; a vitamin C solution, 1 : 6,000, reduces 10 per cent. $AgNO_3$ containing 1 per cent. glacial AcOH. Histochemical pictures showed that the Golgi apparatus and vitamin C in the tissues of rabbits and hens were closely related. The histochemical

* A number of abstracts in this section are reproduced from *Chemical Abstracts* by kind permission of Prof. Crane, of Ohio University, to whom the Editors wish to express their thanks.

pictures of the Golgi apparatus and vitamin C in the tissues were greatly enlarged after an injection of vitamin C into the portal vein of the living rabbit.
RUTH BERGGREN (Chem. Abstr.).

Benzedrine and Brain Metabolism. Mann, P. J. G., and Quastel, J. H. [*Nature*, **144**, 943–4 (1939).]

Benzedrine stimulates the O uptake of brain in vitro when this respires in the presence of certain amines. This is accomplished by an inhibition of the formation of toxic aldehydes. E. D. WALTER (Chem. Abstr.).

Chemical Changes in the Blood Vessels Occurring with Age. Burger, M. [*Z. ges. Neurol. Psychiat.*, **167**, 273–80 (1939).]

In human aortas from individuals aged 10–70 years, the cholesterol, Ca, total P and acid-soluble P contents increased with age, while the lipoid P and phosphatide contents did not change markedly and the total lipoid increased to 50 years and then decreased somewhat. Aortas from cattle aged 1–15 years and from horses aged 1 to over 25 years likewise showed an increase in cholesterol and Ca contents with age. The human, beef and horse aortas all showed decreases in N content and increases in the S/N ratio as the age increased. Apparently the protein in the aortas is replaced by chondroitinsulfuric acid in the ageing process.
MARION HORN (Chem. Abstr.).

Effects of Changes in Dietary Calcium on Neuromuscular Transmission. Brown, G. L., and Harvey, A. M. [*J. Physiol.*, **97**, 330–7 (1940).]

A kid, kept on a diet deficient in Ca, showed a defect in neuromuscular transmission, such that a single maximum motor nerve volley failed to elicit a maximum response from the muscle. With repeated stimulation, at a sufficiently high frequency, each successive response of the muscle became greater until transmission was fully restored at the fifth or sixth response. Chicks on a similar diet reacted in the same way. A diet rich in Ca did not eliminate the normal peculiarity in neuromuscular transmission in the fowl. E. D. WALTER (Chem. Abstr.).

Studies of Human Nervous and Related Tissue by the Röntgen-Ray Diffraction Method and the Petrographic Microscope. Reynolds, Lawrence, Corrigan, K. E., and Hayden, Henrietta. [*Am. J. Roentgenol. Radium Therapy*, **43**, 81–92 (1940).]

Standard methods of X-ray diffraction studies of non-cryst. substances were applied to nervous and related tissues; diffraction patterns obtained in 30 cases are reproduced. The diffraction work was supplemented by observations with a standard petrographic microscope and polarized light; 15 colour reproductions of these slides are given. Orientation can be noted in nerve trunks, which have a highly specialized directional function, in dural tissue and in the periosteal layer. Brain tissue gives a pattern similar to that of neuroproteins. Grey and white matter of the cerebrum give slightly different patterns, the differences being shown clearly after drying. E. H. QUIMBY (Chem. Abstr.).

Chemistry of Lipoidosis. III. Niemann-Pick's Disease and Amaurotic Idiocy. Klenk, E. [*Z. physiol. Chem.*, **262**, 128–43 (1939); *cf. C.A.*, **29**, 6942^{3}.]

The lipoids from the brain in various lipoidoses were fractionated. Compared to the lipoids from Niemann-Pick's disease (three cases) the lipoids from infantile amaurotic idiocy (Tay-Sachs) contain considerably less sphingomyelin and much more of a new glycolipide (substance X). The latter is extracted chiefly by hot $CHCl_3$-MeOH (1–3) from the organ powder after acetone- and ether-solution constituents have been removed. X contains much more sugar than normal cerebrosides. It contains fat acids, a N base very like or identical with sphingosine,

besides the reducing sugar. There is no cerebronic acid present in it. In five cases of juvenile amaurotic idiocy the changes were not so marked, probably because of localization of the lesions to certain centres. MILTON LEVY (Chem. Abstr.).

Metabolism of the Isolated Perfused Cat Brain. Chute, A. L., and Smyth, D. H. [*Quart. J. Exptl. Physiol.*, **29**, 379–94 (1940).]

A method of perfusing the isolated cat brain and an apparatus for recording continuously the O consumption of such a preparation are described. Blood flows were 60–90 c.c./100 gm./min. at pressures of 120–150 mm. Hg. Flows of 45 c.c./100 gm./min. were incapable of maintaining cerebral function as judged by the presence of the corneal reflex. Oxygen consumption was 200–300 c.c./100 gm./hr. Oxygen usage was always in excess of that required for the complete oxidative removal of carbohydrate. Usage of both glucose and lactate were observed. The brain showed a predilection for the former. 32 references.

RACHEL BROWN (Chem. Abstr.).

Acetylcholine Metabolism in the Central Nervous System. Mann, P. J. G., Tennenbaum, M., and Quastel, J. H. [*Biochem. J.*, **33**, 1506–18 (1939); *cf. C.A.*, **33**, 8271[4].]

Glucose (I) at low concentrations (below 20 mgm./100 gm.) brought about the synthesis of acetylcholine (II) in intact brain slices (rat). Fructose and galactose had only slight effects in the synthesis, but mannose had an activity near that of I. The failure of Stedman and Stedman (*C.A.*, **33**, 8271[1]) to confirm this effect of I was shown to be due to limitations of their technique. Preformed " bound " II was found in brain tissue freshly obtained from the rat, and the suggestion that it did not exist (Stedman and Stedman) was based on insufficient evidence. The effect of ether (III) in enhancing formation of II in minced brain tissue at 37° in the absence of an aqueous medium was confirmed. III was highly inhibitory to formation of II in brain tissue in phosphate- or bicarbonate-Locke medium. In brain suspensions in aqueous solutions both III and $CHCl_3$ rapidly broke down " bound " into free II. The effects of III on brain tissue, in the absence of an aqueous medium, closely resembled the accelerating action of K ions on the formation of II in brain slices. The explanation which was suggested for the effect of K ions was also postulated for the effect of III.

I. W. SCOTT (Chem. Abstr.).

The Histidine Content ("Diazo Value") of the Blood in Peptic Ulcer. Schmidt, E. G. [*J. Lab. Clin. Med.*, **25**, 512–14 (1940).]

The blood from patients and controls shows no differences in the values given by various diazotization procedures (methods of Schmidt *et al.*, *C.A.*, **31**, 8646[4], and Theis and Benedict, *C.A.*, **18**, 3398). The data do not confirm the theory that a histidine deficiency exists in the blood of patients with peptic ulcer.

HOWARD W. ROBINSON (Chem. Abstr.).

The Haemato-Encephalic Barrier and Some Physicochemical Properties of the Cerebrospinal Fluid and the Serum. Efimov, V. V., and Lokshina, E. S. [*Bull. biol. med. exptl. U.R.S.S.*, **8**, 287–90 (1939) (*in French*).]

The differences in the interfacial tension and the condition between the cerebrospinal fluid and the blood in patients with schizophrenia, progressive paralysis, brain syphilis, epilepsy and arteriosclerosis of the brain show wide variations from the normal with no regularities and cannot be used for diagnostic purposes. These wide differences are attributed to variations in electrolyte concentration rather than concentration of capillar-active substances at the interface.

S. A. KARJALA (Chem. Abstr.).

Spinal-Fluid Chlorides in Meningitis. Barnes, H. D. [*S. African J. Med. Sci.*, **4**, 97–110 (1939).]

The chloride content of the cerebrospinal fluid is lower in severe than in mild meningitis. The likelihood of death does not appear to be greater in the cases with lower chloride content of the fluid obtained at first puncture. The chloride curve in pneumococcal meningitis shows no tendency to rise. When chloride values are within normal limits or, if initially low, the curve rises during subsequent days, the disease is likely to run a mild course and conversely. The likelihood of death is not significantly greater if the curve falls during the first few days. Two references are given. W. R. HENN (Chem. Abstr.).

The Comparative Iodine Content of Blood and Cerebrospinal Fluid. Klassen, Karl P., Bierbaum, Ruth L., and Curtis, Geo. M. [*J. Lab. Clin. Med.*, **25**, 383–7 (1940).]

Iodine determinations by the method of Matthews, Curtis and Brode (*C.A.*, **32**, 9138[9]) were made on whole blood and cerebrospinal fluid of two groups of patients. In group 1 (10 patients without thyroid disease, fever or meningeal disease, and on a relatively low I intake for at least one month) the average blood I was 3·6γ per cent., the range 2·9 to 5·1; in group 2 (10 patients with hyperthyroidism, who had not received I for one month) the average blood I was 8·8γ per cent., the range 5·1 to 15·7. The increase in blood I was most marked in those patients with a more recent onset of the disease. The average cerebrospinal fluid I in both groups was 0·5γ per cent. Conclusion: Iodine is a normal constituent of the cerebrospinal fluid, and its concentration is not increased in patients with hyperthyroidism without meningeal involvement, fever and I therapy.
HOWARD W. ROBINSON (Chem. Abstr.).

The Sources of the Enzymes of Normal and Pathologic Cerebrospinal Fluid. Kaplan, Irving, Cohn, David J., Levinson, Abraham, and Stern, Beatrice. [*J. Lab. Clin. Med.*, **25**, 495–505 (1940); *cf. C.A.*, **33**, 8782[7].]

A discussion is given of the two possible sources of the enzymes in normal fluid (blood plasma and neural tissue fluid). Tryptic and phosphatase activities of the fluid of purulent meningitis are due mostly to the desmotrypsin and the desmophosphatase respectively of the polymorphonuclear cells; the lipase, tributyrinase and esterase activities are due in part (about 50 per cent.) to the desmolipolytic enzymes, and the amylase activity is due, in a lesser degree, to the desmoamylases of these cells; the remainder of the enzymic activity in this disease is probably due to lyo-enzymes of the same cells and to plasma enzymes which enter the fluid because of increased permeability. The antitryptic power of the fluid of tuberculous meningitis varies with pH in the same manner as serum antitrypsin; this suggests that the antitrypsin enters from the blood plasma because of increased meningeal permeability. The enzymic activity of the fluid in tuberculous meningitis which is not due to the polymorphonuclear cells or to the passage of plasma enzymes across the meningeal barriers is due to the presence of lymphocytes which are particularly rich in lipolytic enzymes. The sources of the enzymes in the fluids in hydrocephalus and brain tumour are discussed. HOWARD W. ROBINSON (Chem. Abstr.).

The Lange Test. II. The Influence of Particle Size and Hydrogen-Ion Concentration of Gold Sols upon Lange Test Readings on Syphilitic and Tabetic Spinal Fluids. Glasoe, P. K., and Sorum, C. H. [*J. Lab. Clin. Med.*, **25**, 534–7 (1940); *cf. C.A.*, **34**, 512[2].]

The sensitivity of the test in syphilitic and tabetic spinal fluids, as in that of paresis, increases with increase in particle size of the Au sol and decreases with increase in pH. HOWARD W. ROBINSON (Chem. Abstr.).

The Cerebrospinal Fluid at Various Ages, with Special Reference to Degeneration and Senility. Riebeling, Carl. [*S. ges. Neurol. Psychiat.*, **167**, 133–46 (1939).]

Graphs are given, showing the changes in the protein ammonia and water contents of the brain, and the protein, cell and ammonia contents of the cerebrospinal fluid from birth to senility in man. Changes in the cerebrospinal fluid are discussed in relation to normal and pathological changes in the brain.

MARION HORN (Chem. Abstr.).

The Xanthoprotein Colorimetric Value of Non-deproteinized Cerebrospinal Fluid in Comparison with the Remaining Humoral Syndrome. Bruns, Trude. [*Z. ges. Neurol. Psychiat.*, **166**, 759–87 (1939).]

The quantitative xanthoprotein test (Becher's method, *cf. C.A.*, **20**, 1666) performed on 229 samples of human spinal fluid gave values which roughly paralleled the results of the usual tests for spinal fluid pathology (lipoid, sugar, globulin, sedimentation, etc.). In general, spinal fluids which were normal by the usual tests showed xanthoprotein values within normal limits (20–32 by Becher's scale), while those which were pathological by the usual tests showed xanthoprotein values occasionally below the normal limit but usually far above, extending up to 1,000. The highest xanthoprotein values were found in meningitis, untreated paresis and diabetic neuritis. However, 32 (14·5 per cent.) of the 229 samples showed no correlation between the results of the xanthoprotein and the other tests: in 11 cases the xanthoprotein values were elevated and the others normal, in 4 the xanthoprotein values were low and the others normal, and in 17 the xanthoprotein values were normal and the others pathological. It is suggested that the alterations in the tyrosine and tryptophan portions of the protein molecules in the cerebrospinal fluid, as shown by abnormal xanthoprotein values, may be the first signs of impending disturbance of the nervous system, and that the xanthoprotein test may hence provide a more sensitive indicator than the previously used tests for spinal fluid pathology. MARION HORN (Chem. Abstr.).

The Vitamin C Content of the Cerebrospinal Fluid. VII. The Passage of Vitamin C into the Cerebrospinal Fluid in Cases of Injured Blood-Brain Barrier. Kasahara, Mitio, and Gammo, Ituo. [*Z. ges. Neurol. Psychiat.*, **166**, 733–4 (1939); *cf. C.A.*, **33**, 8743[8].]

When ascorbic acid was injected intravenously into adult male rabbits, it appeared in the cerebrospinal fluid to a greater extent after meningeal irritation by subdural injection of 0·5 c.c. 3 per cent. aleuronate than it appeared before such meningeal damage. MARION HORN (Chem. Abstr.).

The Cerebrospinal Fluid in the Bovine: Its Composition and Properties in Health and Disease with Special Reference to Turning Sickness. Carmichael, J., and Jones, E. R. [*J. Comp. Path. Therap.*, **52**, 222–8 (1939).]

Thirty-three bovine spinal fluids gave the following average values: 10·6 leucocytes per cu. mm., 34·3 mgm. total protein per 100 c.c., 36·8 mgm. glucose, 685·1 mgm. chlorides as NaCl, 16·1 mgm. nonprotein N, 10·8 mgm. urea N, 1·4 mgm. creatinine and 5·5 mgm. Ca per 100 c.c. The Lange colloidal gold test was negative. In 15 cases of turning sickness increases were noted in cell count, globulin and total protein and in one there was a positive Lange reaction. Five specimens taken from rinderpest, trypanosomiasis and East Coast fever showed little abnormality. RACHEL BROWN (Chem. Abstr.).

Changes in the Chemistry of Cerebrospinal Fluid During Encephalography. Levinson, A., Kaplan, I., and Cohn, D. J. [*J. Lab. Clin. Med.*, **25**, 225–37 (1939).]

The phosphatase, sugar and total protein contents of cerebrospinal fluid are increased after injection of air into the spine and ventricles; Ca and P contents are

increased in some cases; chlorides, nonprotein N, lipase, tributyrinase, esterase, amylase and antitrypsin contents show no significant variation. Probable causes for these changes are discussed. HOWARD W. ROBINSON (Chem. Abstr.).

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2. Pharmacology and Treatment.

Use of Pentamethylenetetrazole (Metrazole) as a Respiratory Stimulant in Acute Alcoholic Depression. McCrea, F. D., and Taylor, Haywood M. [*J. Pharmacol.*, **68**, 41–4 (1940).]

Dogs given 3–5 c.c. absolute EtOH per kgm. intravenously went into a coma from which they were partially aroused for periods of 30–45 minutes by injection of moderate doses of metrazole, after which they again became comatose. If they were given 7 c.c. EtOH per kgm. even large doses of metrazole did not arouse them. Recovery from coma began 3–12 hours after injection of the alcohol, depending on the amount injected. The metrazole had no effect on the duration of the coma or on the rate of disappearance of the alcohol from the blood stream.

L. E. GILSON (Chem. Abstr.).

Effect of Metrazole on Recent Learning. Ziskind, Eugene, Loken, Robert, and Gengerelli, J. A. [*Proc. Soc. Exptl. Biol. Med.*, **43**, 64–5 (1940).]

Preliminary experiments indicate that metrazole impairs the memory of recently acquired learning. L. E. GILSON (Chem. Abstr.).

Effect of Hypnotics and Several Centrally Acting Drugs (Naphthylamine, Picrotoxin) on Glomerular Filtration and Tubular Reabsorption. Koiwa, Makoto. [*Tohoku J. Exptl. Med.*, **37**, 163–78 (1939).]

Chloral hydrate, 0·15 g. per kgm. body weight, subcutaneously injected, increased glomerular filtration 18 per cent. on the average in the 1st hour after administration, with resultant diuresis. Larger doses (0·3 gm. per kgm. body weight) decreased urinary excretion about 58 and 62 per cent. on the average in the 1st and 2nd hours respectively, and decreased the rate of glomerular filtration 62 and 66·7 per cent. on the average in the 1st and 2nd hours respectively. Barbital (2 c.c. of a 10 per cent. solution of the Na salt per kgm.) decreased the quantity of urine excreted on the average 48 and 56 per cent. in the 1st and 2nd hours respectively; this amount correspondingly decreased the rate of filtration 51·2 and 56 per cent. Phenobarbital (Na salt) in doses of 0·1 gm. per kgm. body weight inhibited diuresis 54 and 66 per cent. on the average in the 1st and 2nd hours respectively. These hypnotics act to reduce the blood pressure and slow up the general circulation. Consequently the blood flow through the kidneys is diminished and glomerular filtration reduced. Picrotoxin (1 c.c. of a 1 per cent. solution per kgm. body weight) diminished the urine output 40–70 per cent in the 1st hour and 28–70 per cent in the 2nd hour. Tetrahydro-β-naphthylamine (0·2 c.c. of a 5 per cent. aqueous solution per kgm. body weight) generally diminished urine excretion. These two drugs stimulate the sympathetic nervous system centrally and effect constriction of the renal blood vessels. Forty-six references. MAURICE M. RATH (Chem. Abstr.).

Effect of Potassium Chlorate upon Poliomyelitis Experimentally Produced in the Monkey. Contat, C., and Soycher, C. [*Schweiz. med. Wochschr.*, **69**, 719–22, (1939).]

A virulent poliomyelitis strain was inoculated intracerebrally into *Macacus rhesus*, all of which died in 7–11 days after inoculation. To the virus suspension in vitro was added $KClO_3$ (2·5–5·0 per cent.) for two hours. Injection of the suspension had no effect. When $KClO_3$ (0·1 gm. per kgm. body weight) was given

by mouth every two hours 100 hours after inoculation, poliomyelitis appeared to be checked. Given within 48 hours after injection, $KClO_3$ prevented poliomyelitis from developing. Animals cured by $KClO_3$ proved immune to a second inoculation 10–15 days after the first injection or end of treatment. Five to ten times the therapeutic dose for humans proved nontoxic in monkeys. $KClO_3$ was successfully used to treat 40 patients with acute poliomyelitis.

MAURICE M. RATH (Chem. Abstr.).

The Significance of Neurovegetative Disturbances in Throat, Nose and Ear Diseases and their Treatment with Bellergal. Theissing, Gerhard. [*Münch. med. Wochschr.*, **86**, 1121–3 (1939).]

Bellergal, a combination of bellafolin and ergotamine, together with phenobarbital, gave good results in patients suffering from migraine and Menière's disease. Complex disturbances of the autonomic nervous system, which apparently is hyperactive, are benefited by the use of the three drugs, which are used because they act favourably on both the vagus and sympathetic systems.

MAURICE M. RATH (Chem. Abstr.).

Treatment of Multiple Sclerosis with Lecithin. Miner, I. [*Münch. med. Wochschr.*, **86**, 1038–40 (1939).]

Lecithin (10–20 mgm. in 5 c.c. of physiological saline solution) was injected intrathecally in persons with disseminated sclerosis with considerable improvement in 80 per cent. of 130 cases. Lecithin has a specific antilipase activity and is an activator of cellular processes in the organism. Both of these reactions probably account for its favourable therapeutic action. It may be that lecithin acts further to inactivate the pathogenic virus by fixation of the pathological lipase to an exogenous substrate. Administration by this method caused no apparent toxic reactions. MAURICE M. RATH (Chem. Abstr.).

Tutin : Its Pharmacological Action and Its Antagonism to Sodium Amytal. Swanson, Edward E. [*J. Am. Pharm. Assoc.*, **29**, 2–4 (1940).]

Tutin $C_{20}H_{23}O_8$, a glucoside of *Coriaria thymofolia*, has a convulsant action similar to that of coriamyrtin and picrotoxin ; it is slower in the onset of action but longer in duration. Comparisons were made with coriamyrtin, picrotoxin, metrazole and thujone, in mice and rabbits, by the determination of convulsive and lethal doses, injected subcutaneously and intravenously. In rabbits Na amytal can detoxify 55 minute lethal doses of tutin, 45 of coriamyrtin, 40 of picrotoxin, but only 7·5 of metrazole and 5 of thujone. Intravenously, tutin can detoxify in rabbits a little more than 2 minute lethal doses of Na amytal injected subcutaneously. A. PAPINEAU-COUTURE (Chem. Abstr.).

Two New Substituted Vinyl Barbituric Acids. Hendrix, James P. [*J. Pharmacol.*, **68**, 22–35 (1940).]

5-Ethyl- and 5-propyl-5-(1-methyl-1-butenyl) barbituric acids are potent narcotics showing a wide margin of safety in rats and dogs. The Et compound has been tried in human subjects with satisfactory results. The action was relatively brief. Both compounds were less depressant to blood pressure upon intravenous injection in dogs than was isoamylethylbarbituric acid, and, like the last-named, decreased the O utilization of white rats.

L. E. GILSON (Chem. Abstr.).

The Effect of Certain Barbiturates on the Response of Vaso-Active Substances. Kohn-Richards, Richard, and Grimes, Clyde. [*Anesthesia and Analgesia*, **19**, 31–4 (1940).]

A study of the influence of several barbiturates on blood-pressure changes produced by acetylcholine in decapitated cats showed that some, like pentothal,

increased the depressant action of the acetylcholine, and others, like evipal, counteracted the drug. These drugs did not change the typical effect of histamine. The vasopressor responses to pituitrin were increased 15–20 per cent. by both pentothal and nembutal. G. H. W. LUCAS (Chem. Abstr.).

The Distribution of Bromine in the Organism After the Administration of Bromides. I. The Distribution of Bromine Between the Brain and Blood in the Quiescent Organism and After Excitation with Camphor. Ephstein, Ya. A. [*Arch. sci. biol.* (*U.S.S.R.*), **55**, *No.* 2, 50–6 (*in English*, 56) (1939).]

The ratio of blood Cl to brain Cl in white mice is 2·33. The injection of 136 mgm./kgm. body weight of NaBr yielded a blood Br to brain Br ratio of 3·91 within 1·5 hours. This remained almost constant for 10 days, during which four additional doses of NaBr were given. Brain excitation by the hypodermal injection of 0·2 c.c. of 20 per cent. camphor/25 gm. body weight simultaneously with NaBr did not change this ratio. S. A. KARJALA (Chem. Abstr.).

The Passage of Bromide, Iodide and Thiocyanate into and out of the Cerebrospinal Fluid. Wallace, G. B., Brodie, B. B., Leshin, Seymour, and Brand, Elliott, [*J. Pharmacol.*, **68**, 50–5 (1940); *cf. C.A.* **33**, 2986².]

When the salts are injected intravenously into dogs the anions begin to pass promptly into the spinal fluid, but their passage into the spinal fluid, unlike the case of other tissue fluids, is slower and never reaches the concentration present in the blood serum. Furthermore the serum must attain a certain minimum concentration of iodide or thiocyanate ion before any passes into the spinal fluid. The bromide ion may also have a threshold value, but if so it is very low. When injected into the spinal cistern all three of the ions pass quickly into the blood at the same rate and there is no evidence of any barrier to their passage.
L. E. GILSON (Chem. Abstr.).

The Effect of Intravenous Injections of Sodium Diphenylhydantoinate (Dilantin) on Respiration, Blood Pressure and the Vagus Nerve. Haury, Victor G., and Drake, Miles E. [*J. Pharmacol.*, **68**, 36–40 (1940).]

Na diphenylhydantoinate when injected intravenously in dogs or rabbits produces an immediate 30–65 per cent. fall in blood pressure. This action is peripheral. The compound has a depressant action on the vagus nerve and has a marked depressant action on respiration. Lethal doses produce death by respiratory failure. L. E. GILSON (Chem. Abstr.).

The Action in the Perfused Liver of Acetylcholine, Sympathomimetic Substances and Local Anaesthetics. Chakravarti, M., and Tripod, J. [*J. Physiol.*, **97**, 316–29 (1940).]

In the perfused liver of the dog evidence was found for three effects of adrenaline: (1) opening of the hepatic veins with increased portal inflow and diminished liver volume; (2) increase of resistance due to constriction of the small vessels from the hepatic artery and portal vein; (3) in the presence of pre-existing adrenaline, an increased resistance on the outflow side. When adrenaline is present in the blood, acetylcholine injected into the hepatic artery causes an expansion of liver volume, probably because of increased arterial inflow. Expansion of the liver diminishes the portal flow and the net effect on outflow is a diminution. Tyramine, ephedrine, veritol, synephrine and benzedrine all act like adrenaline, though their effects are more prolonged. Stovaine and cocaine both have a typical adrenaline-like action. Butyn, percaine and procaine have little or no direct action of their own, but all of them enhance the action of adrenaline. E. D. WALTER (Chem. Abstr.).

Antagonism of Evipan by Picrotoxin, Coramine and Cardiazole. Das, S. C. [*Quart. J. Exptl. Physiol.*, **29**, 355–65 (1939).]

The production of a steady state of repiratory depression by continuous intravenous infusion of Na evipan (I) into rabbits affords a convenient method for measuring the efficiency of analeptic drugs and for comparing their relative activities. Picrotoxin (II) causes an increase in the depth of respiratory movement as well as in the rate, whereas coramine (III) and cardiazole (IV) improve the rate of respiration rather than the depth. Three-tenths mgm. of II causes the same increase in amplitude of respiratory stimulation as 10 mgm. of III or of IV. II takes 3–5 minutes to develop its maximum effect, while III or IV reaches its maximum very quickly. When the respiratory depression is severe III often fails to produce a stimulant effect and may even augment the depression. II produces a stimulant effect in such cases. II is detoxified at the rate of 1/10 and the doses of I and the log of the doses of II which balance the continuous infusion of I at first show an increase in respiratory activity and then a fall and a final depression which may be greater than that produced by I alone. RACHEL BROWN (Chem. Abstr.).

The Clinical Applications of Electrically Induced Convulsions. Shepley, W. H., and McGregor, J. S. [*Proc. Roy Soc. Med.*, **30**, 267 (1940).]

The authors state that the electrical method is well tolerated by the patient who is freed from the dread which hitherto was associated with these necessarily continued treatments. The disagreeable sequelae of drug-convulsant treatment are notably absent; such features as vomiting, confusion and psychomotor restlessness which formerly required close " after-supervision " are not evident. The method by its nature is devoid of such former technical complications as thrombosis of veins—a feature of special importance where insulin is used either subsequently or in combination. The method can readily be combined with other treatments such as insulin, and being a physical therapy, removes all question of toxicity or cumulative action. In virtue of the last-mentioned facts, the procedure is completely controllable, a succession of fits not intended being unknown. The method is ideally suitable for the indefinitely prolonged maintenance treatment in those non-infrequent cases where an occasional convulsion is essential to prevent relapse. The method may well reduce the incidence of fracture since their impression was that the fits upon the whole appear less strong. In their series of some 200 induced major fits neither fracture nor dislocation has so far occurred. The method offers of ready repetition without the attendant difficulties of a struggling patient, and indeed the abortive fit induces quiescence and a ready acquiescence to further treatment, in marked contrast to cardiazol administration under similar circumstances. From the administrative point of view the method offers advantages of economy, also less nursing attention and supervision. (Authors' abstr.).

Obituary Notice.

EDWARD MAPOTHER, M.D., F.R.C.P.Lond., F.R.C.S.Eng.

The death of Edward Mapother on March 20, 1940, has deprived British Psychiatry of one who in his own way has done more to alter and develop the specialty in England than any of his contemporaries.

He was born in Dublin in 1881, the son of a distinguished anatomist, a President of the Royal College of Surgeons of Ireland. He was educated in England at University College School, and later at University College and its associated Hospital. He qualified in 1905, after a distinguished career as a student, and during his resident appointments served under Dr. Risien Russell, gaining a knowledge of neurology which influenced his outlook towards psychiatry.

His first regular appointment in Psychological Medicine was at the London County Mental Hospital at Long Grove, Epsom, where he was associated with the brilliant team of workers collected by Sir Hubert Bond, which included among others Devine and Bernard Hart.

He was one of the first to try to join the R.A.M.C. on the outbreak of the 1914 War, even undergoing a minor orthopaedic operation lest he should not be found fit for full service. He served in Mesopotamia and France, returning to England to organize the Neurological division of the 2nd Western General Hospital. After the Armistice he was put in charge of the Maudsley Hospital during its phase as a Pensions Hospital for War Neuroses. Here he again came into contact with Sir Frederick Mott, who had originally organized the hospital on its completion as a treatment centre for neurological and shell-shock soldiers. Mott was still in charge of the Central Laboratory of the London Mental Services, which had been transferred from Claybury to the Maudsley when the latter opened. The association with Mott undoubtedly helped to crystallize Mapother's own tendency to approach psychiatry from the neurological and organic standpoint.

In 1922 he was appointed the first Medical Superintendent of the Maudsley Hospital, when it was opened for its original purpose. He was enthusiastically imbued with the principles for which it was established by Dr. Henry Maudsley, namely, of teaching, treatment and research, and he devoted the rest of his life to promoting these functions.

On the material side, he developed the hospital from six small wards and a small ill-equipped out-patients' department to the present imposing collection of buildings, with an out-patients' department dealing with about 4000 fresh cases yearly, and with a thriving children's department.

Mapother had to fight an uphill battle to attain this development. He was handicapped at the start with few facilities and few assistants, but he overcame prejudice in many directions, and succeeded in establishing a psychiatric hospital second to none, with properly organized departments, and established it as a great centre of teaching in the University of London, so helping towards his ideal of making psychiatry take its proper position in relation to other branches of medicine. It is only fair to add that as the value of this work became apparent to the lay authority for whom he worked, the London County Council, they provided ample funds to help its development.

While his work in linking up the Maudsley Hospital with general medicine was of the greatest value, he was not so interested in maintaining links with the mental hospitals. His enthusiasm for joining psychiatry to general medicine caused him to take a somewhat one-sided attitude towards the ideal of a well co-ordinated mental health service, embracing all branches of psychiatry, and fulfilling all the mental health needs of its area.

The influence of his teaching was always practical and objective. He believed in a psychiatry based on sound clinical neurology and a study of the nervous system, and indeed one of his unfulfilled ambitions was to establish a neuro-psychiatric section at the Maudsley Hospital. He was intolerant of speculations founded on vague philosophy. He always emphasized the importance of the recent as opposed to the remote environmental stresses, in influencing mental illness. Indeed his impatience with the undue claims of some schools of psychological thought made him express in debate a greater antagonism than perhaps he really felt, for he never neglected to study the various aspects of approach to disease, and utilized any that appeared useful to him. He encouraged investigation and research in his co-workers, although impatient of mere compilation without intelligent evaluation. His own trend was towards the clinical side, and purely laboratory experimentation interested him less. Owing to his numerous organizing activities, he left himself little time for systematic personal investigation, but he published work on the Alcoholic Mental Disorders and the Mental Symptoms of Head Injuries, and he also gave the Bradshaw Lectures at the Royal College of Physicians in 1936, in which he indicated his ideas for the progress of psychiatry. He was Physician to and Lecturer on Psychological Medicine at King's College Hospital, and he was an Examiner and Councillor of the Royal College of Physicians, as well as a Fellow of University College, London. He was an Ex-President of the Psychiatric Section of the Royal Society of Medicine, and in 1937 he was appointed to the newly created Professorship of Clinical Psychiatry in the University of London, an acknowledgment of his work as a teacher. He

was consultant to the Queen Alexandra Hospital, Millbank, and also to the Ex-Services Welfare Society, for which body he did much useful work. In 1939 he was elected to deliver the Maudsley Lecture but owing to illness he was unable to do so.

He was a tireless worker, and he devoted his life and energies to the Maudsley Hospital. He has developed the work of Maudsley and Mott, and established a great University Clinic in Psychiatry, and laid foundations which will enable others to do still more for British Psychiatry.

In 1915 he married Barbara, daughter of the late Charles Reynolds, and much of his work latterly was only rendered possible by her help and care of him.

A. A. W. PETRIE.

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The Editors would be grateful if all members of the Association who are on Active Service would send their names, rank and unit to Dr. K. K. Drury, Carlton Hayes, Narborough, Leicestershire, who has very kindly undertaken to receive these.

THE PRESIDENTIAL ADDRESS DELIVERED AT THE NINETY-NINTH ANNUAL MEETING OF THE ROYAL MEDICO-PSYCHOLOGICAL ASSOCIATION, HELD IN LONDON ON JULY 24, 1940,

By THOMAS C. GRAVES, B.Sc., M.D., B.S.Lond., F.R.C.S., M.R.C.V.S.,

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INTRODUCTION.

DR. BOYLE, LADIES and GENTLEMEN,—I offer my thanks to the Association for the honour it has done me in promoting my elevation to its Presidency, and in doing so I desire to express to those who have been able to attend this meeting my appreciation of the effort they have made, in such troublous times, to come here and assist in these proceedings. I much regret that our present circumstances have prevented the holding of even a restricted scientific and social meeting in Birmingham, in an attempt to emulate at least a part of the delightful time we had at Brighton last year, but for pleasure we have to fall back on happy memories and for business this brief gathering has been substituted.

As all our peace-time activities have been cut down to a bare minimum and the justification for this meeting is the business to be transacted, I propose to deal briefly in my address with a subject which is of even greater importance in war than in peace, the subject of treatment applicable to all states of mental ill-health, mild or severe.

I have elsewhere submitted the conception of a common causal bond between the mental illnesses and the bodily disease entities with which they are so frequently associated, and now I purpose to review very broadly the various aspects of treatment which are proper to the several links in the chain of this conception, but with especial reference to those measures in which diphasic vascular variation is an essential factor in the therapeutic action.

I hold this basal common cause to be a residuum left by an acute infective process, associated with which there may have been emotional symptoms preceding, during or succeeding the main body of physical symptoms. This residuum becomes quiescent and even latent in severity and perhaps very cryptic in location.

Nevertheless, just as the main body of the original acute disease was associated with instinctive and emotional disturbances, so this hidden moiety, now developing as a chronic infective process, continues to trouble the instinctive and emotional life of the patient, and reduces or delays the progress of the development and manifestation of his intellectual efficiency from degrees which may be regarded as very well within the range of normal to that extremely abnormal state termed insanity.

A capacity for exacerbation and remission is the great characteristic of this common causal process, but always the remission is less than the extent of the exacerbation, and so its dynamism is displayed even with the inevitability of gradualness ; but whether in the earliest stages, when any symptoms shown are generally regarded as insignificant and the condition " usual and common," or later, when mental symptoms become more certainly obvious, the same fluctuant character is shown.

Links in the Chain of Events emanating from the Chronic Infective Process.

When organisms from an acute infective process gain access to the blood stream they affect the autonomic-endocrine mechanism, and in a similar way, although more slowly, the infective material which reaches the blood stream from a *chronic* infective residuum has a corresponding effect on that same mechanism, which during the acute illness was almost overwhelmed by that same infection and to which it, like the other tissues, is therefore sensitive.

In the full development of the somatopsychic condition arising from a common cause four principal links in the sequence of pathological evolution have to be recognized, for they affect the therapeutic measures which can be applied to curb the progress of the disease and so its remote effects. These links are : the lesions of the common cause ; the blood stream and the secondary and excretory diseases ; the autonomic-endocrine system ; the central nervous system.

The Lesions of the Common Cause.

The chronic infective process usually commences in the adenoid tissue and mucoperiosteal membrane of the upper respiratory tract and the oral periodontal membrane, spreading gradually therein, especially to any area weakened, as by injury, or the subject of maldevelopment.

It thus affects those tissues where the blood supply is scanty and consequently the immunity defences are minimal, but which are just those tissues where mechanical augmentation is a potent factor in assisting the passage of infection and toxaemia from the lesions into the local and general circulation.

In these areas there is room for local spread into regions difficult to examine, but important on account of the many and various disturbances of function which can thus result.

An important consideration therapeutically is the type of infection and whether it is pure or mixed, and similarly important is the condition of the lesion in relation to drainage ; whether the escape of the discharges therefrom is wholly free (open sepsis), or variably impeded and free (defective drainage), or wholly deficient (closed sepsis).

In cases where there are, as is so frequently the case, multiple lesions it is common to find combinations, even all three, of these drainage conditions.

These states of drainage and the extent of the lesions have a relation to conditions affecting the remaining links of the chain and especially the fourth, the central nervous system and the peripheral nerves.

In open conditions of drainage the mucosae are the tissues chiefly involved in the inflammatory process, whilst in closed conditions account has to be taken of the process involving nerve endings and extending to cause actual neuritis affecting the nerve trunks, such as the optic and fifth nerves. Thus, very broadly, conditions of open and variable drainage are more commonly associated with disturbances of taste and smell, whilst those affecting hearing, vision, common sensation and equilibrium appear rather to be the result of completely and variably closed sepsis.

The Blood Stream and the Secondary and the Excretory Diseases.

From entry of organisms into the blood stream a bacteriaemia may ensue which may be mild or severe and of pure or mixed infection, pyogenic or non-pyogenic. Secondary diseases may thus be set up in other tissues. In the body fluids pyaemia and septicaemia are thus met with associated with psychotic states, maybe with death as a sequel.

As a result of the continued activity of the cephalic lesions the rest of the alimentary tract becomes involved, through the passage of the discharges as well as the bacteriaemia, in the infective process, thus favouring the activity therein

of any secondary invaders lying latent, such as the pneumobacillus or the various dysentery and food-poisoning organisms.

It is therefore not surprising that it has been observed that in relation to an attack of clinical dysentery there is usually an exacerbation of an existing psychosis.

There is also reason to conclude that a subclinical state of dysentery or allied infection may be a factor in causing a toxaemia which may assist in many first attacks of psychosis.

In some cases the secondary diseases may be described as excretory because the products of their activity discharge on to mucosal surfaces and thus the absorbed bacterial and toxaemic content from the mother lesions is reduced within the body, whilst the new tissues brought within the ambit of the disease process assist in forming immune bodies available for the body as a whole. When these excretory diseases are active there is a reduction in the severity or even a complete disappearance of the psychotic state, but this returns again, perhaps with exacerbation, when discharges are impeded or the tissues have lost the power to react in this way.

Such apparently paradoxical conditions have been recognized from antiquity. These excretory processes may develop in the alimentary tract, skin, lungs, kidneys, cervix uteri and prostate, etc. There other infections, active or residual, may be present and be exacerbated or activated, e.g. tuberculosis or gonorrhoea ; or, as in the skin or the cervix, a further infection may become superimposed, e.g. streptococcal, on the secondary excretory process.

With these complications obtaining, a local infection, such as gonorrhoea, may prove very resistant to treatment until the mother lesions have been removed. When such conditions obtain the daughter lesions reinforce the mother with their toxaemia and bacteriaemia and thus increase the intensity of the remote as well as the local symptoms.

In organs and tissues which are unable to discharge the products of bacterial activity therein the bacteriaemia causes degenerative conditions which reduce the functional efficiency of the parts affected, e.g. anaemia, cardiovascular disease, iritis, " rheumatic " disease, etc.

With some of these conditions there may, owing to the development of antibodies from the involved tissues, be some degree of remote symptom, e.g. mental, amelioration, but in other conditions the effect is to exacerbate the psychosis.

The next link to be considered is that of—

The Autonomic-Endocrine Mechanism.

The autonomic-endocrine mechanism is affected by the bacteriaemia and the peripheral sensory irritation set up by the chronic infective process, a stimulation being later followed by exhaustion.

The duration, rapidity and severity of these changes can vary, depending on the type and dosage of the bacterial agent and the intensity of the sensory disturbance.

Thus, as a result of the endogenous stimulation of the mechanism there is a sensitization, and even an activation by the sensory irritation, of the emotional and instinctive life, followed later by its gradual or rapid dulling or even collapse as exhaustion of the mechanism supervenes—conditions shown in many cases of acute mental confusion and dementia.

Thus the endogenous sensitization and activation of this mechanism causes the appearance of excessive fear or anger, excessive in relation to the circumstances which seem to evoke the manifestations. In many cases there are, on careful adjudication, checked by responses on recovery after treatment, no real exogenous factors, the actual stimulus being provided by sensory irritation.

The association of disturbances of blood pressure with these conditions of sensitization and activation confirms the involvement of the autonomic-endocrine mechanism in this common causal complexity.

In general it may be said that the treatment of a common causal process is usually followed by a rise of blood pressure in cases with subnormal pressure and a fall towards normal in those cases where the blood pressure is high. In the former group the emotional display is usually one of fear, whilst in the latter group the manifestations are generally those of anger.

In both groups with the swing towards the normal in the blood pressure there is a reduction in the severity of these symptoms, and the patient is no longer unduly responsive to any extraneous stimuli as was the case before the treatment of the common cause.

The last link for a brief review is—

The Central and Peripheral Nervous System.

Here there is for consideration the effects of the conditions discussed in the other links upon the mechanism whereby the individual knows and reacts upon environment.

These effects can be grouped as non-organic and organic.

The non-organic include the disturbances of sensation arising from the toxic-irritative conditions affecting the nerve trunks and the peripheral nerve endings of common and special sensation.

These sensation disturbances are positive, i.e. when there is the addition of abnormal stimuli of endogenous origin, and negative, when there is the removal of normal stimuli of exogenous origin. By these two effects the patient's true appreciation of environment is reduced and distorted. Again, as a result of the sensitization of the reflex arc by the endogenous stimuli, movements which may appear as purposive but which really are out of the

patient's control are induced and these further distort the appreciation of reality.

Another non-organic effect arises from the sensitized over-activity on the one hand, and the exhaustion on the other of the autonomic-endocrine mechanism on the cerebral vessels.

Two conditions are important here—alterations in the general blood pressure and the local vaso-motor changes in the brain.

The organic changes are the sequel to the bacteriaemia.

This can set up myriads of small vascular lesions; each when fresh has a central ischaemic area and around it there is doubtless, as in similar traumatic lesions and thus extending the area of dysfunction, a zone of oedema.

The clinical aspect of these vascular lesions is similar to that of a state of cerebral irritability; they are both exacerbated by similar conditions.

As a result of this widespread vascular disorganization numerous nerve cells in the vicinity of the lesions are destroyed by the continued local anoxaemia. With reduction of bacterial swarming there is a tendency for these vascular lesions to heal: a blocked vessel has thrice been recanalized.

Bases of Therapeutic Considerations.

To deal successfully with conditions of such sequential complexity which have been developing over lengthy periods of time it is important not to be hampered by therapeutic considerations of a limited or short cut nature. "One treatment capable of being given by one man for one mental disease" briefly expresses tendencies which must be guarded against.

It is imperative to recognize that whilst psychiatric classification may be very interesting psychologically it is not so absolute as classification in somatic pathology, and so it is useless to the somato-psycho-therapeutist. A treatment can be valuable, although it is not capable of dealing with all the cases which can be allotted to a group ingeniously devised to meet some psychopathological viewpoint.

As I see the situation many useful measures of treatment have been discarded by some workers because these conditions have not been recognized. It would surely be extraordinary for conditions which must have been evolving over decades to respond immediately to one agent, even if it is given by intravenous injection or applied directly to the skull.

Under the conception of the common cause the possibility of such a duration of development is recognized, and it is further recognized that for the treatment of conditions which have involved mental efficiency the therapeutic net must be spread wide and deep. Treatment should not be confined to the isolated use of one agent or one process, but by using in their proper place all agents which have been shown to have any healing effect in no matter what psychiatric field some good results can ensue.

For this purpose an ordered scheme of treatment based on a somatic pathological concept is available, founded on accumulated knowledge of mental disease going back to Hippocrates. This concept is best expressed by the terms open and closed sepsis. This treatment is applicable and effective, but it needs the co-operation of an efficient and sympathetic team. A therapeutic essential to recognize, however, is that an agent which is beneficial in conditions of open sepsis is the reverse in conditions of closed sepsis, but becomes beneficial when such closed sepsis is converted into open sepsis.

It is possible that failure to recognize this principle is the explanation of the divergent results obtained by different observers and of the discarded therapeutic measures.

Diphasic Vascular Variation.

Stasis of capillary flow is a characteristic feature of the circulation in the later stages of inflammatory lesions.

Agents which stimulate healing in infective conditions do so largely by increasing the vascularity of the lesion, thus bringing, *inter alia*, fresh reserves of immune bodies to combat any infective agent still present. In conditions of open sepsis the discharges resulting from this increased vascularity escape, the potential toxaemia and bacteriaemia are reduced to minor values and there is a rise in mental efficiency.

In conditions of closed sepsis the effect of increased vascularity is to enhance the actual toxaemia and bacteriaemia, thus exacerbating any state of disease or stress secondary thereto, and a fall in mental efficiency.

Consequently any means whereby the general or local circulation is affected tends to reflect itself upon a state of mental inefficiency by acting on any common cause basally responsible for that state.

These means may be by increasing or decreasing the immune body content, similarly the blood volume, and colloidal state, conditions of anoxaemia, conditions affecting permeability as well as those working through the autonomic-endocrine mechanism. Locally the circulation may be influenced by short-wave currents, heat, massage, etc. Conditions of general vascular variation also have a local effect on any site of disease and thus on conditions of open and closed sepsis.

Some of these vascular agents have a pronounced diphasic effect on the circulation, and thus on any diseased part whose tissues are correspondingly affected.

The first phase is one of vasoconstriction, and consequently a transient reduction in vascularity takes place in the first phase and hence a local anoxia effect occurs in the tissues supplied.

In the second phase, which rapidly succeeds, the vaso-constriction is followed by dilatation in usually a well-marked swing so that there is an

enhanced vascularity in excess of the previous reduction. Hence in this phase in areas of old inflammation there is a thorough flushing with blood, and healing tendencies are stimulated in whatever stage the process has reached. It may be that with the infection still active the stage reached may still be that of reactive discharges. If so these are reduced in the first phase, and unless infection is very active they are increased in the second phase. The effect on any bacteriaemia and toxaemia will thus depend on whether there is open or closed sepsis.

The effects, local and remote, of such a diphasic action on open and closed sepsis are not much different from those following simple increase in vascularity. However, in conditions of mixed drainage the effects on the patient as a whole will be harmful, for the increased absorption from the closed will counterbalance any improvement following the increased discharge of toxic matter from the associated open sepsis.

Brief consideration will now be given to therapeutic measures applicable in the various links of the pathological chain, and always the point will be that what appears to be the most diverse treatment will have an effect on remote sequelae, such as mental inefficiency, provided the case is one of open sepsis, but that these same measures will be devoid of effective ameliorative action in cases where the sepsis is closed, although the remote sequelae of mental inefficiency are apparently identical in character to those in the first group.

Treatment in the First Link.

In the first link the prime consideration is the removal of the originating septic state or its effective drainage, and in this matter there should be no ambiguity about the extent of the investigation or the thoroughness, but also the relative innocuousness of the detoxication procedure.

Depending on the type of infective agent it may be necessary to precede intervention by chemotherapeutic or serological measures in order to diminish the bacteriaemia of intervention.

Postoperative measures but also effective in natural conditions of open sepsis are those relevant to the infective agent, such as specific sera, vaccines and chemotherapeutics.

Also acting on the diseased part through the blood stream are agents given enterally and parenterally, such as calcium, and other non-specific agents such as typhoid-paratyphoid vaccine, normal serum or auto-haemotherapeutic measures.

Other agents which also through the general circulation affect the local circulation in the lesions are those whose action is mediated by the autonomic-endocrine mechanism, and therefore in cases of open sepsis, whether occurring naturally or rendered so by surgical means, these agents which may be given

with one object in view can and do effect their, maybe unrecognized, therapeutic action in this manner.

Measures locally applied which have an effect on the lesions do so by their effect on the infective agent, such as chemotherapeutic and serological agents, or on the local circulation, either by causing local vaso-constriction or vaso-dilatation.

Agents which cause a local vasoconstrictor effect such as ephedrine applied to the nose or the icebag to the head, by reducing swelling of mucosae may have an effect in assisting discharges in conditions of variable drainage, although the local action of relief by gargling with an astringent such as by alcoholic beverages is counteracted by the vasodilator action occurring after absorption. This latter action, however, in cases of open sepsis may have an ameliorative result on the lesions, but in cases of closed or variable drainage the astringent action is ineffective whilst the dilator action exacerbates the disease process, and hence its remote effects in the other, especially the fourth, link.

Locally applied measures, such as gargles, washes and irrigations, as of the stomach, colon, antrum and Proetz general nasal sinus irrigation, induce a mild vascular reaction and also assist in bringing away discharges. All these assist in the treatment of the local lesions and are especially useful in cases of open sepsis.

Treatment in the Second Link.

Here are for consideration the measures which are concerned with the blood stream and the secondary diseases, arising from the bacteriaemia and toxaemia.

Investigations in immunity have shown that activity in conditions of infection diminishes the capacity to resist infection and reduces the survival rate. Hence in these conditions of chronic infective disease, whether the patient is manifesting for all to see the common signs of infection, such as a pyrexia with delirium, or is unable, owing to exhaustion, to manifest a pyrexia but is as an alternative exhibiting a reduction in mental efficiency, whether of a severe character or of only mild degree, he should be allowed to rest as much as possible, and be free from any external additions to the internal irritations which have already exhausted him.

Thus measures of general rest will reduce the mechanical augmentation of bacterial inflow and lymphatic distribution.

This reduction can also be assisted by local rest of the parts wherein the mother lesions are situated, and this can be helped by steps taken under the first link by removing sources of irritation and thus of spasm, especially of dental origin. A particular example is that seen in catatonic manifestations arising from abnormal wisdom teeth.

It therefore follows that any induced activity, such as convulsions, in

conditions where a common cause is operative will only increase the bacteriaemia and the pathological conditions which have already been indicated as flowing from it. In sum, a worsening of the somatic and mental manifestations of the chronic infective process.

To combat what has gained entrance to the body fluids the chemotherapeutic agents and sera are appropriate.

To deal with the therapeutics of the degenerative diseases in this very broad review is not necessary to the argument under consideration, but reference can be made to the value of liver extract in the treatment of the conditions of secondary anaemia. Benefit following its use has been observed on the general mental and physical states also in cases where there has been no evidence of gross anaemia, thus suggesting it has also an anabolic-immunity value. Like the sera and chemical agents, this substance appears most effectual in cases of open sepsis, whether naturally occurring or surgically produced.

The therapeutics of the excretory diseases are on the main track of the thesis. These diseases may be regarded as the means whereby the mother lesion is drained, albeit at a distance.

A simple example of this: In a case of acute confusion there appeared a lymphadenitis, which developed in relation to a later found abscessed tooth. When the adenitis suppurated there was a remission in the acuity of the confusional state, but when local healing occurred the confusion returned but again cleared, permanently and more substantially, after the removal of the abscessed tooth.

Thus an abscess, an excretory disease if its discharges are drainable, can be an excellent development.

The fact that mental recovery could occur under such conditions led to the use in the past of setons and blisters in order to induce what was hoped would be such excretory conditions.

Provided the excretory disease has continued to excrete infective discharges many a case has regained and retained sanity, but when the excretory disease ceases to be able to do so then psychosis may return and manifest itself, and vehemently.

Other examples where similar conditions occur have been met with in relation to the following secondary diseases: pyaemia, perineal abscess, calculous nephrosis, appendicitis, cholecystitis.

In such cases, provided the mother lesion attains to open sepsis, and or, the secondary disease continues to discharge, a useful but incomplete mental and physical recovery can ensue temporarily.

However, in cases of inability on the part of the excretory lesion, either owing to surgical intervention or from natural causes, to continue, or to attain to excretion, and especially so in cases where there is closed sepsis, death may close the scene after a stage wherein acute delirium appears. As an

alternative the severity of the infective process may diminish and the patient continue in a state of chronic psychosis.

Malaria may set up pneumonia, and like those excretory conditions which occur naturally, effect some benefit in this link, especially if conditions of open sepsis are present or develop in the mother lesion.

Treatment in the Third Link.

Much treatment of mental disorder in the past, even to antiquity, and much which is in practice at the present day, can be recognized as operating through the autonomic-endocrine mechanism which forms the third link involved in the sequences from an infective process.

Many procedures which are now taboo would have the effect of stimulating that mechanism by exogenous action, such as whirling in the revolving chair until consciousness was lost, keeping a patient under water until nearly drowned, suddenly falling into space or water, and whipping until bruising occurred or the beating, as described in Don Quixote, given to the madman of Cordova. Such methods were termed moral treatment, and it was recognized that they caused, or to be successful should cause, the evocation of fear. It was considered that such methods could help a patient to overcome any lesser fear than that engendered by the method employed.

Among the few means available for the endogenous induction of fear in the earlier days were drastic purgation and blood-letting.

If these methods were followed by the drinking of a large posset, then they resembled the diphasic vascular variation treatment of the present day. It is probable that in cases of open and variable drainage sepsis these crude methods may have been successful; certainly the cases treated by the old and new methods of placing blood under the skin should give parallel results, were it not that the ancient practice rather overdoes the painful stimulation. In conditions of closed sepsis these procedures would exacerbate any physical and mental illness.

The so-called "shock" treatments are the modern counterparts of these methods, and according to some they are regarded as acting in a similar way to the older methods, but the term "psychological" is used instead of "moral" to explain their action.

I consider however that the mode of action of these "shock" treatments is by means of a diphasic vascular variation reaction, and they are only therapeutically effective in conditions of open and possibly variable drainage sepsis, but that they are exacerbatory of the conditions of disease in cases of closed sepsis. What have been included under this "shock" heading are the various pyrexial and the convulsion and coma treatments.

I take the view that whilst these manifestations, viz. rigor and fever, fear, convulsion and coma show their inducing agents are effective, their

therapeutic action is through the diphasic circulatory change they set up in areas of septic disease and the non-organic vascular effects induced thereby, which combats that stasis of capillary flow which is so characteristic a feature of the circulation in the later stages of inflammatory lesions.

As a result of toxic absorption from the mother lesions more and further local and general vascular spasm has been caused, and whilst this effect on the lesions is an advantage, because it limits the amount of absorption, yet any protective action of this kind is more than overcome by the mechanical augmentation which is operative there.

This spasm in some cases relaxes following the removal of its toxic cause, but in other cases it persists to a greater or lesser extent, and thus continues to affect the circulation in the local lesions as well as that in other parts of the body, such as the brain and the peripheral circulation.

If some agent could cause vascular relaxation there would be more discharge and less absorption in cases of open sepsis, but more absorption in cases with closed sepsis.

Hence sympathetic vascular overactivity is reduced by the diphasic variation reaction causing a flushing of the circulation, and this affecting areas of disease assists discharges, reduces toxaemia, and hence the removal of those agents which have been absorbed and which have been disturbing the circulation by general and local spasm.

The fact that there is an improvement in the general circulation following treatment of a common causal state and diphasic vascular variation treatment can be seen very prominently in the effect on both pallor and cyanotic conditions which occur associated with the psychoses ; coincidentally with mental improvement an improvement in the peripheral circulation occurs, both pallor and cyanosis being replaced by a uniform pink colour.

That an alteration in the local circulation around open lesions of the common cause does take place following treatment by diphasic variation agents is indicated by the focal reactions which sometimes occur ; increased discharges may be observed and herpes in the area of the nerve distribution of their location, and this associated with mental and general circulatory improvement.

The agents which are capable of producing these diphasic effects are those ranging between two principal activities : those which stimulate the sympathetic system on the one hand, including the cardiazol group of agents, and those on the other which stimulate the parasympathetic, as by insulin.

Lying between these extremes are other agents which operate through the autonomic-endocrine mechanism, such as the various proteins which given parenterally also induce these vascular reactions ; some of these also cause pyrexias.

Living proteins such as malaria and dead proteins such as those used for specific vaccine and for non-specific protein treatment, such as milk.

In the use of bacterial protein it is necessary to exercise care and not to

assume that one protein is the equivalent of another. Undoubtedly the best bacterial protein to use is the typhoid-paratyphoid combination and not that of *B. coli* or *B. dysent.*; the former is a stimulant to the autonomic-endocrine system whilst the last two are very depressing.

Other conditions which operate similarly although less dramatically are climatic and seasonal changes. Exposure to equable heat and cold are stimulant, and in conditions of health there is a vascular response through the autonomic-endocrine mechanism, but conditions of extreme heat and cold are exhausting to the mechanism.

Owing to its importance I do not feel the repetition is unnecessary that the response to all these therapeutic agents will depend on the condition of drainage of the mother lesions.

Repeatedly it has been observed that a case admitted to hospital with a severe psychotic state and pronounced cyanosis in the summer has after the removal or drainage of closed sepsis, found on investigation, left the hospital in the following midwinter in a normal mental state and with normal peripheral circulation.

Treatment in the Fourth Link.

As a consequence of the radical treatment of the common cause lesions the peripheral cause of the positive sensory disturbances will have been dealt with. Following this treatment it is desirable to allow a pause for the healing to occur of secondary lesions, including the organic effects on the central nervous system, and for any vascular adaptation therein to manifest itself before passing on to drastic circulatory treatment under the third link. As in the treatment of cerebral irritation arising from traumatic causes, so under these circumstances the first essential is physical and mental rest. All exogenous stimuli and fatigue possibilities should be reduced to a minimum. During this treatment the temptation in any one case to resort to sedative drugs should be avoided, for morphia and the barbiturates in particular inhibit the utilization of oxygen by the brain.

The vitamins, antineuritic and anti-infective, are to be encouraged, but they are not likely to be of maximum value until sepsis has been removed.

Reconsideration.

To those who would conclude that the status of "shock therapy," whether by insulin or cardiazol, is not finally established, I would issue an invitation to reconsideration of the problem involved.

Do not, because they will not provide a short-cut panacea which can be given by a team of one, discard them as another treatment incapable of curing all the cases allotted to some psychiatric group or groups.

These agents have their uses if properly applied, and I submit their correct application is along the lines I have set out as part of a linked treatment.

This involves the cessation of the conception of "shock" as a therapeutic procedure. The term "shock" has acquired such a variety of meanings that its use as a measure of treatment is becoming impossible to justify.

To replace it and to start again with a new viewpoint I recommend the perhaps cumbersome, but clearly explanatory term, diphasic vascular variation treatment.

In the *Lancet* of 1932 I submitted that non-specific treatment, including protein given parenterally, was valuable in the treatment of mental illness. This I showed to be the case only in conditions of open or closed converted into open sepsis, but although when given in conditions of closed sepsis very definite shock effects could be observed, such effects were incapable of improving the mental or the physical states, which in fact deteriorated until the closed sepsis was converted into open.

This treatment by non-specific agents was brought within the scope of the linked treatment for use after septic disease has been effectively dealt with, and in a similar way I have brought retarded insulin and cardiazol into the same scheme, but not with the intention of producing any "shock" effect such as convulsion or coma.

However, I am not recommending reconsideration of the use of these agents along these lines in any spirit of compromise, but because I consider they are likely to assist in attaining results for the pathological and therapeutic reasons I have submitted.

By applying the treatment laid down in the first, second and fourth links the possibility of complications occurring when active treatment is applied in the third link is much reduced, and moreover a start has been made and perhaps completed in removing the condition for which the plenary use of cardiazol and insulin were brought into play under the "shock" therapy.

It has been reported that these "shock" therapies, given without any preparation of the patient, are responsible for a wide variety of secondary disease, e.g. lung abscess, reactivation of tuberculosis and secondary dementia. Such are obviously the result of the exacerbation of common causal lesions, whilst the fractures and dislocations which figure so dramatically in the reports indicate the overactivity of muscles weakened by toxaemia also arising from an untreated common cause.

Thus to attain at least two objects the treatment under the first link must be efficiently carried out.

If then after or before pyrexial treatment has been employed it is still thought necessary to employ circulatory stimulants these can be employed in subplenary dosage, and will then probably produce as good a circulatory stimulant effect or better than they would have when the cause against which

they would otherwise have been acting was present, even if the dose had been stronger.

I have thus used both retarded insulin and cardiazol in subplenary doses, and have found them effective as sympathetic and parasympathetic stimulants and with definite curative action on emotional and instinctive disturbances. Fear and anger have thus been permanently reduced by the one agent and fear transiently evoked by the other with such doses.

Other indications of the action of cardiazol even under these circumstances but along the lines I have indicated include the transient blurring of vision, herpes, and slight rises of temperature.

Nevertheless provided there has been drastic treatment of sepsis, improvement in circulation and mental state has occurred with such subplenary doses.

For those who would submit that the outward manifestations of action of these agents, the coma and seizure, are essential to the treatment with plenary doses, I would urge that treatment nevertheless be given in the first link in full, and that the plenary dosage be approached by a number of subplenary doses. With the linked method of treatment very permanent results have been obtained with properly certified cases after even ten, fifteen and twenty years of psychotic manifestations, including treatment elsewhere.

The application of this treatment is therefore not limited to cases of only six months or a year or two years' duration, nor to cases whose prognosis is good or who would attain to amelioration if left untreated, because such being cases of open sepsis, seasonal changes would effect the diphasic vascular variation in due course.

The observation that "shock" treatments have failed to attain any degree of success after a lapse of time is strongly in support of the view that any open sepsis which was present at the beginning of the illness has become closed, and against that barrier even "shock" fails to shake out the mental illness.

If relapse follows the application of these linked therapeutic measures it is because the treatment of the cryptic common cause has been incomplete or another infection has intervened, or that the extremes of seasonal change have strained a mechanism previously severely stressed.

FINALLY.

Finally, I fail to observe that there is any unanimity of opinion that these "shock" methods are at all specific for any form of mental illness, but that they are circulatory stimulants capable of inducing diphasic vascular variation is undoubted.

Now, a diphasic vascular change is exactly what happened at the time of the initial infection from which the common cause was left as an unresolved persisting disease area; hence if these vascular variation treatments, whether given in subplenary or plenary doses, are to attain to their maximum effects,

they are much more likely to do so when the tissues on which they act are not hampered with a toxic state. If these agents do shorten the remote effects of a common cause, such as a mental illness, they do so by renewing those changes which were incomplete at the time of the cessation of the original symptoms of the acute illness.

If the healing processes which are thus renewed are to obtain their best local and remote effects, they will do so when as much as possible of the stubbornly persisting infection which has been isolated and surrounded has been removed.

When this has taken place these agents can then be used effectively in subplenary doses and will fulfil their effects on the sympathetic and parasympathetic mechanisms, with results which have been observed in general medicine, where they are valuable in the treatment of debility arising in the course of chronic infective diseases, during convalescence, and in states of exhaustion.

If such areas of infective disease have not been removed then there will be some justification for the accusation, as has been made in the case of insulin, that the use of these agents is waste in wartime.

Put in simple language, it will be equivalent to driving an engine with both accelerator and brakes full on. The machinery suffers and no progress is made.

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THE ROLE OF THE SEX HORMONES IN PSYCHIATRY.

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I.

THE part played by sex hormones in the genesis and pathology of mental disorders is still the subject of striking differences of opinion among psychiatrists. Much of the evidence adduced is nebulous, and consists of uncontrolled and probably uncontrollable reports of subjective disturbances of the affective life of patients. In this paper an attempt is made to examine critically such evidence as is based on objective data deriving from both human and animal investigations.

It may be helpful at this stage to formulate the questions which it is hoped to answer at any rate tentatively from a review of the available evidence.

1. What variations of brain function can be noted after disturbances in the production of sex hormones ?

2. What variations in the production of sex hormones are to be noted in certain disturbances of brain function ?

3. How far can experiments, concerning the instinctive behaviour and the physiological reactions of animals under the influence of sex hormones, assist in the analysis of the pathogenesis of some disturbed brain functions ?

4. What causal relation exists between these two pathological variations? When is a disturbed brain function and when is a disturbed production of sex hormones the primary cause of the mental syndromes ?

Hypogonadism in Men.

The temperament of patients subjected to prepuberal castration differs completely from that of the normal individual. The persons concerned become shy and reserved, sometimes they are unwilling to work and to think, but they do not show any lack of intelligence. In some cases the intelligence is even above the average. They are often asocial, egoistic, egocentric, sometimes also cunning. Courage and initiative are lacking. Kretschmer (1) emphasizes their psycho-pathological relationship to the schizophrenic syndrome. Libido

is likely to be absent and so are frequently the manifestations of libido. The bodily activity is diminished and fatigability increased. These patients are therefore unfit for hard work, they suffer more than normal people from giddiness and sea-sickness. They have difficulty in dancing on account of their tendency towards giddiness.

The result of castration at postpuberal age is different in the adult male whose secondary sex characters have been completely developed; the libido is unaffected at least for some years after castration. Also in most cases the *potentia coeundi* persists though lessened. The regression in the secondary sex characteristics (diminished growth of beard, gain of weight and fat) is not very marked and takes place very slowly. These facts gave support to the view (Hammond (2) and others) that castration is without any marked influence on the psychological state. Loss of libido, however, is reported to occur only some years after castration in some cases and in others immediately after castration (Lichtenstern (3) and others). There are two explanations possible of the difference between pre- and post-puberal castration. According to one view psycho-physiological reactions once developed do not depend for their continued existence upon the endocrine milieu. But, as the facts reported later in connection with the instinctive behaviour of animals will show, this explanation is not very convincing. The second theory assumes that the testicular production of androgens is replaced by the secretion of another gland in the case of post-puberal castrates. Though there are still many points to be elucidated and the number of hormone analyses performed at different intervals after castration is still far from being sufficient, this view appears certain. The few hormone analyses performed so far have shown that excretion of androgens persists in eunuchs though in smaller quantities (Bingel (4), Chou and Wu (5), Koch (6), Callow (7)). By biological standardization Callow (7) found values varying from 0–39, average 19, i.u. androgens in the urine of eunuchs compared with 20–109 i.u. in the urine of normals. By chemical investigation of the 17-ketosteroids in the urine of eunuchs the same compounds were found as are obtained from normal men's urine (Callow (8)). Oestrogen is also found in the urine of castrates (Quental (9), Eng (10), Bingel (4)). The fact that an increased excretion of androgens occurs in patients with tumours of the adrenal cortex, which will be referred to later, supports the view that the adrenal cortex takes over androgen production in castrates. It is still questionable whether in normal conditions there is also a production of androgen in this organ. Some evidence in support of this view is given by the recent discovery of adrenosterone, a substance with male sex activity (Reichstein (11)).

Apart from mental disturbances of a sexual nature the following symptoms can be observed after castration of the adult. The third or fourth day after castration, a nervousness and hyperexcitability as well as flushes similar to those seen in climacteric women are reported. After some time, however,

these give way to a quiet phlegmatic state of mind and to a temperament similar to that described in the prepuberally castrated. Especially marked is the fatigability ; sleeplessness forms one of the most characteristic symptoms. The psychic reaction results sometimes in an inferiority complex ; sometimes irritability, leading to ideas of persecution, can be noticed. Melancholia, with danger of suicide, has been observed. The question as to whether these symptoms can develop into a state of real psychosis has not yet been sufficiently explored.

In any case it seems to be clear that the psychic disturbances developing after castration and in the other forms of hypogonadism mentioned below are not the immediate psycho-pathological result of the hypogonadism, but the final product of a chain of many progressively developed symptoms. If the androgens in the body should be diminished and, in spite of that, the libido be maintained, whilst the *potentia coeundi* disappears, this loss of balance might give rise to complicated psychic disturbances—either to states of depression or to hypererotism and manic states.

In the light of our present knowledge it cannot be doubted that there are various states of hypofunction of androgen production in the body, grading from slight hypofunction to such a degree of hypofunction as is observed after castration and in the *climacterium virile*. This fact is as a rule neglected by the psychiatrist. In such cases the following symptoms can be observed : diminished activity, increased fatigability, disturbed sleep, sometimes complete sleeplessness, increased excitability, irritability, giddiness, sickness, particularly train and air sickness, hot flushes, headaches, which, when carefully examined, are often found to be associated with indigestion and chronic constipation, diminished potency or impotence, lessened libido, sometimes through over-compensation increased libido. On the mental side anxiety states, paranoia and depression manifesting itself in abundant weeping are recorded. With some of these symptoms as a basis different kinds of psychoses may be developed.

In 1910, Kurt Mendel (12) for the first time introduced the conception of the *climacterium virile*. The symptomatology and the consequences of this state have not as yet been investigated as thoroughly as those of the female climacterium. The following writers have dealt extensively with the subject : Holländer (13), Vaerting (14), Rodhe (15), Juarros (16), Marcuse (17), Wenckebach (18). Hoche (19), who studied the question of the *climacterium virile* in detail, described the growing old of men as follows :

In most men the process of growing old proceeds without any obvious manifestations. The normal process of growing old does not show any definite periodicity or exacerbations. The importance of sexual life diminishes without completely disappearing. The uninstructed patient is unaware of the progressive change. Introspective patients may note with distress, resignation or humour, according to their temperament, that they are declining. Those with ill-balanced mental lives are more likely to succumb to various depressions. In

a certain percentage of cases various features said to correspond to the climacteric changes in women may be noted. A depression lasting from one to three years may occur, accompanied by emotional crises often leading to suicide. These cases as a rule recover.

Mendel gives the following description of the climacterium virile: "Emotionality—tendency to weep, decrease of energy, lack of resolution, unsociableness, hypochondria, self-reproach, suicidal tendency. The bodily disturbances are characterized by headaches, head pressure, stupor, hot flushes to the head, giddiness, faintness, disturbed sleep, dyspepsia, 'heart troubles,' cold in the extremities. As to sexuality, the complaints about the decreasing libido were repeated in all cases without any exception; potency was mostly diminished."

It is natural that the psychiatrist should look very sceptically on the assumed causal connection of the psychic symptoms mentioned above with a decrease of hormone production in the body. But that such a relation exists the endocrinologist knows already, and the psychiatrist will be bound to recognize these facts in the near future. Direct confirmatory evidence is supplied by the fact referred to in detail later on that, by administration of the biologically standardized male sex hormones, most of the symptoms mentioned can be cured. The decisive proof, however, will only be furnished by very systematic and exact hormone analysis of the body fluids of the patients in question. In this direction adequate methods of investigation have only recently been evolved. Isolated investigations carried out without the results being recorded in international units are of little value. It is for this reason that it is not proposed to discuss recent observations by the author on the male and female hormone excretion in such cases. Such observations have been made up to now on a small number of male involutional patients only. They showed a decreased excretion of the androgenic hormone influencing the growth of the capon comb compared with the excretion in normal men and, simultaneously, a disturbance of the relation between androgen and oestrogen.

The excretion of prolan in the urine is of great pathognostic significance, and this will also be found to be true with reference to the female climacterium. After removal of the testicles the prolan output in the urine increases (Ascheim-Zondek reaction I positive), as shown especially by Hamburger (20). The writer noticed an increased prolan output six days after castration. He found also an increased excretion in patients with *climacterium virile*. According to his experiences these patients must be differentiated from another group, in whose urine not a single unit of prolan could be detected, not even in 2,000 c.c. In these latter cases the decreased sex hormone production is not itself the primary manifestation, but only a secondary effect due to diminished production of anterior lobe hormones.

The part played by other hormones in the development of testicular hypofunction will be discussed in the section on the hypofunction of the ovary.

Hypogonadism in Women.

Owing to the existence of the climacterium in women, the mental and psychopathological consequences of hypogonadism in women have been studied for a much longer time and more profoundly than in men. In spite of this there is yet much to learn, both as to the hypofunction of the various endocrine organs and their relation to the many mental syndromes. As the mental and patho-physiological changes due to castration and climacterium are very similar, differing if at all only by their more or less rapid development, they may be considered together. In the discussion of these symptoms the simultaneous regressive changes in the uterus and external genitalia, as well as the changes in the organism as a whole, especially those of fat metabolism, have to be considered. These latter manifest themselves, not in a gain of total fat, but in a different local distribution of fat. Changes of heart rhythm, tachycardia, extrasystoles, increased blood pressure, flushes, giddiness are also reported. Further disturbance of heat regulation may occur, together with headaches, occipito-cervical pain, excitability, irritability, paraesthesia, buzzing in the ears, intractable sleeplessness, failure of memory and the power of concentration, and fatigability. In menopausal melancholia these symptoms occur in an exaggerated form. Another frequent form of menopausal psychoses is paranoia, mania being rare. Some psychiatrists maintain that these psychoses occur much more rarely in married women with many children than in unmarried women, women without children, and widows (Pappenheim (21), Strachan and Skottowe (22)). The paranoia is generally considered to be secondary to a psychopathic family disposition (Donald (23)).

Three to six days after bilateral ovariotomy in women the prolan excretion in urine increases (Damm (24)). This increase, up to 400 r.u. per litre, has been confirmed by many writers (Zondek (25), Oesterreicher (26), Fluhmann (27)). Follicular hormone excretion decreases considerably after ovariotomy, but does not completely disappear. Up to 90 i.u. of follicular hormone may be excreted daily (Laroche, Simmonet and Houet (28), Dingemanse, Borchardt and Laqueur (29)). Androgens are detected in the urine of castrated women (Callow (7), Simpson (30)). Examining the hormone output in menopause, Zondek (31) differentiated four stages: (1) Increased excretion of follicular hormone; (2) decreased excretion of follicular hormone; (3) increased excretion of gonadotrophic hormone and diminished excretion of follicular hormone; (4) disappearance of both hormones.

That a connection between the changes in hormone production and the development of mental symptoms exists is beyond question. There is some evidence for the view that the vasomotor deficiency symptoms may be due not so much to a lack of follicular hormone as to an increase of prolan. They develop only some time after castration, and it is stated that prolan causes an

oversensibility to adrenaline (Albright (32); H. Zondek (33)). The gonadotrophic hormone excreted in the menopause is identical with the so-called A factor of prolan, and is a follicular stimulating hormone produced by the pituitary anterior lobe. It is likely that in some menopause patients the anterior pituitary lobe production, not only of gonadotrophic but also of thyrotrophic hormone, may be increased. Grumbrecht (34) found an increased excretion of thyrotrophic hormone in the urine of climacteric women. In this connection the observation of hyperthyroidism in some climacteric women by Jeanneney (35) and Segond (36) may be mentioned. Those hyperthyrotic symptoms naturally form part of the mental syndrome and their hypophyseal origin is out of the question. On the other hand, hypothyrotic symptoms with dry, scaly skin may occasionally be observed in climacteric psychoses, those cases being very inaccessible to treatment. Considering the antagonism between follicular hormone and thyroid hormone the conclusion may seem justified that, in climacteric psychoses associated with hypothyrotic symptoms, the effect of follicular hormone treatment may be favourable, but in psychoses associated with hypothyrotrophic symptoms such treatment is unfavourable.

Considering the large variations in sex hormone production during the menstrual cycle, it would appear that the menstrual neurosis and psychosis represent secondary disturbances produced by those hormonal variations. At the middle of the menstrual cycle 400 to 600 i.u. follicular hormone are excreted. During menstruation the follicular hormone excretion can cease completely (Siebke (37), Frank (38), Smith and Smith (39), Palmer (40), Gallagher *et al.* (41)).

Investigating preglandiol, the probable excretion product of corpus luteum hormone, Venning and Browne (42) found that it makes its appearance 24–48 hours after ovulation, is excreted for 3–12 days and disappears again out of the urine 1–3 days before menstruation. (Total excretion during cycle 3–54 mgm.) The excretion of gonadotrophic hormone amounting normally to 25 r.u. daily is considerably diminished in the post-menstruum (Zondek (43)). According to Frank and Salmon (44) the biggest amount is excreted between the tenth and fourteenth day of the cycle. There is some evidence mainly based on the results of hormone therapy that certain premenstrual disturbances may be due to lessened corpus luteum hormone production. It has been suggested that the state of premenstrual irritability is conditioned by lessened corpus luteum secretion, whilst the menstrual depressive states are related to diminished secretion of the follicular hormone.

That some relation exists between menstrual disturbances and mental changes cannot be doubted, even though the exact relation has yet to be defined. The variety of these mental symptoms associated with menstrual disorders can be understood if we consider that amenorrhoea can be due not only to decreased but also to increased production of follicular hormone, or can be produced as well by decreased as by increased corpus luteum production.

Puberty.

At puberty a number of hormones connected with the sexual system suddenly appear in the body. The amount of gonadotrophic hormone in the urine increases (Soeken (45), Katzman and Doisy (46)). In girls when the cycle of hormonal production is starting the stresses of the environment assume quite different characteristics. The nervous system exposed to these new stimuli manifests at first some degree of instability (a tendency to giddiness, headaches, irritability). In normal individuals these symptoms disappear with the completion of sexual development. Owing to some predisposition or a developmental anomaly not as yet pathologically determined, the nervous systems of certain persons seem to be unable to deal with the sudden increase of sex hormone influence, with resulting disturbance of cerebral function. It is well known that schizophrenia and epilepsy often appear at puberty. In such cases hormone analysis may show whether disturbance is due to abnormalities in cerebral development, hormone production being normal, or to a disturbed hormone production, cerebral development being normal. In this connection it may be mentioned that some psychiatrists to-day still consider masturbation as a cause of schizophrenia. At first this assumption seems improbable, taking into consideration the frequency of masturbation. Since the process of masturbation may provoke an increased production of gonadotrophic hormone by the pituitary anterior gland, it may be that frequent masturbation during puberty gives rise to disturbances in hormone production with secondary psychological dysfunction.

Hypergonadism, Hyperproduction of Sex Hormones.

As the so-called sex hormones are not produced in the gonads exclusively, it seems more adequate to speak of a hyperproduction of sex hormones rather than of hypergonadism. Owing to the multiplicity of possible combinations of hormonal disturbances which at first result in prematurity the accompanying somatic syndromes may vary greatly. Thus boys, four years of age, have been described who, though completely sexually developed, with strong body structure and a big head, had still their first teeth. The evolution of a schizophrenic syndrome in girls with precocious sex development is generally due to an adenoma of the adrenal cortex. In tumour of the epiphysis, sexual precocity is said to be associated with mental precocity.

Cases of pubertas praecox are reported who at the age of 4 to 6 years, show bodily and sexual development normal to 15 years, but intelligence normal to their own age.

II.

Symptoms of endocrine disturbances are obvious in a great number of psychotic patients. According to some statistics, from one-half to three-fourths of the patients in mental hospitals show some endocrinopathy. These statistics are as yet based only on the more general symptoms, and the percentage would probably be still higher if more refined methods and systematic hormone analyses were employed. An important part is played by disturbances in sex hormone production. It must be emphasized that disturbances of sex hormone production occur only rarely alone, and are mostly associated with disturbances of other endocrine organs such as thyroid and suprarenal cortex. Finally, disturbance of sex hormone production can follow a primary change in the thyroid or suprarenal.

The primary importance of the disturbed sex hormone production in a number of depressions, anxiety states, melancholias and paranoias has been emphasized. Broster, Allen *et al.* (47) in their book on *The Adrenal Cortex and Intersexuality* deal not only with the symptoms of intersexuality, but also with the question as to how far endocrine factors may be concerned in the development of different psychoses. They describe, for example, a case of androgenital virilism with psychosis in which recovery from the psychosis followed adrenalectomy. More recently Allen (48) described a similar case, a woman of 34 years suffering from hirsutism, delusions without systematization and paranoic ideas. The hair of face, legs, arms and pubis was fairly strong in growth and dark in colour. By extirpation of the enlarged right adrenal, the mental state of the patient was largely restored. Before the operation 80 units of androgens daily could be found in her urine. A fortnight after the operation only 8·5 units were found. The excretion of 17-ketosteroids amounted before the operation to 10·8 mgm. daily; there were only 3·7 mgm. after the operation and ten months later 8·8 mgm.

There is no doubt about the intimate relation of schizophrenia to the gonads and the production of sex hormones. The writer has recently noted the external evidence of hormone disturbances in a number of schizophrenic patients. Some of these exhibited a general hypogonadal build, under-development of facial hair, scanty pubic hair, often feminine in its distribution, and in the women there was often disturbed menstruation. On the other hand, cases with increased hirsutism and masculine body build were to be seen. In women there was often a pronounced hirsuties around the nipples, on the legs and sometimes on the thighs. In two cases of this latter category up to 35 mgm. 17-ketosteroids were excreted in 24 hours. Apparently they were similar to the cases reported by Allen as due to a tumour of the suprarenal cortex. The hypogonadal type was, however, much more frequent. Sometimes no prolan at all was found in the urine, together with a decrease of the

17-ketosteroids. The pathological significance of this condition requires further investigation. It will probably be found that several very different pathological states are grouped under the heading of "schizophrenia." Besides the two forms of schizophrenia mentioned above, there are, without doubt, also hypothyrotic types, which respond very well to administration of thyroid (Hoskins and Sleeper (49)). Gjessing (50) deals, in his work, especially with this category.

Mott (51) was the first to conduct systematic pathological anatomical examinations of the gonads in schizophrenia. More than 50 per cent. of cases of dementia praecox showed a complete regressive atrophy and no signs of spermatogenesis were to be seen. Münzer (52) found a similar state in a testis surgically removed from a schizophrenic patient. Mott (51) recorded also a regular decrease in weight of the testes of schizophrenic patients, the average weight amounting to only 12 gr. as compared with an average weight of 18 gr. in other diseases. Mott also claimed that the surface of the ovaries of cases of dementia praecox has usually a white crinkled appearance. Histologically the ovarian follicles are greatly decreased in number and the ovarian cells are degenerated. In most of the cases observed, menstruation had been irregular for some time. MacCartney (53) examined 20 Chinese eunuchs. They showed changes typical of dementia praecox, such as lack of affect, apathy, introspection and purposeless existence. In 110 autopsies performed in cases of dementia praecox, MacCartney found that 60 per cent. of the males were eunuchoid and 52·5 per cent. of the females had disturbances of the ovary. Hutton and Steinberg (54) found endocrine disturbances in 70 per cent. of psychotic patients examined by them, 59 per cent. of them being schizophrenic, and of these 66 per cent. showed hypophyseal and ovarian disturbances. Clegg (55) examined one hundred schizophrenic patients and measured them anthropometrically. Secondary hirsutism, poor muscular development, tender skin and enlargement of long bones were obvious. Only nine of forty-six gynaecologically examined women were normal, the others showing disturbed menstruation and hyper- or hypoplasia of the uterus. In 129 out of 186 schizophrenic women the blood oestrin content was lessened (Sears and associates (56)). There was a diminished prolan excretion in 50 per cent. of forty schizophrenic patients examined (Milco and Borcanesco (57)). In climacterium the prolan excretion of schizophrenic women was lower than that of mentally normals (Turkevitch and Gershanovitch (58)).

Though the intimate relation of schizophrenia to gonadal function cannot be doubted, the question remains to be answered whether the disturbed brain function or the disturbed endocrine function may be primary. Some years ago Kroll (59) reported improvement after vasoligation in four out of twelve patients. Kauders (60) and Pilcz (61) claimed to have obtained favourable results by administration of high doses of testis powder.

Considering that the structural testes changes in schizophrenics described

first by Mott (51) recall the syndrome occurring after hypophysectomy, experiments with gonadotrophic hormone of the pituitary anterior gland would seem to be indicated. Recently Power (62) and Fischer (63) have injected schizophrenics with prolan, the gonadotrophic hormone of pregnant urine. They claim certain favourable results.

In a paper with this title many would expect to find a very far-reaching discussion of homosexuality. From the endocrinological point of view an examination of the literature shows that little is known in this direction. Only the cases which are considered to have ovotestis, arrhenoblastomas or tumours of the adrenal cortex are recorded. Recent reviews on this subject have been published by Moszkowicz (70), and Broster, Allen *et al.* (47). Analytical hormone examinations have rarely been performed and it is impossible to draw any conclusions. Animal experiments show, however, that sexual drive may be influenced by hormones and, moreover, male sexual drive may be obtained in females and vice versa. But considering how often homosexuality may be due to chance and environment the question seems still more complicated. When dealing with this problem, we ought also to bear in mind the intimate relationship of male with female sex hormones regarding their chemical structure. Possibly none of the more obvious variations in gonads or other endocrine organs might be needed to account for homosexuality if disturbances of cholesterol metabolism brought about qualitative changes in the structure of sex hormones. Much more must be known about the production of sex hormones in the body and about the intermediary metabolism before we can differentiate between homosexuality due to hormonal changes and homosexuality due to psychic changes.

III.

An attempt may be made to investigate the relation between brain function and sex hormones by examining the instinctive behaviour of animals in the sphere of sex.

The genital centres in the central nervous system are not yet localized. Using young male rats it was found that even after destruction of as much as 50 per cent. of the cerebral cortex patterns copulatory behaviour may persist. In female rats what appeared to be normal copulation, gestation, parturition and maternal behaviour was seen after removal of 30 to 50 per cent. of the total cortex, whilst all signs of maternal behaviour disappeared after destruction of 65 to 80 per cent. of the cortex. Such females, though they showed characteristic copulatory responses, delivered viable young and sometimes removed the foetal membranes, very seldom brought the young together or built nests for them (Stone (71)). As to the question of localization of the sexual centres, the following writers, Beach (72), Bacq (73), Whiting (74), Bard (75), may be consulted. After abdominal sympathectomy or severance of the two hypogastric nerves in male guinea-pigs, Bacq (73) found mounting, erection,

intromission and rhythmic pelvic movements, but no ejaculations as response to activation by receptive females. In two male rabbits the abdominal chains were removed. Three days afterwards copulation would be seen differing from the normal only in that it was prolonged and did not end with the characteristic tonic clasp with "squeal" and falling on the side at the time of orgasm. Sympathectomy in female rats did not as a rule affect the oestrous cycle, fecundation, gestation, parturition and maternal behaviour, whilst there were deficiencies in lactation (Sweet and Thorp (76)). Maes (77) transected the spinal cord of cats at the first cervical segment. Three to six hours after the transection when the spinal shock had subsided he tested the sexual reflexes of the animals and got completely positive responses. Other oophorectomized animals did not show the reflexes when tested in the same way. But after treatment with follicular hormone the reflexes reappeared. Maes concluded that at least some components of the sexual behaviour are short arc reflexes, the activity of which depends on the hormonal condition, though they can act independently of the higher centres. The existence of a hypothetical "sexual centre" (Dempsey and Rioch (78)) should be accepted with caution, and it may be assumed that such a centre acts not so much as a pacemaker under the influence of which unspecific activities of the spinal cord are transformed into specific sexual reactions, as an *ad hoc* mechanism existing at different levels of the brain stem.

According to Stone (71), hormones from the gonads appear to be necessary for the organization of sexual behaviour in young vertebrates. Castration of male vertebrates in infancy results in a total or almost total lack of sexual responses. Eventful sexual responses shown afterwards have not the same vigour as those in normal animals of the same age and species. After castration, sexual aggressiveness in adult males is generally diminished. Castration of females in infancy or childhood results apparently in complete disappearance of sexual behaviour.

Some facts suggest that the nervous mechanisms that subserve sexual behaviour may already be organized before they are activated by the impulse of puberty. Weston (79) observed a six-weeks-old colt which tried to mount its mother and at the age of 3 months mounted all fillies and calves. Zuckerman (80) studied the behaviour of an eight-months-old pig-tail monkey. Exploring its mother's body in the midst of playing it suddenly peered at her pudendal region. Climbing over her body it remained some moments in a mounting position. At the age of six months it mounted her in response to her repeated presentation and a month later this activity was accompanied by erection and pelvic thrusts. The mother occasionally pulled it off whilst at other times she seemed to incite it. At this time the animal was still suckling and always slept in its mother's arms. There was a threefold relationship between them: the maternal one involving nursing; a social one of playing and protection; and finally the sexual one. Köhler (81) observed similar behaviour in

chimpanzees. According to Zuckerman these responses are increased at puberty, apparently due to the sex hormones, and their previous playful character is then replaced by the purposeful quality of most of the responses of the mature animals.

According to Lang and Evans (82), oestric behaviour, willingness to mate, is in rats coincident with the cornification stage of the vaginal smear. Hemmingsen (83) and Ball (84), however, were able to observe it after injection of oestrone in castrated females. In such animals far larger doses were needed to induce heat than those sufficient to bring about the morphological changes of vaginal epithelium. According to experiences reported by Marrian and Parkes (85) and Wiesner and Mirskaia (86) the same behaviour can be observed in castrated mice. The fact that oestrous behaviour cannot be induced in this way in all animals may support the opinion advanced by Parkes (87) that a second hormone may be needed to bring about copulation. The corpus luteum hormone may be the one in question. In experiments carried out on guinea-pigs Young and his associates (88) showed that corpus luteum hormone administrations must be combined with follicular hormone administration to produce oestrous behaviour. Very small doses of follicular hormone, if followed by progesterone injections, are apt to lead to excitement and mating. In cats (Pompen (89) and Bard (90)), dogs (Kunde and co-workers (91)), sheep (Cole and Miller (92)), cows and sows (Steinach, Stäheli and Grüter (93)), however, heat could be induced by follicular hormone alone.

Castrated male animals showed sexual desire after treatment with male sex hormone. Schapiro (94) castrated male rats before sexual maturity. After nine weeks no sexual behaviour was elicited. After 18 injections of 0·5 mgm. testosterone daily, unmistakable evidence of copulative activity was obtained in the same animals. Stone (95) reports other experiments giving similar results. Similar results are recorded by Fremery and Tausk (96) after injection of 10 mgm. testosterone propionate in male rabbits castrated in infancy.

These experiments confirm the observations made as early as 1848 by Berthold (97) in his classical transplantation experiments on capons and by Steinach (98) in transplantation experiments on guinea-pigs. Freud, Laqueur and Pompen (99) achieved by administration of testicular hormone the reappearance of the strutting and copulation with simultaneous regeneration of the secondary sex characteristics in capons.

Morito (100) and Hamilton (101) produced in baby chicks receiving daily injections of testosterone propionate precocious activation of masculine behaviour. The chicks began to crow and to show evidence of pugnacity at the age of ten days. Mobilizing the endogenous androgen production by injection of gonadotrophic hormone, Domm and van Dyke (102) obtained the same results.

Male sexual behaviour can be induced in female rats by injection of testosterone propionate (Ball (103); Stone (71)). Kun (104) treated normal and

castrated male rats with follicular hormone and produced a marked feminization of behaviour. In normal males the male libido persisted with the female erotization and so obvious behaviour hermaphroditism could be developed.

Many writers report that male animals show feminine copulatory responses when approached by an aggressive male, and that many females at the time of oestrus show spontaneous bisexual behaviour. From the endocrine point of view these facts are not yet explained. (See also Stone (71).)

Experiments supply evidence of the important influence of sex hormones on sexual attraction. Of one hundred female castrated rats kept together in one cage, only one had been treated with follicular hormone. If a male rat in heat or a castrated male or female rat treated with testosterone propionate were put in the cage it found out immediately the female treated with follicular hormone and tried to touch it.

If, measuring the motor activity in revolving cages, two cages each with one male rat were put one beside the other, the lessened or increased activity of one rat was without any influence on the activity of the other rat. But if a cage with a female rat were placed near the one with the male, the activity of the male not only increased but showed also the same periodicity as that of the female. The activity showed the same rhythm, and was synchronous to the ovarian rhythm of the female. If several females, the maxima of activity of which were of different date, were put near to the male, the activity increased still more, but no periodical variations could be observed (Slonaker (105)).

The maternal behaviour of animals seems to depend directly on the hormones. In such cases it is not the sex hormones but the hormones of the anterior pituitary lobe that play the decisive part, especially the prolactin and to some extent the gonadotrophic hormone. Wiesner and Sheard (106) studied the maternal behaviour in rats. Starting about the end of pregnancy it lasts for three weeks after birth. It is mainly characterized by the fact that the rat mother protects the young, keeping them in the warm nest and bringing them back if they have been taken out. She even fosters the young of other mother rats if they are mixed with her own young. The maternal behaviour is completely independent of the mammary gland and persists even after excision of this gland. After treatment with gonadotrophic hormone of the anterior pituitary lobe, even virgin rats may suddenly show maternal behaviour. As yet it cannot be decided whether the latter result may not be due to an admixture of lactogenic hormone with the gonadotrophic factor. Riddle, Lahr and Bates (107) induced maternal instincts in rats, injecting prolactine for two or three weeks. Injecting prolactine for 3–7 days they obtained broodiness in laying hens.

A nervous reflex mechanism, acting independently of hormones, seems to be of importance for the maternal behaviour. Placing of newborn rats in the cage of virgin animals can in itself induce maternal behaviour (Wiesner and Sheard (106), and even hypophysectomized virgin or male mice may behave

maternally if any newborn rats are put in their cages for some days (Lebland and Nelson (108)).

Nest-building activity should be differentiated from maternal behaviour. Richter (109) showed that it is only sometimes combined with the manifestations of maternal behaviour. There is some connection between nest-building and the maintenance of body temperature. After hypophysectomy nest-building is greatly increased—a fact due, according to Richter, to the atrophy of the thyroid after hypophysectomy. An increase of nest-building activity could be obtained by thyroidectomy and by lowering of the external temperature. The general bodily activity is, however, lessened after hypophysectomy and increases again after administration of gonadotrophic hormone.

Castration in rats results in diminished spontaneous activity, increasing again after administration of follicular hormone. This increase after follicular hormone occurs also in castrated males (Richter (109), Wang (110), Gans (111) Miley (112)). In dogs after castration the response to external stimulation was disturbed; new conditioned reflexes could not be established (Arkhangelsky (113)).

It may be possible to establish a certain connection between the decrease of spontaneous body activity as seen after hypophysectomy and ovariotomy and blood circulation in the brain. After hypophysectomy Reiss and Golla (114) found the blood content of brain diminished, and an equally pronounced decrease of blood content after castration. By administration of sex hormones to such castrated animals the blood content could be restored to normal. In normal rats, oestrone as well as testosterone increases the cerebral blood content, and it seems to be immaterial whether males or females are injected with male or female hormone.

IV.

Are disturbances in the endogenous production of sex hormones ever a primary cause of mental disease?

An affirmative answer to this question would be of far-reaching importance to the psychiatrist, and it might be possible to initiate an entirely new line of treatment for certain mental disturbances. In certain psychoses the existence of an endocrine factor cannot be doubted. The mental disorders of the climacterium or those appearing with a suprarenal tumour and disappearing after its removal are obviously of endocrine origin. In many other types of mental disorder the presumed existence of an endocrine factor will only be definitely accepted or rejected when complete hormone analyses are systematically undertaken in the wards and laboratories of mental hospitals.

In a previous paper published in this Journal the author (116) tried to illustrate the neuro-endocrinological relationship by means of a diagram. He

emphasized the presence of a gonadal centre in the hypothalamus, whence impulses proceed to the pituitary, governing its production of gonadotrophic hormone, and this hormone regulates the endogenous production of sex hormones. If there is a lack of sex hormones in the periphery, excitatory impulses proceeding to the gonadal centre provoke an increased production of gonadotrophic hormone by the pituitary anterior lobe. At the same time this gonadal centre is subject to both excitatory and inhibitory influences from the cerebral cortex. Such a scheme illustrates the fact that disturbances of the cortex may give rise to a complete endocrine syndrome similar to those observed after ablation or atrophy of the endocrine glands in question.

It is obvious that the interaction between cerebrum and gonads may proceed in a vicious circle. Primary psychic disturbances, affections or shocks may produce a disturbance in the gonadal function, and the gonadal affection may in turn affect cerebral activities. Such a circle of events may form the start of a pathological process bound to grow worse and worse. To illustrate this vicious circle a case observed by the writer, certainly not a very rare one, may be reported.

A perfectly healthy girl, 19 years of age, was engaged to be married and was very fond of her fiancé. By a tragic accident the young man died. Owing to this shock menstruation ceased and she gained weight. She became depressed and unsocial. The libido disappeared completely, little by little, she became obese, suffered from severe headaches and showed mental irritability and paranoia. This state grew so much worse during a year that a diagnosis of schizophrenia was made and the girl was sent to a mental hospital. Following treatment with gonadotrophic hormone alone (pituitary anterior lobe) her symptoms disappeared, and the patient was discharged from the hospital 5½ months after admission.

It must be recognized that at best gonadal dysfunction can only initiate the first stage of a mental disturbance—whether climacteric or schizophrenic or other changes of brain function. The relation between the different glands—between gonads and thyroid or gonads and suprarenal cortex—makes it clear that a functional disturbance of one of these glands must necessarily affect the function of the others. A case of mental disturbance primarily due to gonadal dysfunction requires for its full investigation a very complete hormone analysis.

The result of therapeutic experiments with hormone administration throws light on the pathophysiology of certain disturbances of the brain function. Such experiments have only recently been possible, as sufficiently purified and concentrated sex hormones have only lately been at the disposal of the physician. Many earlier experiments in this direction can give little information, as the different hormone extracts used had either not been biologically standardized or were of insufficient strength.

Reference may be made to some recent therapeutic experiments which

appear to throw some light on the primary role of the sex hormones in the genesis of certain mental disturbances.

In some cases of prepuberal castration and eunuchoidism studied by the author, the induced mental changes, especially the lessened activity, the slow mental reaction and slowness of comprehension as well as the depression with danger of suicide, disappeared completely after treatment with testosterone propionate—testovirone. Simultaneously some of the secondary sex characteristics began to develop. In one case the treatment lasted for one to two years. During the first six months 50 mgm. testosterone daily were injected, during the next six months 50 mgm. testosterone every second day, afterwards 50 mgm. testosterone every third day. It may be especially mentioned that, according to the author's experiences, the treatment apparently ought to be continued during the whole life of the patient. At least 25 mgm. testosterone propionate twice weekly have to be injected. If the injections be stopped mental irritability appears, eventually leading to depression. In castrates stopping of hormone treatment may be regarded in its effects as a second castration, only that in this case the androgen production is not taken over by another gland as the continuous administration of high doses suppresses the endogenous production. Psychic disturbances due to postpuberal castration in adults disappeared completely following administration of testosterone propionate. In such cases injection of doses ranging between 25 to 50 mgm. twice to four times weekly according to the degree of disturbance was found to be sufficient.

In cases of climacterium virile and of the transitory forms mentioned above the symptoms recorded, consisting of headaches, sleeplessness, irritability, impotence, depressions, could be completely removed by injection of 10 to 25 mgm. neohombreol, perandren or testovirone three to five times a week. This improvement, in some cases observed by the author, proceeded most dramatically. Often following the second injection the patients report better and refreshing sleep. The gait, previously tired and sluggish, was noticed to be much more elastic after about a week. After a week the patient notices a decrease of fatigability and, especially, improved power in mounting stairs—an exercise usually complained of as particularly exhausting. During the following weeks the regression of the other symptoms is completed. Many symptoms, as for example giddiness and sickness, disappear immediately after the start of treatment.

A definite answer to the question as to whether the brain disturbances are due to climacterium virile or represent concomitant transitional stages is supplied by the examination of the prolan output in urine in such cases. Increased prolan output mostly indicates a gonadal hypofunction and, therefore, indicates testosterone propionate treatment.

Numerous experiments are reported and some of them may be mentioned.

Foss (117) reports the case of a man, 38 years of age, who at 19 had lost

both testicles. After treatment with 20 mgm. testosterone propionate daily for a week erections and libido reappeared. Persisting priapism, to which not even coitus could put an end, appeared every night. Therefore the dose was reduced and injections of 20 mgm. twice weekly proved sufficient to maintain libido and erectile capacity continuously. Eight days after the treatment was stopped erections no longer appeared.

Many writers record the disappearance of long-standing impotence after administration of testosterone propionate (Hamilton (118), Huhner (119), Vest and Howard (120), Villaret, Justin-Besançon and Rubens-Duval (121), Schmitz (122), Hass (123), Venzmer (124), Klein (125), Bauer and Koch (126), Bickel (127), and others). Miller, Hubert and Hamilton (128) studied the mental and behaviour changes in two castrates, two hypogonadal men and two patients suffering from a functional impotence. None of these patients showed any sexual desire or erectile capacity; all suffered from symptoms of anxiety or depression. After treatment the sexual power was restored in all cases. The depression disappeared and the intellectual energy was increased. Guirdham (129) described his experiences with four cases suffering from acute anxiety with obsessional traits; paranoic ideas, profound inferiority feelings, acute melancholia with delusions of financial ruin and hypochondriacal delusions. The prognosis was considered hopeless in two of these cases. After treatment with the small daily injection of 5 mgm. testosterone propionate or 5 mgm. androsterone all these cases improved very markedly.

In children with cryptorchidism, aged from 18 months to 11 years, Hamilton, (130) noticed erection after injection of 2·5 to 10 mgm. testosterone propionate 3 times weekly. In senile states muscular activity and mental capacity was increased by daily injection of 40 mgm. testosterone for 15 days (Laroche, Simmonet *et al.* (131)). Fatigability is markedly lessened and the muscular strength measured with dynamometric tests considerably increased (Hamilton and Gilbert (132)).

There are many records of simultaneous improvement of depression, irritability, and impotence after treatment with testosterone propionate in cases of *climacterium virile* associated with prostatic hypertrophy (Mock (133), Schmitz (134), Werner (135)).

These observations indicate that in all the reported cases a primary disturbance in the androgen production of the body leads to secondary disturbances of brain function. The hypofunction of the testicles may also in the prepuberal period have an unfavourable influence on the mental capacity of boys. This is especially obvious in boys with cryptorchidism; their mental capacities, their school work and their general behaviour is greatly improved by treatment with prolan, the gonadotrophic hormone prepared from the urine of pregnancy; simultaneously in such cases the testicles descend (Molitch and Poliakoff (136)). The timidity, anxiety, depression, sometimes associated with irritability and aggressiveness observed in cryptorchid boys, were improved

by the combination of prolan treatment with the usual psychiatric treatment (Mittelmann (137)).

The therapeutic rejuvenation or reactivation experiments may be mentioned. Their history is not as yet completed. In 1920 Steinach (138) performed vasoligature and vasectomy in both animals and human beings. He claimed to have restored sexual power and potency and to have increased mental and physical strength. The operation was said to have resulted in increased endogenous production of androgen due to hypertrophy of interstitial tissue—the so-called puberty gland. Doppler (139) painted the vas deferens with strong phenol solution and so produced a partial obliteration of the spermatic duct. He claims the same results as Steinach. Kammerer (140) reported rejuvenation after application of x-rays, destroying the parenchyma and increasing the interstitial tissue of the testicles. Lichtenstern (3) recorded good results with transplantation of normal and cryptorchid testicles in eunuchs and seniles. Voronoff (141) transplanted testicles of monkeys in man and claimed striking results. To-day the practical importance of these transplantation experiments is minimal as the survival of such transplantations in the body is very limited. The same effect at least can be produced by implantation of testosterone crystals. It is well known that such crystals are not water-soluble and are, therefore, absorbed only very slowly. According to reports of Deanesley and Parkes (142) and the writer's own experiences, they remain beneath the skin for a considerable time. Most favourable results were obtained by the author by repeated implantation of crystals. In patients with so-called *climacterium virile* or *climacterium virile praecox*, for example, the beneficial result of implantation repeated every four weeks so as to accomplish a total deposition of 1500 to 2000 mgm. lasted for two years without any impairment. It is doubtful whether vasoligature and other interventions, influencing the testicular structure, are procedures of therapeutic importance. To-day we have at our disposal the gonadotrophic hormone of the pituitary anterior lobe which is often successful in stimulating testicular function. The results so far seen by the writer after treatment with this hormone are very promising.

Treatment of women with sex hormones has been performed on a very big scale. The psycho-pathological indications are not yet uniformly established. The therapeutic results available up to now support the view that brain function and psychic reactions are directly influenced by the female sex hormone.

The symptoms occurring after ovariotomy, which are wholly in keeping with those in the climacterium and in their most exaggerated form lead to involutional melancholia, can be influenced by follicular hormone in a most favourable way. In fifty-five female castrates Werner (143) observed complete disappearance of all mental symptoms simultaneously with the vasomotor and general somatic disturbances after treatment with follicular hormone. Many reports are given on the follicular hormone treatment of psychosis, depression

and melancholia due to climacterium (Hawkinson (144) recording 1000 cases, Ault *et al.* (145), Suckle (146), Little and Cameron (147), Jones *et al.* (148), Dynes (149)). Little and Cameron (147) administered follicular hormone to eleven women with involutional melancholia and six young women with a psychosis manifested mainly as melancholic negativism. All patients were injected with doses of 1000 i.u. twice a week. Of the eleven climacteric women, eight were fit for discharge from the hospital after a few weeks. In the other three the treatment resulted only in partial improvement. The six young women showed marked improvement. Suckle (146) reports a case of a woman, 47 years of age, whose menstruation became scarce and who simultaneously developed severe depression and attempted suicide. She later became confused, with delusions and hallucinations. After treatment with follicular hormone (1000 i.u. a day perorally and once a week an injection of 5000 i.u.) the state of depression disappeared completely, and after five weeks the woman was able to do some house work.

Certain disturbances seem to be accessible to corpus luteum hormone. In the third week of the cycle during the premenstruum, restlessness, headaches, giddiness, crying spasms, sleeplessness, in some cases nymphomania, can be seen. Israel (150) studied this syndrome in fourteen women, aged 20 to 40, in the course of three years. By administration of progesterone he was able to improve these states markedly.

Attempts have been made to influence different deficiency symptoms due to ovariotomy or menopause by administration of the male sex hormone testosterone. Desmares and Capitain (151), Birnberg, Kurzrok and Livingston (152), Kurzrok, Birnberg and Livingston (153) and Salmon (154) performed successful experiments in this direction.

The results of the many therapeutic experiments performed hitherto in climacteric mental disturbances, depressions and psychoses are very promising. The doses used are still far from uniform, and agreement as to indications for hormone treatment is far from being achieved. The many different disturbances comprised by the name "melancholia" are not likely to be influenced by the same hormones in the same way. An exact analysis of the single psychic phenomena in their relation to the hormones in question would be of great value. But first of all, we have to rely on hormone analysis. So far the relative excretion of female and male sex hormone in women in states of depression has hardly been studied. In this direction the examination of the vaginal smear is of some diagnostic help. Certain signs of vaginal atrophy detected by this method can be improved by follicular hormone. Salmon and Frank (155) checked the efficacy of the follicular hormone doses administered by them with the vaginal smear method described by Papanicolaou (156), and found a parallelism between the changes in the vaginal smear and the state of the patients. When the vaginal smears of climacteric women showed the characteristics of the vaginal smears of normal women in the proliferation stage, the climacteric symptoms

were found to have improved. If the treatment was stopped regression of the changes produced in the vaginal smear and, simultaneously, exacerbation of the climacteric symptoms could be observed. Similar experiences are recorded by Papanicolaou and Shorr (157). Another probably much more important test is afforded by the estimation of the prolan content of urine. As mentioned above, this is increased in certain hypofunctions of the ovary. Dealing with psychic disturbances in women it seems desirable first of all to estimate the prolan content of the urine and, should this be increased, to administer follicular hormone until normal prolan excretion is restored. At present such experiments are being carried out in the Bristol Mental Hospital by Dr. Hemphill and Dr. Martin in collaboration with the writer. The endocrinological factor in the psychic changes of the menopause is obviously not only conditioned by follicular hormone deficiency. Some part in the mental syndrome may be due to the corpus luteum hormone and the testosterone physiologically excreted in the urine of women. Moreover, as mentioned above in connection with the menopause, not only do gonadal disorders occur, but the thyroid seems also to be involved.

Since the effect of disturbance of the hormone equilibrium on the mental state depends on the functional condition of the nervous system affected, it is obvious that the symptoms will vary both quantitatively and qualitatively. To assess the influence of any hormone disturbance it is necessary to have as complete an account as possible of the state of the nervous system, and any attempt to formulate a rigid symptomatology is bound to fail. It is equally true that hormonic treatment to be efficient necessarily predicates a complete hormone analysis; treatment based on symptoms alone may easily do very grave damage. Hormonic analysis has so far been very little used in the investigation of mental disorders, but it is hoped that this paper has furnished indications that the part played by hormonic disturbances in mental disorders is far from negligible, and that a very promising field of investigation lies open to the psychiatrist who will add endocrinology to his clinical resources.

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ON A SPECIFIC PSYCHOTIC REACTION OF SCHIZOPHRENICS TO PHYSICAL ILLNESS.

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THE way in which schizophrenics react to physical illness and injury is a problem worthy of study, especially at the present time when schizophrenia is being so widely treated by methods which bring about profound changes of the physical state. Although schizophrenics, recent and chronic, are very susceptible to physical illness and form a considerable part of the sick population of the average mental hospital, this question has not attracted a great measure of attention. A survey of the schizophrenic population of a mental hospital suggests that there is an apparent lack of specific psychotic reactions to physical illness, so that it would seem as if schizophrenics react to physical illness either in a normal way or more commonly with indifference. It is true that certain paranoid patients include complaints of physical disturbances in their systems of delusions, but as a rule, even in these cases, there is no specific reaction to physical illness, which like other experiences enters into the world of imagination in which the patient exists.

We are concerned here with cases in which a physical illness was followed by specific psychotic reactions and influenced considerably the picture of the psychosis. The problem arises whether specific reactions such as we propose to describe are due to features of the psychosis or to the special character of the physical illness or to constitutional factors, operating individually or interacting.

The schizophrenic personality itself may be inclined to react in a specific way to kinds of physical illness which have an affinity for the psychotic process, and which can readily be related by the patient to characteristic schizophrenic experiences. We propose to treat this problem by investigating the following relevant cases :

CASE 1.—Fanny Y—, aged 41, admitted November 27, 1939.

She had always been rather suspicious and inclined to depression. Her relatives regarded her as hypochondriacal. There was no history of alcoholism. Four years before admission she had undergone a thyroidectomy, which was not followed by any mental symptoms. Her father was an alcoholic, her mother died insane; her maternal uncle and one sister had been treated at mental hospitals for some chronic psychoses (we were unable to ascertain details of their cases). The patient had not been noticeably abnormal until about one month before admission, when she began to express strange ideas and to behave in a peculiar way. The account

that she gave of her illness was borne out by her husband and was as follows: For many years she felt that her neighbours were hostile and used to talk about her behind her back. She became increasingly unsociable, and as years went on turned more to religion.

The course and character of this paranoid illness underwent an extraordinary change when the patient contracted two injuries, the one a burn on the hand, the second a boil on the chin. Some months before admission she burned her thumb while ironing. The burn healed slowly and caused pain, the scar forming a cross; while healing it used to bleed. One day she felt a banging in her head and thought that drops of blood were falling from her forehead. Looking down at the burn, she saw within it "the body of Christ upon a cross." From this she imagined that she herself was being "crucified" in some way by her neighbours, but thought that Jesus was helping her. For a while she heard imaginary voices, and sometimes men running past her door at night. Soon after a painful boil developed on her chin, which pointed through five "heads." As it was healing she noticed that if she looked in the mirror and rubbed the boil she saw through the reflection of the five "heads" the faces of five members of Parliament. She recognized them from photographs in the papers. The faces changed sometimes, and once she saw the Prince of Wales amongst them. There were never more than five faces. She thought that this phenomenon must be due to television, especially as she imagined that people tuned in and listened to her on the wireless. Subsequently she thought that her husband's face had changed. She was unable to look him in the eyes. As she did so his eyes turned in and his face looked like that of the devil. On the last occasion that she consulted her doctor she noticed that when she looked at him his eyes turned in, and his face became swollen. While in hospital she did not experience any of these phenomena, but at first she was afraid to look at people in case she saw the devil, and for about a month she felt that everyone in hospital avoided her. Although during the whole period of hospitalization she behaved rationally, she insisted that the experiences mentioned above had actually taken place.

This is a patient who had held paranoid ideas for some years and who showed acute psychotic symptoms some months before admission. According to the classification of Bleuler, this is a case of a schizophrenic psychosis. The patient had contracted injuries to her skin on two occasions, the first being a burn, the second a carbuncle, each giving rise to specific psychotic reactions. The burn on her hand led to the appearance of Christ on the cross within the injured area. The carbuncle on her chin, in which there were five openings, produced the hallucination of five persons from the outer world within the substance of this part of her body. She could observe these persons on certain occasions when she looked in the mirror. In addition she experienced auditory hallucinations, and noticed changes in the appearance of persons in her environment. Both reactions in this patient have the common feature that a painful lesion of the surface of the body produced a break in the skin, which allowed objects from the outer world to intrude themselves into her body. These objects did not seem to penetrate deeper into the body than the lesions themselves. The psychological significance of these reactions will be discussed after the presentation of two similar cases.

CASE 2.—William J. H—, aged 43. Admitted May 22, 1934. Tram-driver.

He had always been reserved, unsociable and hyper-conscientious, but his behaviour was regarded as normal until January, 1934. At that time he became depressed

and seemed to worry because of the appearance of a small epigastric hernia for which he was to have an operation. On March 9, 1934, he underwent an operation, leaving hospital a week later. On his return home he showed marked psychotic symptoms, resulting eventually in admission to the mental hospital. When admitted he stated that he had felt depressed and nervous before the operation. The day before the devil spoke to him and told him that he would never get well unless he had promiscuous intercourse. The devil ordered him to have intercourse with his daughter, and continually accused him of wickedness. After the operation he used to see the devil by his bed. Shortly after admission he said that the devil was inside his body, that it had entered through the operation wound and swore and talked to him all the time. The devil was under his skin and over his whole body, and took his own shape. In the course of more than five years this idea has not altered. During this time he has been continually tormented in the same way. He can discuss the origin and course of his illness as clearly as when he was first admitted. While he tells of being depressed and changed mentally for a time before the operation, he attaches the greatest importance to the operation itself in connection with his present state. He seems to feel that the chief localization of the devil is in the neighbourhood of his wound, and that it is from the region of the scar that the feeling of the devil inside him radiates.

This is a case of a schizophrenic psychosis (according to Bleuler). For at least three months before undergoing an operation the patient's mental condition had been altering, but it was only at the time of the operation that specific psychotic features appeared, which took their final shape some weeks later when the patient asserted that the devil had entered his body through the operation wound and was now inside him and underneath his whole skin. The remarkable feature of this case is that the devil that he had seen and heard as an external object of his environment before the operation had entered his body through the artificial interruption on the body surface and established itself permanently under his skin. The patient identified himself so closely with the intruder that the latter took the entire shape of the patient and appeared to represent an additional layer round the body. It is quite clear that the appearance of the persecutor was related to the operation, the prospect of which gave rise to great apprehension in the mind of the patient.

There are many obvious points of similarity between Cases 1 and 2. Each suffered from a psychotic illness, an acute stage of which preceded an undue interest in a recent physical illness. The physical illness in each case was associated with an interruption in the continuity of the surface of the body, and provoked a specific psychotic reaction. In each case external objects entered through the wound and were incorporated in the body. They did not penetrate deeper than the superficial covering layers of the body.

The next case illustrates more fully the specific schizophrenic character of this type of reaction.

CASE 3.—Rudolf L—, aged 40. No occupation; single.

He was treated as an out-patient for three months. As a child he was very shy and much attached to his mother. His mother was herself peculiar; she was unusually religious; she encouraged him to avoid other children, fearing that he would contract infections from them. She endeavoured to persuade him to remain

with her always. His father was odd and influenced by his wife. The patient worked as a clerk, losing his employment ten years ago on account of paranoid behaviour. He first showed psychotic symptoms 15 years ago. He thought that he was being watched and that his colleagues were plotting against him. Voices accused him of masturbation and immorality. The principal person in his system of paranoid ideas was a male friend for whom he had formed an attachment of an erotic character some years before. He was greatly upset when this friend parted from him. At the time when he first came under observation his paranoid ideas were unchanged, but hallucinations were not evident. He was suspicious and reserved. He avoided making any contact with other people. He was idle, and interest was centred on himself and the condition of his body.

He complained in a hypochondriacal manner of a peculiar disorder of sensation connected with the alteration of thought processes described below. This disorder was related to a serious physical illness contracted nine years ago, i.e. at least six years after the onset of the psychosis. His account of this illness was as follows: He became acutely ill with a high temperature, headache and vomiting. There were muscular twitchings of the abdominal muscles, double vision and a slight paralysis of the left extremities. In addition, in the course of the illness loss of superficial sensibility on the left half of the face, trunk and upper extremity occurred. He was lethargic by day and delirious by night. The illness lasted about four weeks. When he recovered there remained a squint of the left eye and a numb feeling on the left cheek and the left part of the forehead, most marked close to the left eye. There was no double vision. Ever since that time, about once every month he has an oculogyric spasm when both eyes are drawn up forcibly and painfully for more than an hour. Although the patient was not deeply concerned with any individual physical symptoms, he expressed peculiar ideas about the area of disordered sensation. He said: "I feel as if something is dead around my left eye. I feel that this part does not work. There is no boundary here between me and the outer world. The world pours into me through this gap and I cannot help it. It makes the left part of my body weaker. Sometimes I feel that the left side has no limits. I cannot regulate my will and my thoughts properly around my left eye. If I am thinking of something the right side is all right, and on this side I can change over my thoughts easily when I think of other subjects. I cannot do this around my left eye. My thoughts and feelings there are behind the right side. If I have thought of something or somebody, I cannot free myself from this thought on the left side. When I leave a place the feeling remains for a long while that I am still there with the left side. If somebody passes by, his picture remains in the left side and mixes with other pictures which come afterwards. I feel torn up and have divided feelings. I cannot free myself on the left side from suggestion. It pours into me like a hosepipe, if I meet persons with strong will power. I feel hypnotized on the left side of my face, and there I am too much in contact with the outer world. Everything comes into me through that side of my face when I look anywhere. Therefore I cannot organize myself for this side of my body. It does not obey me. Around my left eye I feel the animosity things and all the persecution which I have been subjected to for many years. On the right side the feelings are natural, but on the left they are unnatural like a sham, and there is a strange rigidity of pictures and thoughts on the left side. During sexual intercourse and masturbation I can enjoy myself only on my right side; the left remains indifferent. It is only in dreams that I feel quite myself. There is no difference then between right and left."

The neurological examination showed the following abnormal features: Ocular movements: Paralysis of the left abductor. Impairment of the ability to converge. Hypoaesthesia to touch, pain and temperature on the left cheek, lower part of left forehead, most marked on and around the left eyelid. Left conjunctival and corneal reflexes diminished. Slight degree of palsy of the left facial nerve, involving all branches. Trunk: Abdominal reflexes diminished on the left side. Upper extremities: Reflexes brisk both sides. Slight rebound on the left. Finger-nose test: Left hand slows down before reaching nose. Lower extremities: Knee and

ankle jerks exaggerated, left greater than right. Left brief ankle clonus. Left extensor plantar response. There was a slight degree of generalized stiffness. There was no disturbance of any form of sensibility apart from what has been described above.

This is a case of a schizophrenic psychosis of paranoid type, which had existed without much deterioration for about 15 years. A physical illness, obviously encephalitis lethargica, intervened six years after the onset of the psychosis, leaving behind as residual symptoms a disturbance of the superficial sensibility in the neighbourhood of the left eye, some degree of ocular palsy, and some slight rigidity. Oculogyric crises occurred periodically. It is possible that there may have been an associated thalamic lesion. A specific psychotic reaction developed after recovery from the physical illness, determining thereafter the main features of the psychosis. From that time the principal complaint was that the outer world intruded itself into the body through the localized area on the surface where there was the sensory disturbance. He related a characteristic form of schizophrenic thought disorder to this localized sensory alteration. That these ideas were related to the disturbances left by the physical illness is proved by the fact that they appeared for the first time immediately after this illness, and were connected only with a sensory aberration having definite and unchanging localization. The ideas of this patient were obviously a schizophrenic reaction to a disturbance of superficial sensibility implying an alteration in the perception of stimuli from the outer world. It may be that a thalamic lesion contributed to the peculiar nature of the reaction. Head and Holmes (1) have demonstrated certain psychic reactions associated with thalamic disorders. Nevertheless, such a possibility does not alter the fact that the main features of the patient's complaint were characteristic of schizophrenia.

Bleuler (2) has mentioned that as a result of the splitting of the personality the patient may experience a loss of " his boundaries in space and time," but he refrains from analysing this phenomenon. In schizophrenia the patient often experiences a loss of the stability and impermeability of the borders of the ego. This is responsible for the common idea that processes which take place in the mind or the body of the patient can take place at the same time in the outer world, and conversely, that processes belonging to the outer world may take place at the same time in himself. The tendency to incorporate objects of the outer world is characteristic of schizophrenia. The term "introjection" signifies the mechanism responsible for this reaction. Our cases seem to show that under certain conditions in schizophrenia the patient may became aware of a localized interruption in the integrity of the surface of the physical ego and therefore of its boundaries. Such an interruption brought about by physical illness in non-schizophrenic patients is not interpreted as a fundamental change in the relationship between the individual and the world around him. The schizophrenic, however, may relate closely changes in his

physical ego with a disturbance of his whole personality, so that under certain conditions such changes may lead to a profound alteration in the relationship between the individual and the outer world. The schizophrenic is inclined to experience the surface of his body as the boundary of his ego. Breaches in the surface of the body are able, therefore, to provoke a specific type of schizophrenic reaction in which the patient feels that there is a localized break in the boundary between himself and the outer world. This localized interruption of the ego borders favours the process of introjection whereby elements from the outer world become incorporated in the patient. It is obvious that the impression of a break in the surface of the body may be caused by an actual destructive lesion involving the skin or by a localized loss of superficial sensibility.

In the third case the disintegration of the personality brought about by an interruption in the subjective representation of the body surface is of a more general nature than in the other cases described. This case illustrates the peculiar connection between thought processes and bodily sensations, often observed in schizophrenia. This patient felt that he thought with his whole body or even with various parts of his body independently. He had, as it were, animated every part of his body. In this case the physical illness had occasioned a special form of splitting up of the personality.

Cases as well defined as the three described above are comparatively rare. An analysis of such cases throws light on a more common reaction to certain types of physical illness, seen in schizophrenic patients. It can be said that psychotic reactions frequently follow physical disorders, which the patient can link with the idea of an intrusion of something from the outer world into the body by the way of the natural body openings. In such cases the natural body openings correspond to the breaches in the body surface described in our cases. The extremities of the digestive tract are regarded as the main entrance and exit of the body. These openings therefore provide easy routes through which the outer world may enter the body and, in the mind of the schizophrenic, are vulnerable points from which the integrity of the personality can be easily assailed. If the schizophrenic patient is made aware that a physical disorder has broken the intactness of any part of the alimentary tract, a specific psychotic reaction corresponding to what we have described is likely to follow. The familiar delusions of poisoning demonstrate the constant apprehension of attack through the alimentary tract which is present in the mind of the schizophrenic. The alimentary tract forms the main inner surface of the body. In a sense too the urinogenital system, especially in females, provides access to an inner surface of the body. Delusional ideas related to physical disturbances in this system are obviously highly complicated and naturally cannot be considered independently of the sexual sphere. They do not lend themselves to the demonstration of reactions of a comparatively simple structure.

One of us (Hemphill (3)) has described two illustrative cases. The first related sensations arising from a painful hernia to devils which absorbed themselves into his abdomen and injected things into his body. In the second case there was a chronic intractable ulceration of the jejunum which led to the belief that the patient's enemies shot at him through his anus. Both cases illustrate characteristic reactions in paranoid patients where disorders of the alimentary system gave rise to subjective sensations.

Although the mechanism underlying the psychotic reaction in all three cases is the same, that is, the experiencing by each patient of an alteration of the boundaries between himself and the outer world as the result of a localized disturbance in the surface of his body, there are special features peculiar to each case. In Case 1 the lesions were not of a serious and lasting character and could not have left much permanent effect. The psychotic reaction was of short duration and had only a temporary influence on the psychosis. In Case 2 the physical disturbance was of an unfamiliar and more extensive character, and the ensuing psychotic reaction left behind a lasting and altogether more significant effect. In each case external objects were actually incorporated in the body itself. In Case 3, although there was no actual break in the continuity of the surface, there was a local change of function which the patient interpreted as if the surface were interrupted. The sensory loss was of a lasting character and was something of which the patient was always aware. The affected area was always experienced as an aperture in the body. The fact that no single object was permanently incorporated in the body, and that all sorts of elements and influences—physical and psychic—intruded themselves in an unceasing flow through this aperture, may very well have been determined by the character of the localized physical alteration which never ceased to attract the attention of the patient. It is notable that at the time when these reactions made their appearance all three patients were in a hypochondriacal state. We do not propose to enter into a more detailed analysis of the reactions of these cases, for we feel that it is clear that the individual character and the consequences of these reactions are determined by the special features of the psychosis as well as of the physical disturbance.

It is not unlikely that in our cases, and more especially in Cases 2 and 3, the physical disorder influenced the course of the psychosis as well as the clinical picture. It is quite possible that the psychosis in Cases 2 and 3 would have followed a more favourable course but for the intercurrent physical disturbance which undoubtedly gave rise to a psychic trauma, resulting in psychotic mechanisms for which the patient had a particular susceptibility at that stage of the psychosis. Such a reaction to certain physical disturbances cannot be expected to appear in every schizophrenic patient nor at every stage of the psychosis. The susceptibility of the psychotic subject to produce psychopathological phenomena as a response to personal experiences is inconstant and subject to great variations.

An interesting comparison can be made between the mechanisms underlying these psychotic reactions and certain types of representation of physical changes in the course of dreams and states of altered consciousness. It is well known that physical sensations, even those of normal physiological origin, are readily projected into the outer world in dreams. It has been shown that in brain disease endogenous sensations give rise to the same mechanism. One of us (Stengel (4)) has recorded illustrative examples. The most striking was a case of acromegaly, in which the patient in her dreams projected her physical alterations into an animal, with unmistakable features of acromegaly. The mechanism of projection was responsible for these reactions, and any evidence of introjection as observed so clearly in our schizophrenic patients was lacking. Projection is of course a common feature of schizophrenic reactions. Schilder (5) has described how actual physical illness is projected in hallucinations. In our first case, in which the psychotic reaction was the least serious, there was some attempt at projection. The patient in her second reaction observed the introjected material only in the mirror. Furthermore, she projected the experience of personal change into persons of her environment. It is of interest that projection occurred after introjection in Case 1 alone, which was the only case of the series in which the traces of the reaction to physical illness disappeared. In the other cases no such attempts at projection appeared. This is quite in keeping with the view that projection is a compensatory mechanism and indicates the effort of the individual to free himself from psychopathological elements.

Summary.

Three cases in which a peculiar reaction to physical illness appeared in the course of a schizophrenic illness of the paranoid reaction type have been described. In each case the physical illness was responsible for a local interruption of the surface of the body. An impressive psychotic reaction followed the physical disturbance. In one case this reaction was transitory, but in the other two it endured and determined the picture of the psychosis. The feature of this psychotic reaction common to all cases was the incorporation of objects of the outer world in the patient by way of the break in the body surface. It has been shown that the special nature of the psychotic reaction was determined by the existing stage of the psychosis at the time when the physical injury was incurred, as well as by the character of this injury. The psychotic reaction described is related to loss of stability of the boundaries of the ego in schizophrenic states and the tendency towards introjection of external objects. The loss of stability of the boundaries of the ego renders the schizophrenic more susceptible to psychotic reactions to damage of the body surface.

It has been pointed our how examination of the reactions described above assists in elucidating certain more common psychotic reactions, by which the

patient relates an existing physical disturbance to the entrance of a noxious agent through one of the natural body openings.

Attention has been drawn to the way in which physical disturbances are represented in dreams and twilight states, and a comparison has been made between these reactions and the psychotic reactions described in our cases.

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STUDIES IN CERTAIN PATHOPHYSIOLOGICAL AND PSYCHOLOGICAL PHENOMENA IN CONVULSION THERAPY.

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DURING recent years so much has been written about convulsive therapy that it would seem rash to burden still further the very extensive literature on this subject. Nevertheless, in spite of the admirable work that has been done, it cannot be said that the implications of convulsive treatment are fully understood, nor that the fullest possible use has been made of this treatment for research into the pathophysiology of epilepsy. Furthermore, the recent introduction by Cerletti and Bini (1) of a method of treatment with electrically produced epileptic fits has increased still further the scope of research. I have had at my disposal case material provided by the treatment of various forms of mental disorder with cardiazol for more than two years, and with the electrical method in collaboration with Mr. Grey Walter for about six months. This has enabled me to conduct certain investigations of a sort that have received little or no attention hitherto, and to make observations covering various aspects of the physiology and psychopathology of induced epileptic states.

Observations on Motor Phenomena.

The attention of the observer is first drawn towards the exhibition of powerful motor activity which succeeds the injection of an adequate dose of the convulsant. Much of this activity conforms with that of the typical fit of spontaneous epilepsy, but there are, in addition, other types of movement which occurs only in certain individuals and have therefore not attracted general attention. These motor phenomena are seen either immediately before the clonic stage of the convulsion or during the period of unconsciousness which follows the clonic stage or, less frequently, during an incomplete fit. The phenomena to be described made their appearance fairly consistently in certain individuals early in treatment, but tended to disappear after a number of fits. Some of these movements have been observed and commented on by

others in both insulin and cardiazol treatment. I have observed types of movements which can be classified as follows :

1. *Purposeful movements.*—These occur most frequently. Usually they are grasping, groping or reaching movements of the hands and arms. The purposeful character of these movements is well demonstrated by actions such as rubbing the eyes or repeatedly grasping a part of the body. Occasionally these movements have an athetotic character.

2. *Rolling movements.*—Some patients habitually roll over, sometimes completing the whole circle several times. The rolling movements frequently terminate by the assumption of a foetal attitude in which the patient sleeps. The direction in which the patient rolls is always the same, and it is notable that it is usually towards the side to which the patient turns when sleeping after the fit and in normal sleep.

3. *Hemiballistic movements.*—Extensive and violent rotation of one or the other arm, similar to hemiballism, is occasionally seen.

4. *Opisthotonic movements.*—These are of a powerful character. They are relatively common, and not infrequently occur in association with other types of movements.

5. *Automatic movements of the lower limbs.*—(*a*) Thrashing : Beating movements of the extended lower limb, usually accelerating and increasing rapidly in amplitude. (*b*) Bicycling : Rhythmical alternating movements of the lower limbs, similar to the action of the cyclist in pedalling. This action starts slowly, and works up to a maximum speed of about six cycles per second. In certain subjects bicycling was succeeded by blind running with great violence, strongly reminiscent of epilepsia procursiva.

6. *Cataleptic postures.*—These are chiefly observed in the incomplete fit. They are often of several minutes' duration and are of the nature of flexibilitas cerea. They are more marked in the upper than in the lower limbs.

Other types of movements may be observed, but it would seem that the above classification covers in a general sense most individual categories. Tonic movements of the eyes are probably of a different nature, and as they have been described by others they will not be referred to here.

Most of the above movements represent types of abnormal motor activity seen in lesions of lower motor centres. Involuntary movements of a purposeful character have been seen in disorders of the striate body and the frontal lobes. Hemiballism has been found to follow lesions of the body of Luys. Slow bicycling movements have been observed in cases where there was softening of the anterior part of the globus pallidus. Thrashing and bicycling, as well as opisthotonos, resemble movements seen in lesions of the mesencephalic motor nuclei, observed clinically in tumours of the midbrain and produced experimentally by stimulation of these regions (Graham Brown, 2). Fraser and Reitmann (3) have shown recently that bicycling accompanies the return of motor activity during the recovery from experimentally produced anoxaemia. A similar complex of all the movements described before has been observed by various workers (Wagner-Jauregg, 4; Gerstmann, 5; Strauss, 6; Gamper and Kral, 7) in individuals during resuscitation from severe transitory anoxia of the brain produced by attempts at hanging, or avalanche disasters. Localized lesions in the basal ganglia were demonstrated in cases which had succumbed. This may suggest that these movements are due to the return of activity of

deeper centres as the effects of anoxia are subsiding. The fact, however, that such movements occur both in the incomplete reaction and before the development of the clonic stage, when anoxia could not have been severe, suggests that in certain individuals cardiazol can affect certain deeper parts of the brain to an unusual degree at a time when its effect upon the cortex is not fully developed.

These movements, which are not the usual accompaniments of the spontaneous epileptic fit, appear to occur less frequently in the electrically induced fit, and obviously only in the post-convulsive stage. This would suggest that in the electrically induced fit certain parts of the brain which are involved in the cardiazol fit are not usually affected, and when atypical movements occur they are probably due to anoxia. This would conform with the experience that the electro-fit is considerably shorter than the cardiazol fit, being very constantly about 45 seconds (Fleming, Golla and Grey Walter, 8).

Relationship between the Motor Reactions and Individual Features of the Patient.

Observation of a long series of induced convulsions creates the impression that individual patients seem to favour a particular type of reaction to convulsant measures, in both the complete and incomplete fits. Naturally, individualities are most evident where the reaction is particularly mild or contains uncommon features.

Even with the so-called normal reaction one notices small peculiarities, such as the sequence in which the march of the fit occurs, the type of the cough, or the way in which the eyes are screwed up or the mouth opened. Furthermore, it would seem as if the amount of discharge during the convulsive stage of the fit varies in different individuals.

The motor reactions appear to be either of or between two extremes, namely, fits of a mild nature unaccompanied by great motor activity, and fits associated with a storm of movements. The " mild " fit is nevertheless a typical fit, but is mild by comparsion with those fits where the motor discharge is extreme.

With regard to the mild type of reaction, one gets the impression that those individuals whose reactions are mild with a comparative paucity of motor activity are, in their behaviour during their illness, simple and devoid of aggressive action. I have not observed any case whose reaction to cardiazol was mild in whom, during the period of detention in hospital, strong spontaneous psychotic motor activity or a high degree of negativism could be seen. The conduct of these cases, in spite of a variety of delusions, hallucinations, states of fear or apprehension or apathy, did not take the form of active and violent opposition to the environment. It was not uncommon to learn that such patients had been particularly good tempered or docile before the development of the illness.

With this type of personality, muscular activity before and after the fit is slight, and no marked muscular energy nor extraordinary movements accompany the incomplete fits. Such patients usually tend to sleep on quietly after the convulsive stage without exhibiting restless behaviour. At the other extreme are those patients who react with a great expenditure of muscular energy, showing not only an extreme motor discharge during the fit, but also various movements before and after the convulsive stage, and whose incomplete reactions are rich in motor phenomena. In the psychosis of such patients negativism and motor activity are prominent, expressed in violent action against property and staff or against themselves, and in resistance to treatment. Their histories do not show that they had been noticeably submissive and gentle prior to the mental illness, and sometimes the reverse seems to be the case. Between these extremes are patients whose reactions to injections and whose psychotic behaviour cannot be assigned to one type or the other.

These observations show that there is a relationship between certain forms of involuntary motility and features of the personality. If it is true that the atypical movements described are related to activity of deeper parts of the brain, and that such movements appear chiefly associated with certain personality features, then it could be inferred that there is an intimate relationship between personality features and the activity of deeper parts of the brain.

A Postconvulsive Reflex Phenomenon.

In the majority of individuals treated there is a short period of reflex excitability during the postconvulsive stage. This stage of excitability appears shortly after breathing has terminated the postconvulsive apnoea, and lasts for upwards of a minute. During this period, a brisk stimulus applied to the skin of the trunk produces a brisk flexion contraction of all four limbs with anteroflexion of the neck, accompanied by some protrusion of the eyeballs and some dilatation of the pupils. This phenomenon seems to be related to respiration, as it can be elicited only immediately after the end of inspiration, no reaction being obtained to stimuli applied at any other moment in the respiratory cycle. The susceptible phase in some patients seemed to be not more than a few seconds ; it is therefore likely that in the few patients who did not show this reaction the stimulus had been applied when the susceptible phase was over. This reaction, which can be demonstrated in many cases during cardiazol therapy, was seen only once in 12 cases treated with electrically induced convulsions.

The phenomenon may be regarded as resulting from the state of hyperactivity of the motor cortex, which persists for some time after the convulsive stage and which gives rise to motor discharges in response to external stimuli. This reflex hyperactivity has some resemblance to what is seen in strychnine poisoning, where external stimuli provoke motor discharges. The relationship

of this reaction to the passing off of anoxia, and to the restoration of more normal circulatory conditions, indicates that it marks the return of activity in parts of the brain which have been exhausted or suppressed in the course of the epileptic discharge.

Reflex Movements of the Eyes.

The occurrence and features of spontaneous ocular movements during the cardiazol fit suggested that it was desirable to investigate in some way the reflex behaviour of the eyes. The eyes did not respond reflexly to alteration of the position of the head during the fit and reflex compensatory eye movements could not be elicited. It was of interest to investigate the response of the eyes to the stimulus, which under normal conditions invariably produces a certain sequence of eye movements, that is, irritation of the labyrinth, leading to physiological nystagmus. As far as I am aware, investigations of this sort have not been conducted during epileptic fits in human subjects.

The method employed was that of syringing the ear with cold and hot water as in the usual tests for labyrinthine function. Only patients free from any disorder of the auditory apparatus or labyrinth were investigated. Syringing was performed with the patient lying on the back—

(*a*) Under normal conditions on the day before cardiazol injection.
(*b*) In the post-convulsive stage immediately apnoea had ceased.
(*c*) During the convulsive period.
(*d*) During an incomplete fit.

The results were striking, both because of their form and of the absolute consistency with which they appeared. They were as follows:

(*a*) *Under normal conditions.*—All patients examined showed normal physiological responses.

(*b*) *In the post-convulsive stage.*—One or two seconds after syringing with cold water, the eyeballs turned towards the side of the irritation, reaching an extreme deviation. This deviation could not be altered by turning the head. Between 10 and 30 seconds later the eyes left this position and moved slowly towards the middle line. Sometimes the movement of the two eyes was not synchronous, and the eye of the irritated side lagged behind the other. The eyeballs did not remain in the middle position, but showed a slow rhythmical movement to right and left of 2–4 mm. amplitude. These movements were of the type of pendular nystagmus. This pendular nystagmus was followed by some jerky movements of the type of the normal labyrinthine nystagmus. On several occasions deviation of the eyes was accompanied by active turning of the head towards the side of the deviation, but the head could be moved in the opposite direction without much resistance. Just before the end of the period of deviation, and also when nystagmus had commenced, it was sometimes possible to produce compensatory deviation of the eyeballs by turning the head forcibly. For example, turning of the head from the middle position to the left, when the eyes were already deviated to the left, caused the eyes to leave their position of deviation relative to the head and to remain in their position in space, thus preserving their original angle of deviation from the body axis.

(*c*) *During the period of convulsion.*—Syringing with cold water was performed in the tonic and clonic stages. The results were largely the same. The eyes turned, as described before, to the side of the irritated labyrinth. Compared with the results of syringing in the post-convulsive state, there were the following differences:

(i) There was a latent period, sometimes 5–10 seconds, before the results of syringing appeared. This period was especially prolonged when a tendency to spontaneous deviation in the opposite direction existed already, so that although deviation towards the side of irritation always occurred, it obviously took some time to overcome the impulses drawing the eyes in the opposite direction.

(ii) The appearance of muscular tension of the eyes and the very extreme degree of deviation gave the impression that the eyes were being turned with far greater muscular force than in the post-convulsive state.

(iii) Occasionally the eyes moved from a position of lateral deviation to that of extreme deviation obliquely upwards. Tonic deviation remained until the end of the clonic stage; return to the middle position occurred as described above, with occasional squinting, or a phase of pendular movements, to be succeeded by a few jerks of physiological nystagmus. No patient complained of dizziness or nausea when questioned immediately after the return of consciousness.

It was felt that syringing of the ears might not be without effect on the general condition of the patient, and observation seemed to suggest that that was the case. Reflex activity in all patients seemed to be somewhat increased and to persist for a longer period than usual when the ear was syringed in the post-convulsive stage. Stimulation of the skin and front of the abdomen provoked a more brisk and more frequent reaction than it had done hitherto without syringing. This effect was not evident when syringing was done during the fit. When syringing was done during the fit the return to normal respiration seemed to be much smoother, and cyanosis and pallor seemed to disappear more quickly than usual, and it seemed as if the motor discharge of the epileptic fit was more complete.

(*d*) *During the incomplete fit.*—Syringing was performed during incomplete fits, when the patient was in a state of semi-consciousness and was not accessible nor co-operative. The threshold obviously had to be nearly reached. The result was essentially the same as in the post-convulsive stage.

Syringing with hot water produced reactions similar to syringing with cold, except that deviation of the eyes occurred away from the side of the irritation.

Summary of the Findings in the Labyrinthine Investigations.

The notable results of these investigations are as follows:

Syringing of the ear, both during and immediately after convulsion, fails to cause the normal physiological nystagmus.

Syringing with cold water consistently causes an extreme deviation towards —with hot water away from—the side of labyrinthine irritation, in each case followed by a period of pendular nystagmus, followed in its turn by a short period of nystagmus of expected physiological type.

Reflex irritability in the post-convulsive period seems to be increased by syringing in this stage.

Labyrinthine stimulation during the fit seems to facilitate the return of normal respiration and circulation.

It is not intended to enter into a full discussion of these findings. It is only possible to consider a few of the factors involved. As the direction of deviation corresponds to the side of the slow component in the normal physiological nystagmus, it is possible that this deviation is the result of the suppression of the quick component during the epileptic state. The phenomenon would therefore be an example of an inhibition of a certain action, namely, of the

quick component of the normal nystagmus, which component is generally considered to be related to the cortex. It has been shown by Wilson (9) that inhibition as well as discharge of activity takes place during the epileptic state. However, it is not likely that such an extreme and powerful deviation of the eyes takes place without some positive influence on the part of the cortex irrespective of the inhibition of the cortically controlled quick component. The experiments of Spiegel (10) have shown how labyrinthine stimuli under certain conditions can influence the cortical activity of animals, thereby demonstrating the existence of connections between the cortex and the labyrinth. Further investigations on problems arising out of these findings are not yet completed.

It is of interest that labyrinthine stimulation was found to have a marked effect on the re-establishment of circulation and respiration. It can therefore be assumed that stimulation of the labyrinth affects in some way the vasomotor and respiratory centres. This has already been suggested to explain certain vasomotor and respiratory alterations which occur in various conditions, such as Menière's disease, where irritation of the labyrinth exists.

Conditions Influencing the Response to the Convulsant Drug.

Various observers have reported on factors which influence the threshold, i.e. the minimum dose of the drug necessary to produce a fit. Such factors are—the speed of injection, the concentration of the drug, the administration of sedative drugs or substances such as histamine with a vasodilating action. (Dennyson and Watterson, 11; Watterson and Macdonald, 12). My observations show that there are other factors which have an effect upon the threshold. Such factors are :

(*a*) *Follicular hormone* :—A number of female patients suffering from amenorrhoea were treated with 50,000 units of oestrone, injected five times in 21 days, while undergoing treatment with cardiazol. In almost every patient the threshold was considerably raised while oestrone was being absorbed, and in one patient it was impossible to induce a fit with doses of less than 50 per cent. more than what had been effective previously. At the conclusion of hormone treatment the threshold returned to its original lower level. Furthermore, it was observed in certain other patients that on the days immediately before the menstrual period there was a reduced susceptibility to cardiazol. Although this appears to be somewhat at variance with the common experience that there is an increased incidence of fits in epileptics at the menstrual period, it may be that in cardiazol epilepsy follicular hormone influences the susceptibility to the blood-borne drug by causing alterations in the cerebral circulation. Recent experimental work by M. Reiss and Y. M. L. Golla (13) has shown that the administration of sex hormone markedly increases the cerebral blood content in animals. My observations indicate that the same conditions may

be true in the human subject and may be responsible for raising the threshold to cardiazol.

(*b*) *Behaviour of the patient at the time of the injection.*—Patients who were obviously terrified and struggled violently, showing physical signs of extreme fear, with a rapid pulse and pale face, failed to respond to the injection more often than those who were co-operative or apathetic, and if the degree of anxiety was great, anything but a very large dose was ineffective. At first sight one would expect to find that in states where cortical excitation was already present, and where the rate of circulation of the blood was increased by the rapid and pounding heart-beat and the extreme muscular activity, the threshold to a given dose of cardiazol would be lower rather than higher; there must, therefore, be other conditions related to states of anxiety and emotional tension, unfavourable to the production of a fit. In the literature it appears that Ribbeling alone refers to this problem. He mentions that it is necessary to give an increased dose of cardiazol in agitated states.

It is possible that the raised threshold to the cardiazol fit in states of anxiety is related to changes in the cerebral blood-flow. Furthermore, it may be imagined that physiological conditions similar to those described by Cannon (14) exist in the anxious and agitated human being, and if so may contribute to the inhibition of the fit. Perhaps the liberation of a substance with an action similar to histamine produces circulatory changes affecting the distribution and local concentration of cardiazol.

Changes in the Optic Fundi During the Induced Fit.

In genuine epilepsy there is seldom an opportunity for making a systematic examination of the fundus throughout the epileptic fit. Hughlings Jackson (15) records vasoconstriction, and Rossi (16) a paraxysmal angiospasm of the retinal vessels in the course of the epileptic fit.

I have investigated the optic fundi of a number of patients during cardiazol treatment. The patients were also examined from time to time on days when cardiazol was not administered. Homatropine was used as a mydriatic. At first no mydriatic was used, but it was found that, although not strictly necessary, its use greatly aided a full inspection of the fundi, especially at times when deviation or movement of the eyes occurred. As similar results were obtained in the same patient whether homatropine was used or not, it can be assumed that this drug has not influenced the findings.

The first essential was familiarity with the appearance of the fundi of each patient under normal conditions, for individual fundi and discs differ, some showing marked pallor. Therefore, what one can call the "complexion" of the fundi had to be taken into account before comparisons could be made.

It is hardly possible unless the patient co-operates fully to observe the fundus until unconsciousness has supervened, and at the onset of the tonic

stage it may be impossible if there are extensive movements of the head or trunk or eyes. With the aid of an assistant the observations can usually be made during the tonic stage. These difficulties do not exist later, when the eyes remain open or even staring and, except for the inconvenience of deviation of the eyes, or the more rarely seen violent postconvulsive movements, the fundi can usually be kept under observation continuously until consciousness returns.

In all patients examined some changes were observed in the condition of the blood vessels and the appearance of the discs, which were as follows: During the tonic stage there is marked contraction of the arteries accompanied by a growing pallor of the whole fundus and disc. In some cases this blanching seems to cause the disappearance of small vessels. The veins also become less distinct. This picture remains until the end of the first half of the clonic stage. During the second half of this stage the vessels dilate, veins and arteries become more prominent, and the pallor subsides. In some cases, vessels which were not obvious before become visible. This state of hyperaemia deepens, and the disc loses something of the sharpness of its outline ; in some cases one even gets the impression that swelling of the disc has occurred. By the end of the clonic stage the hyperaemia reaches its climax; the whole fundus and disc have then a distinctly reddish appearance, considerably more red than is seen in the fundi of the patient under normal conditions. The hyperaemia gradually subsides during the postmyoclonic stage, but even when breathing has become normal there is still a trace left. The fundi are usually normal when consciousness has returned, but occasionally a certain amount of hyperaemia and even a slight degree of swelling of the disc remain for a considerable time afterwards. In one patient the discs never regained the original sharpness of outline during the whole period of treatment and several subsequent weeks.

The literature on cardiazol therapy contains the following observations: Meduna (17), quoting Fesus, who investigated Meduna's patients, states that there is no constant change in the fundi during the cardiazol fit, except " a certain degree of increased vascularity of the connective tissue with slight dilatations of the vessels of the episclera." He (Meduna) considers that these observations are in contradiction to the behaviour of the cerebral vessels of animals during experimental convulsions. Kennedy (18) reports that there is no change in the retinal vessels except the widening of the veins during cyanosis. Watterson and Macdonald (12) observed retinal vasodilatation only during the cardiazol fit.

The behaviour of the retinal vessels that I have reported is of interest, as vasomotor changes in the brain have received so much attention in the discussion of the causation of epileptic convulsions. This behaviour is in keeping with the processes of vasoconstriction and vasodilatation on the brain surface that have been observed in experimental epilepsy. Fischer and Lowenbach (19) photographed the surface of the brain during a cardiazol fit. Their photographs

showed that the visible arteries and veins became dilated during the fit, and tiny vessels were seen which had previously been invisible. Foerster (20), Dandy (21), Leriche (22) *et alia* have observed vasoconstriction when epileptic fits took place during an operation on the brain surface.

It has been suggested that the epileptic fit is caused by vasoconstriction of cerebral vessels. This theory has found and still finds support. Certain changes in the brain tissues in epileptics—for instance, the well-known lesions of the cornu ammonis—have been ascribed to vasomotor disturbances. Alf. Meyer (23) has recently demonstrated that similar changes in other parts of the cortex, the "dropping out" of nerve cells, are related to the distribution of blood vessels. These findings agree with Jackson's (15) idea that anæmia of the brain might be responsible for the epileptic fit. It is true that this theory has met with opposition from the beginning. It was denied by Gowers (24), and more recently Golla (25) has argued that, although the presence of vasomotor disturbances in the brain cannot be denied, there is no direct evidence that they are responsible for the epileptic fit. My own observations show that vasomotor changes take place in the fundi during the whole cardiazol fit, and that these changes occur in the same sequence and are of the same order as those observed in the cerebral circulation during epileptic fits. It is very likely that the respective changes take place at the same time in the fundi and the brain. But, as Wilson (26) has pointed out, whether the undeniable association of vascular changes with the paroxysm is one of cause or effect has still to be discovered.

Some Observations on the Psychopathology of Convulsive Therapy.

It is clear that an understanding of the mechanisms responsible for a change of symptoms in shock treatment cannot be gained from study of the physical events alone. It is unnecessary to refer in detail to the rich literature on this subject. I propose to record certain observations which are of special interest because they have attracted little attention up to the present, and to draw attention to certain psychological events with regard to which my experience differs somewhat from that of others.

Attitudes of Patients Towards Treatment.

The various attitudes which patients may show towards treatment may be classified as *co-operation, indifference, hostility, fear, pathological terror.* Of these co-operation is probably the most frequently observed and is certainly the most favourable from the point of view of prognosis. Indifference and hostility seem to be related closely to the fundamental features of schizophrenia, and where they are present treatment has little effect. Fear should not be considered as identical with what I propose to call pathological terror. Fear can be observed in many patients irrespective of the nature of their psychoses,

and does not differ from the usual apprehension shown by so many individuals for physical interference or painful forms of treatment. Pathological terror is a most impressive and extreme degree of fear with widespread manifestations of terror. It is remarkable in that it does not necessarily appear after the first injection, and that in certain cases it disappears later in treatment. It is generally assumed that failure to produce the complete reaction on one occasion leads to pathological fear of subsequent injections; in my experience any such connection is fortuitous. The occurrence of states of terror is not derived from a fear of undergoing pain, but is obviously determined by something entirely different. Nightingale (27) found that states of anxiety occurred in four patients who never missed a fit, and that 10 of his 44 cases who frequently showed the incomplete reaction exhibited no fear.

Without discussing this phenomenon at length it may be stated that a careful examination of patients showed that the underlying factor was a conscious fear of death expressing itself by the fullest possible opposition to being rendered unconscious. It is remarkable that the organism is capable of some successful opposition, for, as has been already pointed out, pathological terror can raise the cardiazol threshold to a very considerable extent. Perhaps this can be compared to the experience of anaesthetists that some patients can by an effort of will resist the hypnotic effect of the anaesthetic to an unexpected extent. Some patients cannot be hypnotized, even with the aid of hypnotic drugs, if the psychic resistance is too great. Vasomotor changes have been shown to raise the threshold. It is reasonable to assume that such changes accompany the state of pathological terror and inhibit the fit, but do not operate to any significant extent in the milder reaction of fear. Pathological terror was confined to schizophrenics and did not occur in any of the melancholics treated, irrespective of the fact that they may have been by nature timid or that anxiety was a prominent feature of the illness. This is an illustration of the so-called psychic anaesthesia of the melancholic.

The Stages in the Returning of Consciousness.

From the psychological point of view, the period following the end of the clonic stage can be divided into various stages:

(1) *The stage of complete inactivity* while the vascularization and respiration are being restored to normal. In this stage no response can be obtained to the application of external stimuli.

(2) *The stage of involuntary movements*, the pathophysiological character of which has been described. This stage is not always clearly defined and sometimes cannot be observed. The patient sometimes gives the impression of indulging in these movements, sometimes of trying to suppress them. He is not quite inaccessible to external stimuli, as is shown by the return of the blink reflex. If one tries to restrain him in this stage he resists or avoids

restraint in a purposeful way. For example, a patient who tried to leave the bed would brush aside obstacles placed in his way. He would even turn in the direction of spoken words and withdraw from painful stimuli, but he obviously could not understand speech nor would he speak himself.

(3) *The stage of semi-consciousness*, where contact between the patient and his environment is gradually being re-established. At first the patient looks round in apparent bewilderment. He does not speak spontaneously, and shows an obvious resistance on being pressed to speak. Mental activities take place slowly at this stage. Some patients try hard to overcome the difficulties. Others give up the struggle and turn away and try to sleep. Such patients give the impression not only of being disinterested, but of objecting to being disturbed. They curl themselves up in a foetal attitude on one side and draw the bedclothes over them. One sees from the expression and gestures of those who try to rouse themselves that the world around them appears to be unfamiliar, and they give the impression that they are trying hard to remember something that they once knew and have forgotten. While this bewilderment is prominent the patient's response to questions is poor and there is little attempt to fulfil commands. Questions, if answered, are met by "I don't know."

(4) The next phase can be described as *the period of aphasic reactions*. This phase is very short and cannot be observed in all patients. During this phase the patient tries to answer questions and obey commands; in his responses he shows aphasic phenomena. These phenomena occur in the following order:

At first the patient is unable to name any object or thing perceived. If asked to name an object he seems to search for words he has forgotten, sometimes employing circumlocutions. He is, however, able to volunteer remarks the extent of which seems to depend upon his power of attention. He will sometimes say "I don't know," or "I can't say."

Next the patient can name parts of his body and obey the examiner correctly and without obvious difficulty.

Following this, the ability to name familiar objects returns. The knowledge of names is still very limited, and at first only objects with which the patient has some personal connection are remembered. For example, a gold ring is easily named by married women at a time when a bunch of keys or a pen can be named only with difficulty.

Paraphasias do not seem to occur. There is, however, in some patients a form of expression in the naming of objects which, although not aphasic in itself, is observed only in this stage, while the difficulty of naming objects persists. This is the use of a particular qualifying adjective with each noun. The adjectives used are usually one of these, namely, "real," "little," "lovely," or a combination of two. For example, a wallet is named as "a real little wallet"; a ring as "a real gold ring"; a pen as "a lovely little pen," etc. That these expressions are peculiar to this stage is shown by the fact that they were not employed by the patients either before the fit or after complete recovery from it.

There is a wide variation in the purity and the development of this stage in different individuals or in the same individual on different occasions. Sometimes the entire aphasic stage seems to be too brief to permit of examination. On the other hand, the stage of aphasic reaction in certain patients may be of several minutes' duration. Perseveration is commonly observed.

Typical results of the examination of patients in this stage are the following :

CASE 20.—Strong epileptic fit, with dilatation of pupils and turning upwards of eyes. Fit lasted 65 seconds, followed by strong rolling movements with outward flinging of the arms. Cyanosis of face lasted two minutes. Four minutes after the end of the myoclonic stage various parts of the body were named correctly, quickly and without difficulty. When asked to name other objects, the patient was very slow and seemed to have an obvious difficulty in doing so, expressing itself in perseveration, e.g. :

Objects presented :	Fountain pen.	Answers : Pen.
	Nail file.	Pen.
	Pencil.	Pen.
	Purse.	No answer.
	Money.	No answer.

The patient would make no further attempt until consciousness was complete. In this case the greater facility in naming parts of the body than external objects was very obvious.

CASE 21.—Typical fit. Immediately after the fit patient was restless, with rolling movements, combined with slow movements of the eyes to both sides, more to the left. Attempts to name objects two minutes after the fit gave the following results :

Objects presented :	Watch.	Answers : White and black.
		White, green, blue, black, white, gold.
	Nose.	Nose.
	Eye.	2 eyes.
	Coin.	3 eyes.
	5*d*. bus ticket.	5 D.
	Nose.	A little nose.
	Bunch of keys.	A real little key, not all alike.
	Watch.	A real little watch.
	Stethoscope.	A real —— ?
	Pen.	A real little pen.
	Mouth.	My mouth. Tooth and nose.
	Right arm.	Left arm.
	Golden ring.	A real gold ring.
Three minutes later :		
	Red tie.	The colour of real red.
	Blue pencil.	A real blue pencil.

This examination gives examples of the use of qualifying adjectives and of perseveration. At the time when it was conducted any difference in the relative ease of naming parts of the body and external objects which may have existed had disappeared.

The aphasic phenomena described suggest that there is a short stage of what has been called amnesic aphasia, or in Head's (28) system, nominal aphasia. But in distinction to the typical amnesic aphasia, in these cases there is a short period in which naming of parts of the body alone is intact. That the aphasic reactions cannot be attributed to confusion or gnostic failure is shown by the general behaviour of the patients and the use of circumlocution.

Aphasic reactions of a similar type have been observed in chronic epileptics

following fits, and in epileptic twilight states, where the reaction sometimes persisted for several days. A similar reaction, too, has been seen during the re-awakening from insulin coma (Stengel, 29).

The peculiarity of applying qualifying adjectives to objects, noted before, occurs also in chronic epileptics. In descriptions of Stengel (29), a chronic epileptic after a series of fits applied the adjective " real " to objects presented to him. It is well known that chronic epileptics habitually use qualifying terms such as " lovely " or " beautiful," which adds to their conversation a verbosity and unctuousness. This form of speaking is recognized as the result of a change of character in epileptics. It is surprising that this peculiarity, which in epileptics takes years to develop, can appear for a brief period after a cardiazol convulsion.

When the last traces of speech defect have disappeared, the patient seems to show a certain slowness of mental activity, with the desire to sleep and to avoid contacts.

The reactions described are not specific to cardiazol. I have been able to observe them in a smaller series of patients undergoing treatment by electrically induced convulsions.

Amnesia.

It has been suggested that the effects of amnesia contribute considerably to favourable results in cardiazol therapy, and that the amnesia is retrograde. The theory was put forward that abnormal mental contents, hallucinations and delusions, were also subjected to the amnesic process and were eventually forgotten altogether. The real facts of the amnesia were investigated in a group of ten cases undergoing treatment, chosen irrespective of prognosis or history. Eight pictures were presented to each patient 30 minutes before the injection. These pictures were chosen from subjects likely to be of general interest. In order to make quite sure that the material of the pictures had been understood, the patients were asked to describe the pictures at the time of showing. About an hour after the injection each patient was asked whether anything had been shown to him that morning. No patient, at any time, failed to recollect having been shown a series of pictures; three remembered all the pictures, and the remaining patients remembered a fair part of them; no patient remembered less than three of the series. Incidentally the three patients with the best scores were responding very favourably to treatment and afterwards recovered, while those with the lowest scores were those who seemed to have the poorest power of concentration.

The absence of a retrograde amnesia after the electrically induced fit was easily demonstrated. Many patients remembered the electrodes being strapped to their foreheads, and even the passage of the small calibrating current, just before the initiation of the fit.

Examination therefore showed quite clearly that a retrograde amnesia is not one of the common after-effects of convulsive therapy, and cannot be regarded as a mechanism essential to cure.

However, there is always an amnesia for the period of the convulsion and for the time after it when consciousness is still clouded. No patient could recall features of behaviour during the period of semiconsciousness, irrespective of how long this period lasted. Many patients complain that there is some disturbance of memory during treatment. But the existence of such a disturbance can only be demonstrated within a period of an hour or so after the convulsion.

These amnesic features agree with what Gillespie (30) has described in an account of a personal experience of a cardiazol convulsion.

Induction of Symptoms.

In the course of recovery of patients during cardiazol treatment, I have observed a remarkable tendency which as far as I am aware has not yet been described. At the time when interest in personal delusions and hallucinations is fading, patients show a great interest in the experiences of others and sometimes a tendency to adopt their psychotic ideas.

For example, when one patient of a group of six was questioned about her menstrual condition, the other five within a day or two reported spontaneously irregularities in their own, although not one of them had sought advice on menstrual troubles before. It was obvious that their concern was not very deep-seated and had been inspired by the remarks of the first patient.

The increase of interest in others can be extended to cover hallucinatory experiences. One patient who had apparently lost her own characteristic delusional ideas reported that she was dead and had no body ; she had copied another patient, who was then under treatment and expressed these beliefs. She admitted as much in examination, and no great difficulty was experienced eventually in persuading her that this idea was untrue. Another case, who had the idea that her " bowels were stopped up " and that she had been " wicked," transmitted these ideas to two other patients under treatment at the same time, who asserted quite emphatically that they " must be wicked too." These ideas were expressed each morning before treatment and persisted for a few days.

These are instances of the " induction " of pathological mental products, which occurs in *folie à deux*, and which is most frequently seen in paranoic subjects ("induced paranoia") and sometimes in cases of hysteria (Coleman and Last, 31). They are evidence of an increased susceptibility to influences from without the patient, in opposition to the autism of the schizophrenic, as if the wall between the schizophrenic and the outer world had become less impervious and less definite. At the same time, they are further evidence of the interest

that the patient takes in the outer world, and of the tendency to enter into groups with common interests. Therefore this symptom, although in itself pathological, is a sign of growing sociability. It is of great practical importance for, as the examples suggest, the increased susceptibility of the patient may lead to injurious results if he is subjected to strong pathological elements in his environment. In addition, this heightened susceptibility may provide a good reason for refraining from questioning the patient about pathological ideas which are becoming less real to him. There is a certain danger of confirming delusions which the patient hopes to forget, by a process of what may be called re-induction.

I have been unable to ascertain from the literature or from personal experience if the induction of symptoms described above occurs in the course of spontaneous remissions. It seems probable that it does not, and if this is the case it provides one definite point of difference between the mechanisms of spontaneous and of therapeutic recovery.

Some Considerations on the Mechanisms of the Change of Symptoms.

It must be conceded that, irrespective of the ultimate therapeutic result, a certain change in the clinical picture occurs in almost every patient in the course of convulsive therapy. In what way the observations recorded in this paper can assist in throwing light on the mechanisms of the change of symptoms can now be considered. The importance that may be attached to a particular set of observations depends upon what personal conception is held as to the nature of the psychoses under treatment. For those who are inclined towards an organic aetiology, the pathophysiological observations will be of greater interest than the psychological. But in the present state of limited knowledge neither aspect can be neglected.

There is no doubt that the cardiazol fit brings about a repeated change of functional relations between cortical and subcortical parts of the brain. This is shown by the transitory appearance of types of movements related to the deeper centres, which, as has been described before, occurs before and after the fit proper, in addition to the typical motor phenomena of epilepsy. This indicates that the relationship between different systems of the nervous organization is deeply disturbed by the action of the drug, and that a great readjustment and re-establishment of this relationship must take place before full consciousness returns. It is not unlikely that the process of readjustment has some lasting effect upon the nervous organism as a whole, and that in the course of repeated disturbances and reorganization of neural relations some fresh orientation takes place, bringing the parts of the nervous system into a state of more normal balance.

If one feels justified in regarding schizophrenic symptoms from a neuropathological angle, as Kleist (32) *et al.* have done, one finds in schizophrenics

various signs of physical change that can be related to neurological syndromes. The states of hypo- and hyperkinesis in schizophrenia have their counterparts in forms of postencephalitic Parkinsonism. The disturbance of affectivity has been related to functional disorders of deep centres, especially the hypothalamus. Similar views have been expressed with regard to the affective psychoses. Cushing (33), Foerster and Gagel (34) and Alpers (35) record manic states in hypothalamic disorders. These views received practical importance in the works of Moniz (36), who has reported successful results in schizophrenia and melancholia, after severing the connection between the deeper parts of the brain and the frontal lobe.

Therefore, it may be suggested that a physical agent which brings about repeated alterations in the functional relation between deeper and higher levels of the brain, such as has been observed in induced epilepsy, may lead to a re-establishment of normal functional relations between these centres. Although such a theory is far from proven, it has the advantage of being related to clinical observations, and it may have some value as a working hypothesis.

The possible objections to the " organic " theories have led some workers to seek a psychological approach to this problem. The psychological theories have the advantage of embracing a wider field and being non-exclusive to other forms of shock treatment. Further, they are based on what is known of schizophrenia, and the conception of schizophrenia itself is after all psychological.

In dealing with the psychological mechanisms, use will be made of observations recorded earlier in this paper. There are three psychological events in the course of a single therapeutic convulsion, each of which provides an interruption in the psychotic life of the patient.

The first event is the realization of being treated. This realization is evidenced by various attitudes on the part of the patients, and it is striking that, irrespective of their behaviour, nearly all patients seem to realize that the therapeutic interference is intended to be beneficial. The treatment seems to stir up an innate tendency to be restored to normal health.

The second event is represented by the return from the death-like state of the epileptic fit to reality. It has been shown that this return is gradual and that mental functions return in a definite order. The state of aphasia is of special interest for an interpretation of the psychic readjustment towards reality. It has been described how the patient in this stage is able to identify and name parts of his own body before any object of the external world. This phenomenon can hardly be ascribed to a disturbance of organic function alone, but must be determined to some extent by psychological conditions. Hughlings Jackson (15) has shown to what extent psychological and personal conditions can influence the capabilities of the aphasic. If one regards the order in which the faculty of naming is restored as reflecting the re-establish-

ment of the patient's relation with the world, one finds self-interest, or rather an awareness of the ego, returns first, to be followed by an awareness of other objects and the relationship they bear to him.

In chronic epilepsy similar phenomena can be observed, and seem to suggest that personality changes may influence or even determine certain features of speech disorders. Chronic epileptics, as is well known, are highly self-centred, and their personality undergoes a change in the direction of restricted egotism. Another point of similarity between the reactions of chronic epileptics and those of patients awaking from induced convulsions is their habit of using certain adjectives which are evidence of an exaggerated emotional attitude towards objects of the environment. It may be that this similarity is not accidental, but has a bearing on the psychological readjustment of the psychotic patient towards his own personality and the outer world. Repeated induced epileptic fits in schizophrenics might lead to what has been described as an epileptic feature of the personality. It may well be that the appearance of such features of the epileptic personality might prove antagonistic to the schizophrenic dissociation and result in benefit to the patient.

There is one fundamental difference between the epileptic and the schizophrenic; the epileptic experiences his personality as a whole, even to an exaggerated extent, while the personality of the schizophrenic is "split up." From the psychological point of view these features are really antagonistic. It is possible that the epileptic seizure, which overwhelms the whole organism, compels the schizophrenic to re-establish the unity of his personality. It may be for a similar reason that autistic schizophrenics have been known to react normally in situations of real danger. The assumption that the temporary imposition of epileptic features produced by convulsion therapy contributes to the change of the schizophrenic personality, is in no way related to Meduna's unjustified assumption of a biological antagonism between schizophrenia and epilepsy.

The third event is the encounter with the environment after re-establishment of consciousness. This takes place when the patient is fully conscious and in full possession of his mental capacities, but still experiencing the physical aftermath of the shock. In this stage the patient feels dependent and shows a tendency to attach himself to persons in his environment. Aggressiveness is usually absent. This stage might last for hours, or even endure. The convulsive episode has forced the patient to assume an infantile relationship towards his environment, absolutely opposed to the psychotic attitude. The nature of the new situation is sometimes indicated by an outpouring of eroticism, which obviously has the same source as the tendency to express a pleasant emotional feeling towards objects during the stage of aphasic reactions, as described before. Repeated occurrences of the state of dependence on others, which replaces for a while the psychotic attitude, may very well lead to a definite breaking of the psychotic withdrawal from human society.

Such a conception as this of the return to an infantile state may have been in the minds of those workers who have attributed the therapeutic action of shock treatment to psychic death and rebirth. The interpretation given above seems to be in closer relationship to objective clinical observations.

Such psychological considerations are applicable to all forms of shock treatment and other forms of treatment that operate through the production of a change of consciousness, e.g. continuous narcosis and general anaesthesia. It is, however, necessary to realize that the disturbance of consciousness in continuous narcosis is not so profound as in epileptic fits, and therefore the adjustments which the patient must make in the process of recovery from these conditions are necessarily less extreme.

This theory is also applicable to improvements observed in melancholic depression and mania treated by forms of "shock." In these states, too, the relationship of the individual to the outer world and also to himself is disturbed, and perhaps in the course of shock treatment readjustment takes place. Observations are not sufficient to allow the analysis of the course of this readjustment. It is not uncommon to encounter cases of melancholia where marked improvement has followed a serious and unsuccessful attempt at suicide, especially where, as in gas poisoning, hanging, and drowning, the attempts were followed by unconsciousness. Such cases may be examples of the beneficial influence of forms of shock in affective psychoses.

It might at first sight be argued that a psychological theory must be an alternative to an organic. But if it be held that the manifestations of affectivity are the expression of processes taking place in the deeper parts of the brain (and this can be regarded as proved by what is seen in certain brain disorders, such as postencephalitic Parkinsonism), it becomes clear that the psychological theory for an alteration of affectivity is not necessarily opposed to a theory derived from observations on organic activity. Both theories really postulate the same mechanism, but reach their conclusions by the investigation of two entirely different forms of human behaviour, motility and affectivity.

In the interests of economy of space it is not possible to publish case-histories nor to discuss the therapeutic results, which in my series were not markedly different from those obtained by the majority of other workers. The presentation of the views of others and of bibliographical references have for the same reason been reduced to the minimum.*

I should like to express my gratitude to Dr. J. J. B. Martin, Medical Superintendent of the Bristol Mental Hospital, for permission to publish the result of these investigations and for his constant interest and encouragement, and also to Mr. Grey Walter, of the Burden Neurological Institute, who was responsible for the application of the electrical treatment.

* The last number of this Journal, published in May, 1940, contains several interesting papers dealing with various aspects of convulsive therapy. This paper was completed before it was possible to consider these contributions.

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CEREBRAL FAT EMBOLISM AS THE CAUSE OF DEATH IN A CASE OF SCHIZOPHRENIA TREATED WITH TRIAZOL (AZOMAN).

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THERE has been an extensive literature on accidents occurring during cardiazol treatment, and since the largely conflicting pathogenic view-points have been discussed in recent reviews (Gross and Gross-May, 1939; Kennedy, 1940; Wyllie, 1940), there is no need for their detailed enumeration. Gross and Gross-May, whose paper was unfortunately not available to us in the original, recently summed up the more important causes of accidents, grouping them into mechanical disorders, particularly of the osseous, tendinous and muscular system; disturbances of the vascular system—arrhythmia, auricular fibrillation, syncope and vascular spasm due to the specific action of cardiazol; and finally, respiratory disturbances—arrest of respiration, pulmonary embolism, and abscess due to thrombophlebitis at the site of injection.

Published deaths following the use of triazol are very few; in principle, however, the same mechanism may be assumed to be at work as in death after cardiazol. Wyllie reports four deaths in a series of 85 cases, giving details of two resulting in *status epilepticus* after intramuscular injections respectively of 4 c.c., and of 2 c.c. plus 1 c.c. after 15 minutes. In both cases death followed immediately after the fits. At autopsy of the second case there was intense venous engorgement, particularly of the lungs; the brain was also intensely congested; on the inferior surface of both lobes of the cerebellum there was an area of oedema and softening; it was considered that the cerebellum had possibly exerted pressure on the vital centres lying on the floor of the fourth ventricle and had so brought about paralysis of the respiratory system; no histological study seems to have been made. The author considers that supplementary doses are unsafe when using the intramuscular route, and that in the first case quoted the dose was excessive. Atkin (1939) has recorded a series of 12 cases in which there was one death, from pulmonary tuberculosis after the

fourteenth treatment in a very long-standing case of schizophrenia, the triazol having apparently reactivated an old lesion.

The following case seems to be of interest, firstly as an addition to the small group of fatal cases during triazol treatment, and secondly because the changes found are of an unusual and unexpected nature. The case is the first death among 59 cases so far treated with triazol at Brentwood Mental Hospital since July 1938.

Clinical Report.

The patient was a married woman, aged 33, with two children, born 1934 and April 1939. She was of normal intelligence; her temperament was described as "cheerful"; she was an alcoholic abstainer, and her previous history revealed no significant illnesses and no mental abnormalities. Her menstrual periods were regular, the first having occurred at the age of 14, and her pregnancies were uneventful. An elder sister was a voluntary patient in the same hospital in 1934 for two months, suffering from an anxiety attack. No family or personal history of epilepsy or of epileptic equivalents can be traced.

The onset of her psychosis occurred suddenly on July 4, 1939, up to which time she had been feeding her younger child, when she complained of insomnia and was noticed to be agitated; the next day she became very excitable and was admitted to hospital for observation. Whilst there, she attempted to attack the staff and would neither speak nor feed herself. On July 7, 1939, she was sent to Brentwood as a temporary patient. On admission she was seen to be a well-built woman of 154 lb. weight, very toxic and covered with bruises. Her temperature was 101° F., pulse 130, heart sounds regular and normal, blood pressure 165/80 mm. Hg, lungs clear. All her reflexes were brisk with flexor plantar responses, cranial nerves normal. Her teeth were carious, and she had sordes on her lips and was lactating. Her urine contained albumen, a trace of sugar and was loaded with acetone; pus cells and very scanty granular casts were found in the centrifuged deposit. Wassermann reaction was negative. Mentally she was wildly restless and confused, extremely resistive and vicious; she spat her food out, was dirty and incontinent; she could give no coherent replies to questions and her attention could not be held. She readily became exhausted and did not sleep. A clinical diagnosis of katatonic schizophrenia was made.

Her physical condition improved with treatment and she became less restless, though for several weeks she needed frequent tube-feeding. During August she developed a *B. coli* bacilluria and in the same month went into a state of katatonic stupor. It was not until October that her general condition improved sufficiently for convulsion therapy to be started, and on October 17 she was given cardiazol. After five injections triazol was substituted, as the smallness of her veins made the less bulky injection preferable. The technique of administration followed throughout was that recommended by Walk and Mayer-Gross (1938) with premedication with atropine. Her mental condition only improved slightly, and rapidly varied between confusion and comparative clarity, when she was able to converse and to occupy herself to some extent at simple routine ward work; at her best she was hostile, abusive and negativistic. Whilst she was in the hospital she sustained no known fracture, and although no X-ray of her vertebral column was taken, there was no clinical evidence to suggest that any fracture might exist in this region. The following table summarizes the doses used, the dates on which treatment was given and the results obtained.

It may be considered that some of the later intravenous doses were rather large (*cf.* Braunmühl's (1938) weight-dose tables), as the patient's weight in December was only 115 lb., but it has been our practice to increase the intravenous dose when the previous fit was delayed by a long myoclonic stage; moreover, the therapeutic

Table of Doses.

No. of treatment.	Date.	Dose.	Result.
	1939.		
1	October 17	10% cardiazol, 5 c.c. intravenous	Major fit statim.
2	„ 20	„ 5 c.c. „	„ „
3	„ 24	„ 5 c.c. „	„ „
4	„ 31	„ 5·5 c.c. „	„ „ (very apprehensive).
5	November 3	„ 6 c.c. „	Major fit statim, violent before.
6	„ 8	Triazol, 2·0 c.c. intramuscular	Major fit after restless period.
7	„ 10	„ 1·25 c.c. intravenous 0·75 c.c. added after two minutes	A few myoclonic twitches only. Major fit 5 min. later.
8	„ 14	„ 2·0 c.c. intravenous	Major fit statim; great apprehension.
9	„ 18	„ 2·0 c.c. „	Major fit statim.
10	„ 21	„ 2·0 c.c. „ (injection partly extravenous)	Delayed major fit.
11	„ 24	Triazol 2·0 c.c. intravenous	Major fit statim.
12	„ 28	„ 2·0 c.c. „	Delayed major fit.
13	December 1	„ 2·5 c.c. „	Major fit statim.
14	„ 4	„ 2·5 c.c. „	„ „
15	„ 9	„ 2·5 c.c. „	„ „
16	„ 12	„ 2·5 c.c. „	„ „
17	„ 16	„ 2·5 c.c. „	Major fit after long myoclonic stage.
18	„ 19	„ 2·5 c.c. „	Major fit statim.
19	„ 29	„ 2·5 c.c. „	Prolonged period of myoclonic convulsions, followed by 3 fits in an hour.
	1940.		
20	January 2	„ 2·75 c.c. „	Ditto, 3 fits.
21	„ 5	„ 2·75 c.c. „	Major fit statim.
22	„ 9	„ 2·25 c.c. „ (dose reduced owing to accidental wasting).	„ „
23	„ 12	Triazol 2·75 c.c. intramuscular	9 major fits, the first 5 min. after injection, the last 2½ hours after.

advantage to be derived from a reasonable number of multiple fits has been appreciated. As the above table shows, her 23rd and last treatment was given on January 12, and consisted of 2·75 c.c of triazol intramuscularly, a dose no larger than she had previously had intravenously, the intramuscular route being used on this occasion after failure to penetrate a vein. This injection was given at 11.50 a.m., the first major fit occurring at 11.55 a.m. and the ninth and last at 2.15 p.m. The exact times of the intervening fits were unfortunately not recorded, but they were observed to follow the usual rule of increasing intervals. No attempt was made to terminate these multiple fits, as this particular woman had never had more than three following any one injection and other patients have had from six to nine entirely without ill-effect. The patient remained very confused for the rest of the day.

On January 13 she was drowsy and stuporose—not an unusual state for this patient—but her general condition gave rise to no anxiety and she was able to take her diet when hand-fed.

On January 14 she awoke in a comparatively alert mental state at about 7 a.m., and at 7.25 a.m. (43½ hours after the triazol injection) she suddenly had a major fit lasting about five minutes and described by a reliable and experienced nurse as being a "typical epileptic fit." She was restless and plucked at the bedclothes

until 8.30 a.m., when she had an attack of generalized myoclonic twitchings, lasting three minutes, similar to those so often seen after a subconvulsant dose of triazol; she then became comatose with stertorous respiration and a thready pulse. Her pupils were moderately dilated and reacted to light, corneal reflexes were absent and she had a right external strabismus. All her tendon reflexes were diminished and her plantars flexor. Temperature was normal and remained so. Her urine showed a trace of albumen, but no sugar or acetone. She was incontinent at 10 a.m., her condition being otherwise unchanged. At 3 p.m. she was still deeply in coma, but the neurological picture had developed; her pupils were now very much contracted but still showed a slight reaction to light, corneal reflexes being absent; no strabismus was now seen. Arm, knee, ankle and abdominal reflexes were now absent, all limbs were flaccid and her plantars both extensor; a little later this extensor reflex was replaced by a mass-withdrawal response.

At 7.30 p.m. she was cyanosed and dyspnoeic, with moist râles at the bases of both lungs. All reflexes, including the plantars, were absent, and she died at 9 p.m., having been in coma for 12½ hours.

Pathological Report.

A post-mortem was held on January 15, 22 hours after death. Nutrition was good and there were no external signs of disease. Body weight was 116 lb. The macroscopic findings were as follows:

Heart (230 gm.): Muscle pale, slight atheroma of aorta, coronary arteries patent, valves healthy, right-sided dilatation.

Lungs (right, 400 gm.; left, 380 gm.): Patches of haemorrhage, terminal oedema.

Liver (1,340 gm.): Pale and fatty.

Spleen (125 gm.): Pulp soft.

Kidneys (right, 160 gm.; left, 150 gm.): Small pin-head cysts on the right kidney surface; both kidneys congested.

Brain: The meninges showed intense venous stasis. there was a thrombosis in the circle of Willis. In the right frontal lobe was an area of haemorrhagic softening near the surface, of about the size of a walnut. Its precise situation was not indicated. Other macroscopic abnormalities were not noted. The dissected brain and small pieces of the organs were embedded in paraffin and sent for histological study to the Central Pathological Laboratory; the following is the result of the investigation:

There was no noteworthy finding in the organs; in the liver there was some central congestion and brown atrophy combined with moderate fatty change. In the kidneys congestion and cloudy swelling were noted. In the lung small bronchopneumonic patches were seen alternating with areas of intense congestion, haemorrhage and oedema. No evidence was obtained from these paraffin-embedded sections of the presence of fat embolism.

The histological investigation of the brain in the first place confirmed the observations already made on naked-eye inspection. Thrombosis of one of the arteries in the circle of Willis is shown in Fig. 1; it was of recent date, but organization in the parts next to the intima was already taking place (the hole in the middle of the thrombus is an artefact); otherwise the vessel wall was healthy and there were no signs of arteriosclerosis, syphilis or of any gross vascular disease. In addition, more or less complete thrombosis was found in a number of large and middle-sized meningeal blood vessels on the convexity of the cerebral hemispheres. Where there was no thrombosis, the vessels were filled with blood to capacity and were very distended; however, in a number of blood vessels, blood corpuscles were absent or filled only a part of the lumen as if they had been pushed aside by an unstained foreign substance; occasionally a circular or crescentic zone near the intima of the vessel wall was left free. Fat stain provided the explanation for this phenomenon. It was seen in Scharlach-R preparations that many blood vessels contained fat emboli

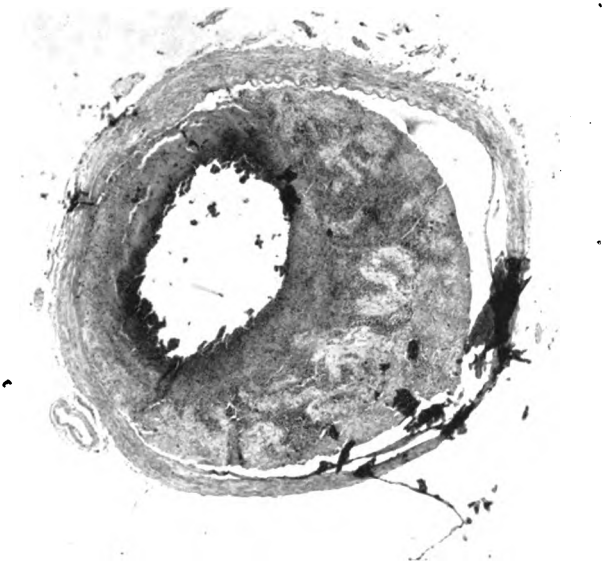
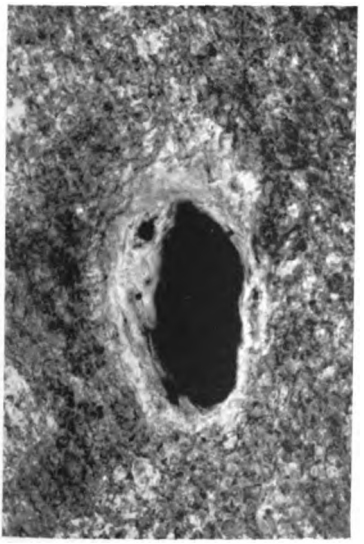
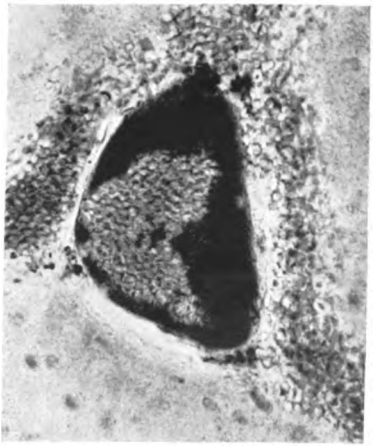


FIG. 1.—Large thrombosed artery (haematoxylin-eosin).

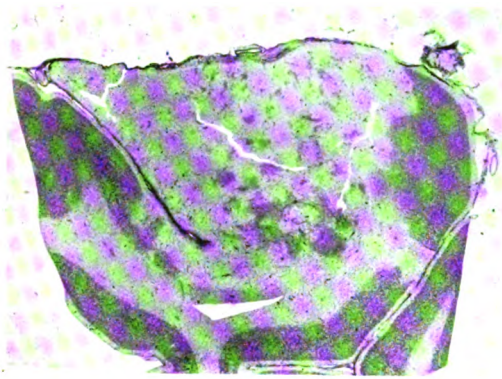


a

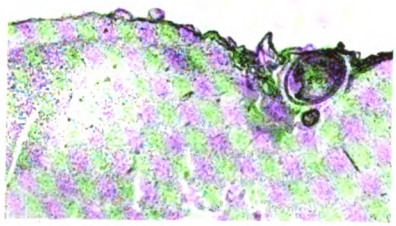


b

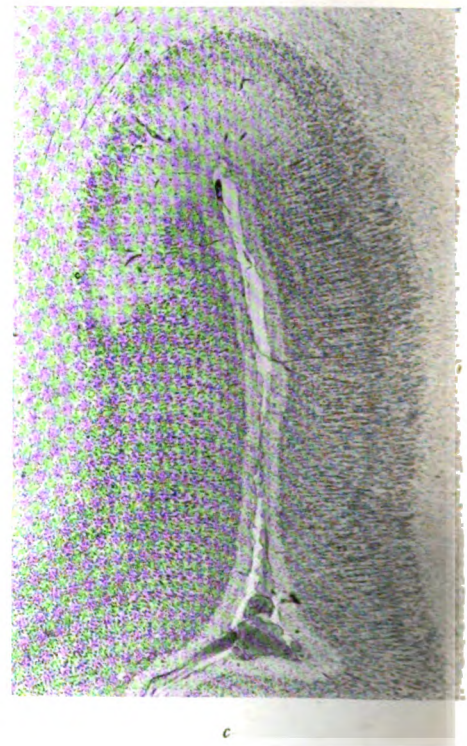
FIG. 2.—Fat emboli (Scharlach-R stain).



a



b



c

FIG. 3.—Ischaemic necrosis and early softening of the cerebral cortex (Nissl stain).

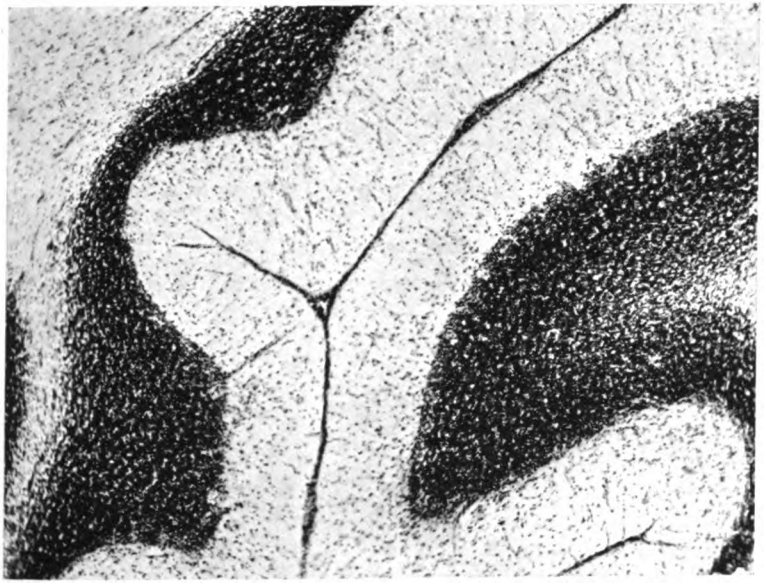
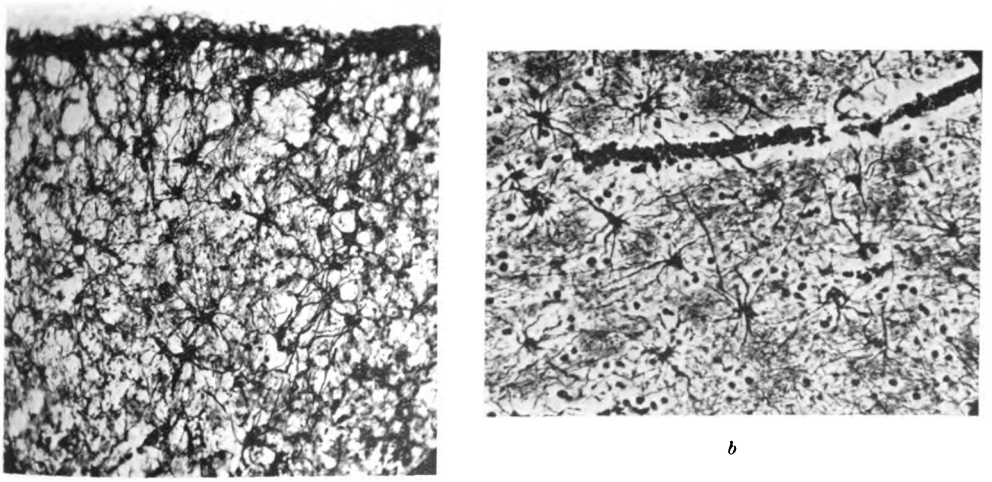


FIG. 4.—Ischaemic necrosis of the cerebellum (Nissl stain).



a *b*

FIG. 5.—Astrocytic proliferation in the subpial layer of the cerebral cortex (*a*) and in the white matter (*c*). (Hortega's variant for astrocytes.)

which either filled the whole lumen or a part of it (Fig. 2). The empty circular or crescentic zone contained fat which seemed to be pressed against the vessel wall by the red corpuscles, as seen in Fig. 2*b*. Although fat emboli were found everywhere in the brain, their total number was not very large; they occurred in the grey matter not more frequently than in the white matter, they were found particularly in small-sized vessels of the pre-capillary type, less frequently in capillaries, and occasionally only in the larger meningeal vessels. A great number was seen in the region of the cornu ammonis, and particularly in the vessels which emerge from the hippocampal sulcus and supply the Sommer sector. The cerebellum was also severely affected, while the dentate nucleus and the inferior olive did not contain a conspicuous number of emboli.

In addition to the extensive lesion in the frontal lobe already seen on naked-eye inspection, a small area of cortical necrosis was found in the parastriatal region of the occipital lobe. Considerable damage was also noted in the cerebellum. The nature of the lesions in the frontal lobe was that of an ischaemic necrosis; the nerve cells were entirely wiped out either over long stretches of the cortex or in more circumscribed foci (Fig. 3*a*). In the neighbourhood of the areas of total necrosis, characteristic ischaemic nerve-cell change was seen, the nucleus becoming triangular and deeply stained, the cytoplasm homogeneous and the margin beset with extracellular basophil incrustations. There was intense microglial proliferation, and some of the proliferated microglia were being transformed into compound granular cells. The endothelial cells of the small blood vessels were in active proliferation and new capillaries were formed by budding. The whole picture corresponded to that of an incipient softening. In some parts of this area of softening many small haemorrhages were seen; Fig. 3*b* demonstrates a thrombotic vessel in this area of necrosis.

The lesion in the parastriatal region of the occipital lobe was much smaller. It consisted of an area of ischaemic necrosis in the depth of a sulcus with a nearly symmetrical position on both sides of the sulcus (Fig. 3*c*). The histological detail was the same as that of the frontal area, though haemorrhages were missing; nearby a thrombotic pial vessel was seen.

In the cerebellum there was "dropping out" or homogenizing change of the Purkinjë cells in many lobules with marked proliferation of the Bergmann glia and the characteristic shrub-like formation of the microglia in the molecular zone (Fig. 4).

The rest of the brain was free from ischaemic necrosis and haemorrhages, even in those regions such as the cornu ammonis in which numerous fat emboli were found to be present. There was, however, some diffuse change. Fat was abundant in both nerve cells and blood vessel cells; the fatty change in the vessel-wall cells was not more marked in vessels with emboli than in those without; there was also a diffuse proliferation of the macroglia in the subpial layer of the cortex and in the white matter throughout, as demonstrated in Fig. 5*a*-*b* after staining with Hortega's variant for astrocytes. For an unknown reason, Holzer stain did not bring out this proliferation well, although in some parts it corresponded roughly to the gliosis seen in the silver preparations.

Discussion.

There is little doubt that in this case death was due to cerebral fat embolism. Epileptiform convulsions, followed by confusion, drowsiness and coma, is a well-recognized sequence of events in cerebral fat embolism; there was, however, no petechial rash of the skin, which is considered to be of high diagnostic value. It is difficult to assess the exact time of onset of the cerebral condition, since there was no conspicuous signal, such as a fracture. The period between onset and death varies greatly; according to Strauss (1933), who has collected most of the literature published up to 1933, it may be

a few hours or even eleven days; most cases die on about the third day. Epileptic fits often initiate the syndrome, but they may also occur in later stages. In this case the situation is still further complicated by the occurrence of two sets of convulsions on January 12 and 14 respectively, and by the fact that delayed fits may occasionally occur after cardiazol injections (Hobson, 1938; Harris, 1939; Thorpe, 1939), although the nature of this phenomenon is not yet understood. The great majority of cases of fat embolism follow fractures, particularly those of the long bones (*vide* the statistical figures given by Strauss). Other less frequent causes are contusions or lacerations of adipose tissue, operations in fat tissue, orthopaedic procedures, rupture of the liver, burns, etc. (Strauss, 1933; Cammermeyer, 1937; Wilson, 1940); even concussion may under certain circumstances lead to fat embolism, as is evidenced by animal experiments carried out by various workers (quoted after Strauss).

It is difficult to assess which of these pathogenic possibilities apply to our case. The patient was badly bruised when admitted to hospital, but the interval between admission and the terminal embolism was too long for this to be considered as a possible cause. Nothing is known of a fracture in our case, but the possibility that one had occurred without being noticed cannot be excluded. Vertebral fractures, which are easily overlooked if occurring during cardiazol treatment, have been reported as a source of cerebral fat embolism (Strauss), though only as a very small percentage among other fractures. Considering the importance which osseous complications have recently attained in cardiazol treatment, our case would point to a new indirect source of danger associated with the occurrence of fractures. Whilst it is admitted that the case is exceptional, cerebral fat embolism may well be found more frequently now that attention has been drawn to its occurrence. So far, most workers have considered the functional disturbance of the circulation the most important cause of cerebral complications in idiopathic epilepsy and induced convulsions, but there are cases in which this explanation is considered to be insufficient; Jansen and Waaler (1940) recently reported, in a case dying during cardiazol treatment, gross lesions for which they postulated an organic affection of the vascular system of the brain, such as thrombosis. In idiopathic epilepsy, gross lesions, transient or permanent, are occasionally produced in the brain, differing from those typical after-effects which are said to be caused by vasomotor disturbances or other types of oxygen deprivation of the tissue; epileptics may die suddenly without a satisfactory cause of death being found at post-mortem. It would therefore be worth while to study cases of this kind with fat embolism in mind. It is interesting to note that fractures occur also among idiopathic epileptics.

Fractures are not the only source for the mobilization of fat, as has already been pointed out; epileptiform convulsions of whatever nature may give rise to contusion, laceration and even concussion, any of which are said to be a potential cause of cerebral fat embolism. The question has been discussed

as to how clinical methods might be improved for the discovery of fat embolism ; the general opinion (Strauss) seems to be that the blood-fat level, the secretion of fat by the urine and fat in the cerebro-spinal fluid are not reliable indicators ; whether the observation of fat in the retinal blood vessels might be of diagnostic value remains to be seen, otherwise the diagnosis rests upon the free interval, the sequence of neurological and mental symptoms, and the occurrence of petechial haemorrhages of the skin.

The histological changes in our case correspond in principle to what has been described in previous cases of cerebral fat embolism and in animal experiments (Neubuerger, 1925 ; Weimann, 1929 ; Bodechtel and Mueller, 1930 ; Cammermeyer, 1937). In our case there was no patent foramen ovale to allow the passage of the fat from the right heart into the systemic circulation, thereby avoiding the respiratory circulation ; moreover, this communication was found missing in the cases of Weimann and Cammermeyer, and it has been proved experimentally that passage of fat through the lung capillaries is quite possible. Nothing is reported in our case of fat emboli in the lung or in other organs. At autopsy no specific attention was paid to their possible occurrence, and the small paraffin-embedded pieces of the lung, liver, heart, kidney and spleen gave no sufficient indication of their presence. The changes in the brain in our case, as well as in those of cerebral fat embolism previously reported, present the picture of ischaemic necrosis and haemorrhagic softening. In our case the changes were well circumscribed, apart from some diffuse glial proliferation ; only two cerebral regions, the frontal and occipital lobes respectively, and parts of the cerebellum had undergone necrosis. In the cases of Neubuerger, Weimann and Cammermeyer the extent of the lesions was much greater ; the areas of pallor in Cammermeyer's case were so numerous that in his own words " not a single slide was free from them." The cornu ammonis, inferior olive, dentate nucleus and periventricular regions, all of which were a favourite site for lesions in previous cases, were preserved in our case. One reason may be that fat emboli, particularly in the capillaries of the grey matter, were not so numerous in our case as in previous ones ; another explanation is that through the occurrence of thrombi in the large basilar vessels, death occurred before the signs of an early ischaemic necrosis could develop in many places. The widespread occurrence of thrombi, even of the large arteries at the base, is a significant feature of our case ; their relationship to the fat emboli is not quite clear. The opinion has been voiced that the emboli do not merely act as a local mechanical obstacle, but give rise to secondary functional disturbances of the whole circulation of the brain ; Neubuerger and Weimann particularly have emphasized the intermediary rôle of the vasomotor disturbances which may produce lesions in areas in which emboli themselves are absent ; from their point of view the general slowing down of the circulation would account for the thromboses. This interpretation has, however, been contradicted (Bodechtel and Mueller ; Cammermeyer) partly on the strength of

experimental evidence ; according to Cammermeyer, the distribution of lesions in the brain is mainly determined by the " haemodynamic laws " which govern the passage of emboli. Since, owing to previous dissection of the brain, a close topographical investigation could not be carried out, no conclusive view can be advanced on the relationship between emboli and thrombi in our case.

It is interesting that regions, such as the cornu ammonis, dentate nucleus, inferior olive and cerebellum, which are generally susceptible to ischaemic necrosis, may also be a favourite site of fat emboli. The question arises whether Cammermeyer's haemodynamic factors might not be partly or wholly identical with those responsible for the selective vulnerability of the regions concerned.

Summary.

A case is reported in which death occurred from cerebral fat embolism during treatment with triazol. The pathogenesis is discussed, particularly with a view to the accumulating reports on fractures occurring during spontaneous as well as induced epileptic convulsions.

Whilst the exceptional nature of the case is fully recognized, it contributes a pathological view-point which may prove of some value in the study of convulsive conditions.

We have to thank Dr. W. Gordon Masefield, Medical Superintendent of Brentwood Mental Hospital, for his permission to publish this case. Our thanks are also due to Mrs. E. Beck, assisted by a Rockefeller research grant, for her help in the preparation of the slides and microphotographs.

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FORCED GRASPING AND DISTURBANCES OF ATTENTION.

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As a result of two operations which were performed on a rhesus monkey with the object of working out an approach for the destruction of the anterior nuclei of the thalamus, not only were the latter involved, but lesions were also produced in the frontal lobe. The lesions were largely caused by the removal of firm adhesions which had developed after the first operation. The motor disturbances and the mental changes which appeared after the second operation revealed some features which had much in common with a clinical syndrome previously observed in a patient who had died from a frontal lobe tumour in the same region. For this reason it seems worth while to record and to discuss these two cases. The experimental operations may be described in some detail in order to explain the extent of the lesions produced.

FIRST OPERATION, MAY 30, 1939.

Under nembutal anaesthesia two large bone-flaps were turned down to expose the frontal and parietal areas on either side, the right flap extending across the midline, and a bilateral subtemporal decompression was made. Two small dural flaps were reflected towards the longitudinal sinus, while two others were made in the decompression areas. Two large veins were sealed immediately before they opened into the sinus, and the anterior half of the callosal body was brought into view without difficulty. The corpus callosum was then split by means of a blunt instrument, and the anterior horn as well as the body of the lateral ventricle exposed. Some traction was required to bring the foramen of Monro into view. This served as a landmark for the identification of the anterior pole of the thalamus which, in the monkey, is completely hidden under the large fornix. Several blunt punctures about 1 mm. in depth were then made in the region of the anterior nucleus. It was impossible, however, to expose the body and the tail of this nucleus which extend far backwards and, as the animal meanwhile had grown extremely restless, the operation was ended. It was then decided to expose the anterior nuclei more completely at a second stage and by a modified approach. There had been only slight bleeding from the thalamus and the other parts of the brain.

POST-OPERATIVE COURSE.

Although the animal had grown restless at the end of the operation it only recovered from the anaesthetic some time later. Two hours after the operation it reacted to strong stimuli with inco-ordinated movements. Four hours later the first spontaneous movements appeared, the right arm, however, being less used than the left. On the following day the animal was moving freely in its cage, using all four extremities, without apparent disability, but there was some general slowing up of movements and possibly some slight inco-ordination while climbing.

On the fourth day there was some transitory weakness in grasping, affecting both lower extremities. For the rest of the post-operative period, however, the animal revealed hardly any gross abnormalities.

Second Operation, July 13, 1939.

Owing to shrinkage of the dura following the first operation, the bone and the brain-surface had come into contact, but the adhesions which had developed between the bone and the leptomeninges were removed without inflicting severe damage to the brain. The dura itself, which was also found to be adherent, could be dissected away from the brain-surface by means of small pledgets of cotton-wool

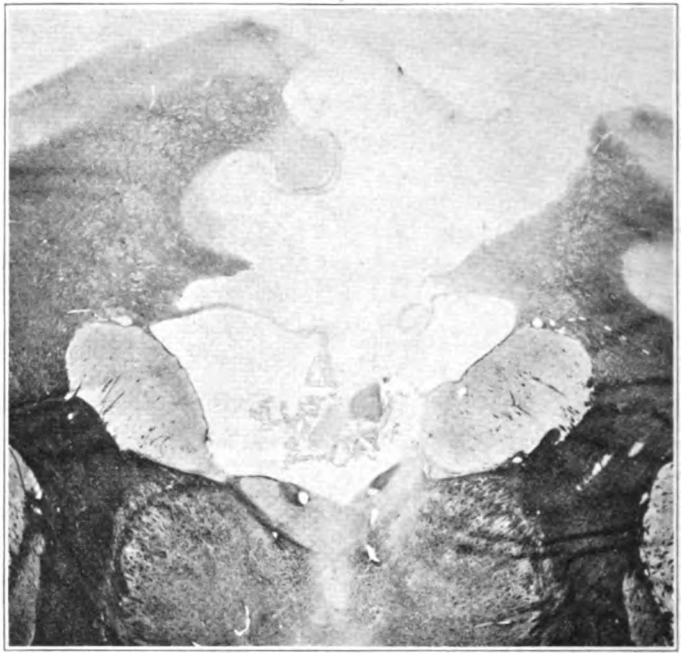

Fig. 1.—Coronal section through the brain of the rhesus monkey immediately behind the foramen of Monro, showing the extent of the experimentally-produced lesions involving the medial parts of the hemispheres, the corpus callosum, the left fornix and the right anterior nucleus of the thalamus; the latter is atrophic and demyelinated. Necrosis of the anterior cerebral artery is also present. (Weil's stain, 30μ, × 5.)

soaked in saline solution. A certain amount of damage, however, of the most superficial layers of the cortex, and the opening of some small blood-vessels, could not be avoided. The approach to the corpus callosum proved to be much more difficult than previously, as the adhesions were found to be firmer in the region of the falx than on the convexity of the brain. When the corpus callosum was finally brought into view the trans-callosal incision was easily identified. It was impossible, however, to make another incision above the roof of the third ventricle, as the falx cerebri, which was found to be in close contact with the callosal body, did not give way. It was decided, therefore, to resect a part of the falx. After occluding some surface-veins on the right side, which narrowed the field, the brain

was gently brushed away from the falx until on this side, too, the surface of the corpus callosum could be seen. At this stage of the operation the falx was resected between clamps. When the longitudinal sinus was coagulated in front and behind, brief convulsions occurred. After the middle third of the falx had been removed, it was found that the anterior cerebral artery, which had been in close contact with the anterior margin of the falx, but which could not be seen in the depth of the field, had been damaged by the coagulating current; a sudden pallor had spread over the surface of the brain situated immediately above the corpus callosum when the inferior longitudinal sinus, and presumably the artery, had been caught by the clamp. This pallor could be seen, if only for a moment, in spite of the venous congestion and the inevitable traumatic changes caused by the removal of the adhesions. The callosal body was now fully exposed, and an incision was made in the midline beginning at the level ot the foramen of Monro including the left fornix and extending backwards, but sparing the region immediately in front of the splenium as well as the splenium itself. The velum interpositum was split and brushed away to either side, thus exposing the right and left thalamus. The exposure of the right thalamus was more complete, and the impression was gained that the punctures which were subsequently made into the anterior nuclei were deeper and better placed than the lesions previously made on the left side. After small pieces of cotton-wool soaked in warm saline solution had been put into the depth of the field the wound was perfectly dry. The bone-flaps were loosely sutured in position as the danger of increased intracranial pressure due to oedema seemed imminent.

Post-operative Course.

The first voluntary movements of the animal appeared five hours after the operation. There was, on the first post-operative day, a very marked weakness of both lower extremities and the left upper extremity. The animal was able to walk a few steps and sit up, but was quite unable to feed itself. On the next morning, however, the monkey was found to sit high up on its perch and there could not, therefore, have been any considerable difficulty in climbing at that time. Feeding, however, was impossible, as the left upper extremity was still paretic and could only be used when mass-movements were performed, and the right hand proved to be practically useless because forced grasping had developed. It is noteworthy that forced grasping, at that time, was not severe enough to make climbing impossible. Later in the day the animal was found lying prone and frequently fell asleep, but it could easily be aroused. From the third post-operative day until a fortnight after the operation, the following, more or less constant features were observed:

(1) A gradual disappearance of the weakness of both lower extremities.

(2) Inability of the animal to feed itself because the left upper extremity was still paretic and the right hand, which was clinging to the bars of the cage most of the time, could not be used for any isolated movements.

(3) Very pronounced forced grasping, as already suggested by the previous point: when the grip of the right hand was forcibly released, and the hand touched with a stick, the latter was firmly grasped and the monkey would often hold it with a firm and steady grip for a long time. There was no forced grasping when objects were placed into the left hand of the animal, but its right hand would then immediately get hold of them.

(4) The animal would mostly sit on the floor of its cage with an empty and emotionless expression. When frightened, however, it would jump up on the wall of its cage and try to climb to the roof; while doing so, the lower extremities were brought up with great difficulty to the level of the upper extremities and even higher, there being long intervals between these movements, but the grip of the right hand could not be relaxed and the animal would, after some time, stop its vain efforts. It would maintain its posture for several minutes and appear quite motionless during this period. Gradually, however, the flexed posture of its

extremities relaxed, the latter becoming more and more stretched, until the animal touched the floor of its cage with its back while the grip of the hand and the feet would relax only some time later.

(5) When the animal started feeding itself with its right hand, the left upper extremity remaining paretic, it would move the food towards its mouth, but stopped in the middle of the movement for a considerable period of time. It became evident, on several of these occasions, that the animal's attention had been distracted, as revealed by a sudden change of expression on its face; a source for this distraction could not always be detected, except possibly for the movements of the other animals in adjacent cages, which, however, do not distract a normal monkey under similar circumstances. The animal would also seemingly forget to chew food just taken until it was repeatedly pressed into its mouth.

(6) The animal could not see the monkey in the cage next to it except through a hole in a partition. It was often found peeping through this hole in a rigid and motionless attitude even if its fellow, at which it had been looking, was no longer in view.

The forced grasping could be elicited, although to a less marked degree, until August 23. The animal was then killed, for the clinical examination revealed no further new symptoms, and those already described had been confirmed by repeated examinations.

At autopsy both frontal lobes appeared markedly reduced in size, large parts of their medial aspects being transformed into areas of softening. One of the serial sections showing the full extent of the lesion in the transverse diameter is demonstrated by the accompanying illustration.

The main features of the syndrome which are important from our point of view are the *grasping movements*, the *akinesia* and the *disturbances of attention*. The history of a patient who was observed by the author in a hospital in Vienna some time ago will accordingly be reported only in so far as it has a bearing on our present problem.

Previous to the clinical observation, G. St—, an official aged 57, had been manifestly ill for six weeks only. His general behaviour was first suggestive of a patient in the first stages of general paresis, as far as could be conjectured from the report of his wife, but this impression could not be confirmed by the subsequent examination. For some time he had been annoying the other members of his household by his lack of initiative. For instance, he would not get up in the morning even if he was repeatedly told to do so, or when finally his blankets had been removed and the windows widely opened. He then apparently would take no notice of the icy air that streamed into the room, for he would continue to lie motionless until forced to sit up. Later on he had to be dressed, otherwise he would sit about without moving for almost any length of time. When shaving he would suddenly stop, being unable to perform the necessary movements in one continuous succession. When walking in the street his attention would be caught abruptly by articles displayed in the shop windows for what his wife called an excessively long time, or by advertisements of any kind, which he would read loudly. He would also make loud, tactless remarks. When reading, or appearing to do so, he would hold the paper motionless for a surprisingly long time, failing to drop it even after the lights in his room had been turned out. However, he was able

to report the contents of the newspaper articles he had read quite correctly and to comment on them, sometimes in a rather clever way. He was also completely orientated as to time, space and his own personality.

The neurological examination revealed forced grasping on the right side; at times the grasp reflex could also be elicited on the left, and on touching the sole of his foot, or his toes on either side, feet and toes were slowly moved towards the hand of the examiner. The other neurological symptoms were (1) a right-sided hyposmia, (2) a left-sided incomplete hemiparesis with a positive Oppenheim phenomenon and vague sensory disturbances on the affected side, (3) a static and locomotor ataxia with a tendency to fall backwards. As various other symptoms suggested increased intracranial pressure, the diagnosis of a right-sided frontal lobe tumour was made. The patient died suddenly during a severe attack of raised intracranial pressure.

At autopsy a small round glioma was found projecting over the medial surface of the first frontal convolution on the right side, in front of the precentral lobule. Its position coincided to a large extent, therefore, with Brodmann's area 6. The tumour must have exercised a considerable amount of pressure upon the symmetrically situated part of the left hemisphere. There was a very marked oedema on the side of the tumour, as the swelling of the brain-substance extended into the region of the internal capsule and the basal ganglia.

Discussion.

The mental phenomena accompanying forced grasping have been dealt with by various observers and there appears to be considerable disagreement regarding their significance.

Schuster (1923, 1926) and Schuster and Pinéas (1926) express the belief that in their patients, who were mentally impaired, grasping movements were involuntary and were not under volitional control. Adie and Critchley (1927) claim that the grasping movements occur either unconsciously or against the patients' will, and that their patients were psychically normal at the time the movements occurred. In the first case reported by Adie and Critchley, persistent grasping movements were noted to occur in spite of the patient's effort to relax or to prevent them. In the second case the patient was unable to open his hand in spite of "obviously genuine" efforts. In the third case, which is particularly instructive, the patient stated that she was unable to relax her grasp upon objects once she had taken them into her left hand. "When I try to use a knife and fork, I cannot let the fork go when I want to. Sometimes when I get hold of the tablecloth I cannot let it go. Once I pulled the cloth right off the table that I had just laid."

Walshe and Robertson (1933), however, maintain that the grasping movements are volitional (1) because they are under the patient's control in that he

can prevent their occurrence, (2) in view of their delicacy of adjustment, necessitating the participation of the cortex in their production, and (3) on account of their occurrence in response not only to tactile, but also to visual stimuli. They must be looked upon as some kind of volitional movement, different from ordinary volitional movements only in so far as they occur in individuals whose psychomotor functions have been impaired by the disease of the brain. The concluding description by Walshe and Robertson deserves to be quoted in full, as it brings out the essential difference between the two concepts very sharply: "Anyone who has carefully observed the grasping movements of the hands we have described, who has seen the high degree of purpose and skill they display in achieving their object, their perseverance until this has been attained, their subordination under the patient's will—when he can be induced to exert this—and also the extremely specialized stimuli which are necessary to invoke them, receives the ineradicable impression that they are voluntary movements. There is an adaptability behind them that allows of no other interpretation, and their dwindling and disappearance with the waning of the patient's consciousness seems to confirm this impression."

Adie and Critchley, however, maintain, as stated above, that their patients experienced these movements as something imposed upon them and were quite unable to prevent them despite their normal mental state. This mental state, to be true, appeared grossly abnormal to Walshe and Robertson, as shown by their critical remarks concerning the conclusions of Adie and Critchley. However, in the first case of the last-named authors the range of the voluntary movements is stated to be complete, and the patient must have been able, therefore, to understand the orders which were given to him. In the second case no intellectual or temperamental changes were noted, and we would give the authors sufficient credit to rely upon their judgment. The third case, finally, gave the graphic account of her grasping movements which was reported above. None of the patients could have really been in a mental state which would have rendered the observations of the grasping movements unduly difficult, and their interpretation as to their voluntary or involuntary character doubtful. In our own patient the grasping movements were obviously of a reflex-like character.

Moreover, the quotation given above, summarizing the views of Walshe and Robertson, appears to be somewhat inconsistent in itself, for the very fact that the movements can be subordinated to the patient's will " provided he can exert this " proves that the grasping movements, at least in some instances, could not have been executed under the patient's control. It would be quite impossible to assume that the grasping did occur as a genuine effort of the patient's will, while the very same will-power, when stimulated to resist the grasping tendency, should suddenly have become inactive or inefficient. The high degree of adaptability of the grasping movements makes it no doubt

very probable that they are performed under cortical guidance ; this, however, would not necessarily involve their truly volitional character.

The essential aspects of the matter would seem to be covered, in our belief, by the following points, which refer to the psychical situation *preceding* the grasping movements :

(1) Any patient who is alert or co-operative enough to try to prevent the occurrence of grasping movements must make a distinct effort to suppress them, whether he succeeds or not being of secondary importance.

(2) Grasping movements, once performed, have occurred without the patient's intention, as contrasted with the unmistakably deliberate movements of everyday life which are merely links in one intentional chain—however inconspicuous the successive volitional acts may have become as a result of long training and experience.

Forced grasping, therefore, would seem to be the result of a disorganizing process which affects the relationship between the deliberately selecting and deciding individual and its subordinated hand. Although the hand is still capable of performing appropriately co-ordinated movements as a response to various stimuli (regardless of whether they are tactile or visual), it is reduced to some sort of independent instrument following its inherent type of action. Whether the patient is able to prevent the occurrence of forced grasping, by " reconnecting " himself to the hand which tends to get out of his control, depends solely on the intensity of the grasping-tendency in relation to the counteracting volitional power he is able to develop at a given moment. Grasping movements are not volitional even if the concept volitional is reduced to " least volitional " and " most automatic," as no volitional movements, however automatic they might have become in the course of time, could possibly occur without preceding intention. Furthermore no movement which requires, once it has started, a conscious effort to be stopped, instead of merely a natural impulse, can be regarded as intentional. Obviously it requires a true effort to stop the patellar reflex, but only an impulse to " suppress " a voluntary extension of the leg.

We have, so far, dealt with the *occurrence* of the forced grasping only. The *persistence* of the muscular contraction over a considerable period of time, however, requires a few additional remarks. This perseverance must be regarded as the outcome of two conflicting forces :

(1) The original stimulus which, while persisting, maintains the posture of the hand or, if increased, intensifies the grip, and—

(2) The intention of the patient to loosen the grip of his hand upon the object, provided he is alert or co-operative enough.

If a brief formulation of the grasping phenomena is attempted, it could perhaps be compressed into the following sentences : the performance of the flexor muscles of the patient's hand, as well as the central apparatus on which it depends, is liable to be provoked into action at any moment and on any

occasion, and the hand is in continuous danger of being trapped; the patient may be or may not be able to prevent this or to free the hand from its own grip.

A quite similar formulation would seem to apply equally well to the pathological state of attention observed in the monkey, and in the patient whose pathological behaviour was described in full at the beginning of this paper. Just as any object which happens to touch the hand is firmly grasped and held for an abnormally long period, the attention, too, may be trapped by any visual stimulus and remain focused upon it and, just as no selection is made among various objects and they are all treated alike by the grasping hand, no analysis is made of the objects of the outside world as to their relative importance.

In the more severe cases a combination of maintained grasping and attention may conceivably occur if a variety of objects has to be handled in a definite succession in order to perform a certain task or to achieve a certain aim; as a result of the prolonged action of his muscles, the individual will not only continue his hold upon the object longer than necessary, but will have great difficulty in releasing his attention from this object too. Since the focused attention severely restricts his field of vision, the patient can receive practically no impulses from the proper sources which may counteract and terminate the pathological state of mental fixation. Eventually this may happen after a long period when the maintenance of attention or the muscular action have exhausted themselves, just as most pathological reflexes eventually cease.

The common feature, therefore, which characterizes grasping and attention in our cases is the increased tendency of these functions to be brought into action as well as to persevere, and the question naturally arises how this identical type of disturbance can be best explained. There is obviously something fundamentally similar in the process of both normal grasping and normally concentrated attention. This may be regarded as an element of direction or orientation towards an object with the intention of establishing some sort of connection. However, it would be idle to indulge in any speculations as to a presumably common root of these functions, and we would rather confine ourselves to the statement that, under certain pathological conditions, something like a "forced grasping of attention" occurs. At the "lower level" of grasping the element of direction may be represented by the association of grasping with groping movements, and even the rotation of the whole body towards the object which is grasped. This phenomenon has been repeatedly described in the literature as a "magnetic reaction." At the "higher level" this common element is represented by the inherent factor of direction to be found in attention itself.

It is necessary, at this juncture, to define (1) the disturbances described with regard to the normal state, and (2) similar pathological disturbances, in order to circumscribe them more sharply.

(1) In *normal states* volitional impulses necessary for the performance of certain actions are produced in a sequence which is adapted to the achievement of the predominant aim prevailing at the moment, and the performance of these actions is practically never hampered by an undue amount of attention being allotted to one or more of them.

(2) In states of *true akinesia* no volitional impulses are formed or they are greatly reduced.

(3) In states of what may be called *secondary akinesia*, volitional impulses are formed, but they are soon immobilized as the central control is weakened. In normal circumstances the central control governs the allotment of attention in accordance with the requirements of the main or central aim, and prevents more than a very limited amount of attention from being paid to inessential objects. Thus, attention may be caught and fixed by anything and maintained, for the field of attention, and consequently of action, is limited—like the grip of the hand on the object.

It is not suggested, however, that pure types of akinesia are more frequent than mixed forms. In the latter one or other element may prevail.

In our patient there was a very obtrusive element of fixed attention, however the formation of impulses might have been at times, for he would be attracted—and remain attracted unduly long and sometimes even too intensively—by anything that happened to enter his field of vision. He would, for instance, read loudly anything written he might happen to see or comment loudly on anything he might happen to observe. Signs of distraction or unduly fixed attention, leading to secondary akinesia, were also readily recognizable in the monkey operated upon and were particularly impressive, since they occurred even when the animal was feeding itself.*

In the syndrome observed, therefore, two main components can be isolated :

(1) A disturbance in the formation and utilization of volitional impulses, the difficulties in utilization being produced by a high degree of distractability, and—

(2) The grasping movements of the hand.

It would be tempting, at this point, to localize a basic function, recognizable in both the similarly disturbed mechanisms of grasping and attention. Before an attempt can be made to consider this possibility, however, it is necessary to review the evidence laid down in the literature, as the number of our own observations is too small.

Watts (1934) did not observe any neurological symptoms after the experimental occlusion of the main trunk of the anterior cerebral artery in monkeys and, at autopsy, the brains appeared normal. Subtotal interruption of the callosal fibres, made by Meagher (1933) and performed incidentally, like our own operations, in order to work out an approach to deep-lying parts of the brain, and subsequent complete transection of the corpus callosum in a series

* Fulton saw forced grasping in some of his experimental animals disappear at feeding-time.

of monkeys and dogs which had been partly trained, likewise failed to produce any demonstrable difference in their motor behaviour.

Kennard and Watts (1934), after ligation of the anterior cerebral artery in monkeys, followed by the transection of the callosal body, observed no paresis or forced grasping, but there appeared a deliberateness and a lack of initiative of movements. It seems, however, from the description of the authors, that these symptoms were only slight. When, in addition to the ligation of the anterior cerebral artery and the transection of the corpus callosum, the left premotor area (area 6) was extirpated three weeks later, the course was unaffected, save for a transitory hemiparesis on the right side. Transections of the corpus callosum following left-sided extirpation of the motor and premotor areas did not aggravate the symptoms produced by the cortical lesions, which consisted of transitory forced grasping opposite the extirpation and a constant disinclination to use the right hand for finer movements.

When area 6 alone is extirpated in the monkey on the medial as well as the lateral surface of the brain down to the level of the corpus callosum, forced grasping occurs, while the motor activities of the animal remain otherwise undisturbed. Removal of one premotor area produces forced grasping transitorily in the opposite hand, but bilateral removal brings it out permanently (Richter and Hines, 1932).

Fulton, Jacobsen and Kennard (1932) observed, after bilateral removal of the frontal and premotor areas, a retardation in the initiation of movements, e.g. grasping for food, and the mental state of the monkeys appeared to be one of rather marked torpor. If, however, only the frontal areas were extirpated, the premotor areas being left intact, a greatly increased spontaneous motor activity was noted.

It seems fairly certain, with regard to these reports, that the coagulation in the anterior cerebral artery and the interruption of the callosal fibres in our experimental animal have contributed no essential features to the syndrome observed, although it might have aggravated some aspects. The author, too, has reported (1940) a certain slowness of movements in a rhesus monkey after partial interruption of the callosal fibres, which was also observed, after the first operation, in the animal described in the present communication. It appears after the interruption of the anterior as well as of the posterior half of the corpus callosum, but it is very slight and only transitory. It may be that this slowness lasts longer when the corpus callosum is completely interrupted, although in view of the negative findings of Meagher, this would not seem to occur regularly.

It may further be regarded as certain that the appearance of forced grasping in the monkey was caused by the severe bilateral involvement of area 6, although the lesion extended well beyond these territories. That the involvement of area 6 in man produces forced grasping can no longer be doubted in spite of the view still held by some authors that this phenomenon is due to

lesions of the brain-stem, for it has never been noted to occur without involvement of the frontal lobe, while coincident lesions in the deeper parts of the brain have been present in a small number of cases only (Adie and Critchley). In our patient the glioma was situated in area 6 and also involved, by pressure, the corresponding territory on the opposite side. The extent of the oedema produced by the tumour makes the case still more readily comparable to the extensive traumatic changes in the brain of the monkey. The lesion of the anterior nuclei could hardly have contributed to the syndrome described, for the reasons which have just been given, but it has probably contributed to the involvement of the cingular gyri, which, according to Le Gros Clark and Boggon (1932), are connected with these nuclei.*

A review of my own cases in the light of the experience of previous workers reveals, therefore, that lesions involving the anterior cerebral artery, the entire corpus callosum and the anterior nuclei of the thalamus, are not necessary for the development of forced grasping and akinesia, but that these disturbances appear after the destruction of the pre-motor and frontal area.

It appears to be of particular importance that lesions confined to the frontal areas give rise to greatly increased spontaneous motor activity, while destruction of both the frontal and pre-motor areas not only adds the feature of forced grasping, but completely *reverses* the symptomatology of the frontal lobe. It may be concluded, therefore, that with regard to spontaneous activity the pre-motor area is the functionally predominant territory, and responsible, as such, for the production of the syndrome described in our two cases.

The psychological analysis and the anatomical evidence can be related to each other from different angles ; while it is not surprising that a lesion situated just between the frontal and motor area should influence both motor and mental processes, it appears to be rather striking that disturbances of these functions (and, indeed, the functions themselves) should also bear a common mark, in spite of the different levels they represent.

The observations described in this paper would seem to be covered by the concept of Goldstein (1936), who stresses the importance of a specific directional element in every function of the frontal lobe regardless of whether the function is somatic or psychic. It would appear, however, that directional elements are also present in the performances of other areas of the cortex and even in the brain-stem, while in our patient and in the experimental animal no frontal symptoms, apart from forced grasping and the disturbance of attention, were detected which could possibly be explained by a disturbance of a basic directional function.

According to Held (quoted from Kleist, 1933) the midbrain contains structural elements for the integration of grasping, looking and listening in a

* It may also be mentioned that the insertion of foreign bodies into the anterior nuclei of rabbits performed by the author (bilaterally in one and unilaterally in five animals) produced no signs of akinesia within two months.

certain direction. This would still further substantiate, within the framework of Jackson's doctrine, the view put forward in this paper that there is a close interrelationship between attention and grasping.

Summary and Conclusions.

(1) Grasping movements, as a pathological phenomenon, are executed by the same neuromuscular apparatus which, under normal circumstances, works under volitional control; they occur, however, without the patient's intention and must, therefore, be regarded as reflex-like actions even though they may be highly co-ordinated.

(2) Attention, normally under volitional control and guidance, may be diverted and kept in a state of "forced distraction" with the production of akinesia by the same brain lesion which produces forced grasping.

(3) The determining factor of this syndrome which was found in the monkey and in man alike, and which occurs in association with states of primary akinesia, is the destruction of the pre-motor area (area 6), although at least a partial involvement of the remaining part of the frontal lobe is also necessary for the production of the syndrome.

(4) It would seem that a lesion situated in area 6, as the intermediary zone between the motor area and the frontal lobe proper, not only produces motor and mental symptoms, but also establishes a common type of disturbance which is readily recognizable and has been analysed in this paper.

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MORBID ATTENTION—A FACTOR IN NERVOUS DISORDER.

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IT is not surprising that the treatment of mental disorder should have brought in its train a clearer insight into the ordinary course of events in the human mind. In this as in every other department of medical experience the hidden processes of nature are revealed to advantage when they become manifest in some abnormal form. One has only to think of the importance of the part played by the recognition of heart-block and of muscular paralysis in elucidating the meaning of the successive phases of the cardiac cycle. In a wider field a greater claim can be made for clinical pathology in its contributions to knowledge of the structure and function of the nervous system. In the work of Hughlings Jackson (1) alone may be recognized the foundations of a new era not only of neurological medicine and surgery, but also in the more scientific spheres of anatomy and physiology. The subtle complexities that underlie the apparently even tenor of nature's average path may first come to light when disturbed by disease.

The application of this generalization to mental experiences as such must be made with certain special considerations in view. While psychological medicine deals with a field peculiarly its own, it should be recognized that in the long run there is no hard and fast boundary between the realm of mind and the scenes of biological activity through which it finds expression. The brain is, of course, the main centre of these vital processes to which we look for an explanation of such mental phenomena as come within the range of scientific observation. It is there for example that the functions of the organs of special sense become articulate in the behaviour through which they contribute to the life of the organism as a whole. The progressive integration of the stimuli of touch and light and sound through advancing stages of evolution bring the organism into relation with an ever-widening and more varied environment. Various theories have been invented to account for the way in which psychic phenomena are associated with the vital processes with which they appear in a general manner to be co-ordinate.

According to one theory the apparent co-ordination is merely incidental; the correspondence is described as "parallelism" inasmuch as the mental

and neural events are regarded as following independent courses. The theory of "interactionism" presumes conditions in which "mind and matter" exercise a mutual influence on each other. "Animism" sees, in the relations, the determining control of unseen agencies, in the varieties of behaviour, a response to the demands of spiritual forces which find expression in a totality of mental experience and organic reactions.

In sharp contrast with these more or less speculative theories there is "materialism," the conventional hypothesis of modern science, a framework of thought which has been constructed by measured observation and experiment. This is an elaborate fabric woven from the concepts of physics, chemistry and biology, and used as a standard of reference in the interpretation of the physiological and pathological activities of living matter. In the hands of the great majority of those who apply it, it is merely a convenience or an instrument for practical purposes. Its origin and character and ultimate significance are rarely subjects for critical inquiry. The utility of the materialistic framework is its main justification.

There have been those however who, like the great physiologist, J. S. Haldane, while admitting and demonstrating on a large scale its usefulness, have called in question the validity of the doctrine. Haldane, in his works, emphasizes, again and again, that however indispensable physics and chemistry may be in biological investigation, the secrets of life as manifested in the internal milieu of the organism can be explained in the long run only in terms of the peculiarities of life itself.

When we come to regard the data of mind in the light of materialistic teaching the difficulty is still greater. Materialism assumes that mental phenomena, cognitions, emotions and will power are the *product* of nervous activities and so ultimately depend on physical and chemical factors. If the hypothesis is to be accepted in the sense in which it obtains in these departments of natural science, then it also implies that invisible and intangible thoughts and fears and aspirations are subject to a reversible process in which once more they become subject to the laws of time and space in the light of which physical and chemical processes are interpreted. This metaphysical speculation to which materialism naturally gives rise would itself have no practical importance, were it not that there is a general tendency for physiological and pathological study of the brain to be pursued on the assumption that perversions of the mind can in the long run be explained in terms of neural structure and function, and their underlying chemical and physical conditions.

It would, of course, be misleading to overlook or even to minimize the invaluable contributions which have been made to an understanding of the mind and its relation to the brain in the light of biological theory. The faculties of the human mind have evolved *pari passu* with the evolution of the nervous system. On no other hypothesis is it possible to form an intelligent conception of the manner in which the living organism is adapted, according to species,

to its environment through the mediation of its special senses ; and when we think of the distinguishing peculiarities of the human mind itself, its rational and creative intelligence based on biological and social inheritance, ever in process of constructing, demolishing and reconstructing a world of its own, we can picture this feature of the course of nature in an intelligible fashion only when it is seen as part of the struggle for existence. This somewhat vague generalization does not however lend itself to analysis and proof by the inductive methods of science. The limitations of the intellect are such as to render impossible any more than partial explanations of certain aspects of the great condominium of mind and life which is the scene of human activity. The procedure of investigation thus resolves itself into the choice of a particular field, and the examination of that field in the light of the knowledge, experience and technique suited to its cultivation.

Where there is such diversity of disorder as may occur in the mind it is obviously difficult to choose the line of inquiry most likely to lead to diagnosis. This is more particularly the case in the early stages of disease when the question usually arises whether it is " functional or organic." There is, of course, in the long run no justification for any such mutually exclusive distinction. Every disturbance of " function " must be related in some way or other to disorder of " organic " process ; and whether such disorder of organic process can be recognized as grossly structural, histological or chemical (toxic) is merely a matter of refinement of observation. On the other hand considerable organic defect or disease may occur without any recognizable disorder of function. Cerebral tumours, arterial brain disease, or the chronic degeneration of latent syphilis (general paralysis) may be in course of development over varying periods before they give rise to signs of organic disease.

The clinical convention of distinguishing between functional and organic nervous disease is thus a practical device in conformity with the methods of scientific analysis. In one sense it may be justified by the doctrine of Cartesian dualism, by the hypothesis that our framework of thought has reference to two distinct worlds which are fundamentally different in their attributes ; on the one hand to a material world, animate and inanimate, but in either case subject to the " laws of nature " as these are recognized in natural science ; and, on the other, to a non-material world, to a realm of experience whose content is invisible and intangible, and so without the criterion of the standards of time and space which apply to the physical order.

The validity of this dualism is a metaphysical problem with which we are not here concerned. But even if it be questionable on logical grounds, that is no reason, in itself, why in certain circumstances it should not be applied for practical purposes. There is no other standpoint from which it is possible to get a rational view of such mental derangement, for example, as paranoia or systematized delusional insanity. It becomes manifest in morbid emotions, strange notions and aberrant behaviour ; it begins insidiously and progresses

gradually till its victim becomes estranged from the ordinary world of social intercourse.

As the disease is insidious in its onset, the significance of its initial signs is recognized only at a later date. Abnormal sensitiveness or shyness, a defect in "social instinct," does not of itself betoken disease, in the conventional sense, but when once the course of events has reached a stage at which there is more or less isolation from social relations, it is seen to have been an important feature of the groundwork on which the whole morbid power has become articulate. The progressive development of isolation or aberration in the paranoiac takes place, in so far as it can be revealed by observation, in the invisible and intangible realm of mind, and the concepts of biology provide no clue to an explanation of its origin and character. The mental outlook which dominates the ideas and behaviour of the paranoiac is not in itself lacking in logical structure. The fears and suspicions, delusions and hallucinations and the aberrations of conduct are all comprised in a self-consistent "little whole" in which the paranoiac may gyrate quite regardless of the wider ambit of understanding sentiment and social activity in which, if his mind were normal, he would be playing a part.

A striking feature of this morbidly restricted and self-contained mental state operating in comparative isolation from its human environment is that it is not accompanied by evidence of disease of the brain or of any other part of the body in a pathological sense. Delusional and hallucinatory states may of course be associated with poisoning or with structural abnormalities of the brain, but the paranoiac shows no signs of somatic disorder which can be correlated with his mental peculiarities. The average span of life may be run and decay occurs without evidence of change other than that which attends advancing years.

Differing essentially from the permanent disorientation of the paranoiac, though possessing some features in common, is the peculiar form of mental instability known as "double personality." This strange disorder may, like paranoia, occur without any manifestation of organic disease. The abnormality presents itself as essentially mental. But here the patient as a rule passes abruptly into a new phase of existence sharply demarcated in thought and behaviour from the immediately preceding experience. The suddenness of transition resembles what takes place in an epileptic fit. It is in fact a state to which some epileptics are prone. In it however there are no convulsions, and the loss of previous "consciousness" is replaced by a new kind of consciousness involving an aberrant type of behaviour. Similar aberrations have been described also in general paralysis of the insane.

It is however with cases in which, as in paranoia, there is no evidence of reaction which can be attributed to toxic or "organic" factors that it is proposed to deal. Such cases may be regarded as suffering from a temporary loss of memory and it may be convenient to describe them from this point of view. A superficial review of the history points to interruption of the natural

flow of conscious experience by the intervention of a new kind of consciousness which finds expression in a corresponding novelty of behaviour. Some of the characteristic features of these dramatic disorders were seen in the following cases.

Case 1.

S. M—, now aged 62, was a non-commissioned officer in a Territorial regiment in Palestine during the last war. Up till the time of the war he had enjoyed good health. He was not wounded, but had an attack of malaria, and in the second battle of Gaza was said to have been "shell-shocked." On returning to England he was still suffering from shell-shock and was sent to a hospital for psycho-therapeutic treatment. On discharge from the hospital he had not quite recovered but was considered to be sufficiently well to undergo training as a ship's cook. He went through the training with apparent success, but on its termination he got "lost" and was missing for several days. On "coming to himself" he was in a state of extreme nervous excitement, and after being brought home from Liverpool to Glasgow was placed in hospital. This was in March, 1920. Since then he has been totally incapacitated for work by reason of mental instability. During this period of twenty years he has had comparatively good health so far as his nutritional state is concerned. He eats well, but his sleep is restless and disturbed. He has had occasional attacks of excitement rendering hospital treatment necessary. There has however been no abnormal decline in his physical condition. He is well preserved for his years and there is no evidence of organic disease.

The outstanding feature of the disorder shows itself in a general nervous instability, and this again finds expression in signs which are both somatic and psychic. In what might be called his average state he is nervous and tremulous, his equilibration is faulty and his gaze wanders in various directions and he has at times a "far away" expression. When he talks he is usually somewhat exalted; his memory for certain events is excellent, and he can retail with accuracy accounts of such experiences as he can recollect. His character is excellent. He leads an exemplary life, is kind and considerate to his family and is careful to avoid experiences which he has found to conduce to excitement. He does not go to football matches or to the cinema.

The dramatic features in his case are phases of what may be termed a "second personality" which occur in certain circumstances. No merely verbal description of these "turns" could convey an adequate impression of the effect they produce on the onlooker. We see him in a somewhat animated nervous state, not unhappy, retailing an account of the entrance of his regiment to the valley at the second battle of Gaza. He tells his story in an ordinary way, describing the scene with the Turks on the hill-tops on either side. Proceeding with his tale as he recollects the incidents his *attention becomes concentrated on an aeroplane*, and simultaneously his whole demeanour and behaviour

change. The story stops abruptly, the tremors cease, his expression becomes fixed and serious, he shouts "Down, boys!" and flops on his face on the ground. He then rises partially, and posing on one knee makes movements indicating the seizure of his rifle, which he loads and he then takes aim and shoots. He then stands up, walks forward a few paces and looking to the side sees a wounded comrade lying on the ground. Approaching him he pulls round his water-bottle and raising the wounded man's head gives him a drink. During all this time he remains perfectly steady. The tremulous agitation and spurious gaiety which characterized his "normal" or average state have now completely gone, and he presents an appearance of calmness and seriousness consistent with the part he is now playing as an actor in the old scene. He is quite oblivious to his immediate surroundings. He appears to see what he is doing, but the immediate objects of his surroundings while presumably pictured on his "visual fields" form no part of the stream of current consciousness. He actually is, for the time being, where he was over twenty years previously, in the valley of Gaza. His behaviour as expressed in his reactions to an imaginary environment gives the impression of being intelligent and it is not in itself coloured by emotional disorder. On the contrary, it appears, compared with that of his average state, to be remarkably free from excitability. He appears to proceed from one act of the drama to another with calm and deliberation.

It is not difficult to awaken him from this sleep-acting performance, from a course of behaviour which might be dictated by a dream. Though he pays no attention to words spoken quietly, he can be wakened by a sharp remark and by shaking his body in the way in which one would try to arouse a person from sleep. On emerging he immediately begins to shake, looks round and appears to be somewhat frightened and rubs his head, complaining that it is sore. He is once more in his "normal" average state, and has not the slightest recollection of what has happened.

Apart from the absence of tremor and replacement of shaky "cheerfulness" by a more serious and placid demeanour, there is nothing in the "second" state so far as his physical condition is concerned to distinguish it from the average state. There is a notable absence of the reactions of fear; as a matter of fact his normal condition is more suggestive of morbid excitability, and when he comes out of the "amnesic period" he immediately shows signs of great agitation.

What, then, is the point of view from which it is possible to interpret in a rational fashion this curious interlude in the course of conscious experience? There is no suggestion of association with organic nervous disease, so that the data in the problem are exclusively psychic in character. That it had its origin in war impressions is obvious; but the comparative rarity of such states among the multitudes exposed to the same or similar conditions indicates that the essential factor was in the constitution of the patient. The only trace of abnormality in this context lies in the fact that he is the father of an imbecile.

and it is difficult to appraise the significance of this incident, more especially as the mother of the child suffers from myxoedema. There has been nothing in his character or behaviour to indicate the presence of the so-called " psychopathic personality." A good husband and father he neither drinks nor smokes, he takes a keen and practical interest in his family and domestic affairs, talks intelligently and politely, and conducts himself like a self-respecting citizen. But, as has been pointed out, there is no mistaking his " nervousness " in his ordinary conscious state, a nervousness which suddenly disappears when he enters a phase of " second consciousness " such as has been described.

The aetiology of a condition of this kind raises questions of a metaphysical character which are beyond the scope of clinical inquiry. The clinical problem may, however, be stated in a way which avoids these more speculative issues by selecting for discussion features of the disorder which are easily recognized.

In the first place the dissolution of continuity represents an interruption of *memory*. There is a complete break with the immediate past, and again at the end of the morbid scene there is an abrupt return to the current of normal consciousness, with no recollection of what has occurred in the interval. The morbid state has all the appearance of conscious behaviour, except that the reactions occur without any regard to immediate surroundings. This would appear at first sight to imply the alternation of two distinct states of consciousness. That the states are distinct and independent there can be no doubt. If consciousness means, as the term suggests, " the knowing of things together," it is clear that the things " known together " in one phase are quite different from those " known together " in the other phases. This interpretation is not prejudiced by the fact that the consciousness or " knowing together " of the " second " state is itself fictitious in relation to the time and place and circumstances in which it finds expression in behaviour. The behaviour as such comprises rational and purposive movements co-ordinate with the perceptions and feelings which animate and colour the contracted and isolated circuit of his mind for the time being. That he has been translated into an island of the past and so completely isolated from current environment implies rather a loss of self-consciousness by the transference of *attention* to a limited field in which it becomes completely absorbed, and in which behaviour has become automatic. It may be assumed that at this remote date the impressions then received were such as to produce shock with dissolution of continuity, and that as a result of instability of his nervous system proper redintegration never took place. On the recurrence of impressions which by suggestion or associations tended to revive the old scenes he immediately loses contact with his environment, to find himself in the forgotten past displaying the activities relevant to that period alone.

In the second place let us consider the part played by *attention* in the process of events. He is seen in his average mood and mode of behaviour, nervous and

anxious, interested in an ordinary way in what is going on and comporting himself in what for him is a normal manner. Led in conversation to the scene of his Palestine exploits we leave him there *without any further suggestion* about his experiences. He proceeds like an ordinary person to recount what happened. It is a simple historical review of the incidents which occurred in so far as they recur within the range of his memory. The tale is told in a more or less disinterested fashion without any apparent increase of excitement. It is merely an account in retrospect, an abstract summary of what he thinks took place. It may be taken for granted that his visual memory is at work, and that it is culling from the details a sufficiency of data to make a rational story. This is just what happens in ordinary normal life. He is proceeding with his story without any apparent intensification of interest when suddenly *his attention is concentrated on a particular object.* On one occasion he hears an aeroplane overhead, looks up and sees it, and shouting " Down, boys ! " throws himself on the ground ; on another he sees " Johnny " on the hill-top at the side of the valley, loads his rifle and fires ; while on yet another he may see a comrade lying in front and take appropriate steps to help. This sudden change of attention is accompanied, as has been pointed out, by a complete alteration, equally sudden, in his emotional state. The expression of suppressed fear has been replaced by a calm, and he behaves in a manner consistent with a rational response to the illusions which make for him the scene.

To say that he is in a trance or that he has hypnotized himself is merely to classify the incident without throwing any new light on its more intimate character, or on the conditions of its occurrence. Nor does it contribute much to its elucidation to recognize in his aberrant behaviour the eruption of suppressed memories. It is highly probable that during his initial psychological treatment successful attempts were made to revive and co-ordinate the experiences through which he had passed, and that the treatment had an effect which enabled him to establish himself for the period of apparently good health which he enjoyed while undergoing his training as a ship's cook. The question then arises as to an explanation of the recrudescence of nervous disorder. It is, of course, feasible to suggest that the memories had again been suppressed, but this does not dispose of the fact that their revival, when it did occur, was accompanied, not by a restoration to health, but by complete dissociation in which the " memories " were no longer memories to him, but the concrete environment in which he was displaying his reactions.

When it is suggested that " attention " plays a decisive part in the dissociation it is well to indicate the sense in which that term is used. Attention is not merely a psychic process confined to the invisible and intangible realm of spirit. It is essentially related to the motor activities of the organism. It is only as a muscular *process*, in posture or active movement, that it becomes attention at all. It is an aspect of behaviour firmly rooted in nervous organization, for the behaviour of any animal species may be described in terms of the

manner in which it attends to, that is, tends towards or away from its environment. Viewed in this light attention is seen to be *automatic or involuntary* on the one hand, and *deliberate or voluntary* on the other. The fundamental framework of attention in the animal world is involuntary. This is seen in the automatic or spontaneous or forced movements of animal activity usually referred to as instincts. Somatic habits appropriate to the species are engrained in the constitution and preserved by heredity. On the basis of these there arise in the human subject, related no doubt to cerebral development, a new realm of attention concerned with the field of rational intelligence and creative purpose. Here memory which was originally " tissue memory " (Hering) and involved in heredity acquires a new significance. It becomes conscious or self-conscious memory, a picture in mind of the past and of a possible programme for the future. Here attention is active in a voluntary role, though of course still subordinate to feeling, emotion or sentiment. This new realm of invisible and intangible experience which we call the " mind," while it is cultivated by vision, hearing, touch, taste and smell, exists for the individual mainly as a picture or standard of reference in his imagination. But to be reliable it must conform in principle with the standard or picture of the world which he shares with his fellow men. There must be at any rate a degree of consent in the meaning and implications of what is seen and heard by those who live in the same social medium, and not only that but the behaviour, the attitudes, movements and talk of those who share this common world must tend to the solidarity of that community of which each individual forms a part. The human struggle is a process of attempting to find adaptation in this common task. No expression of the mind in word or in deed is effective except in so far as it forms an integral part of reciprocal relations with environment. Talk has no real meaning in the absence of a listener, and behaviour which takes no account of surroundings is futile. The movements of attention are one of the best tests of mental ability and stability. The capacity to concentrate attention or to move it deliberately from one object to another in accordance with the requirements of the situation is a reliable criterion of mental capacity.

Bearing these considerations in mind it is not difficult to realize how attention may become morbid. Put in its simplest form it may be said to do so, by becoming (1) concentrated in excess or (2) diffuse and incapable of concentration.

(1) *Morbid concentration.*—There is abundant evidence in clinical observation of morbid concentration of attention. The mind of the paranoiac is an outstanding example of mental isolation in which understanding, emotion and will power become more and more confined within the orbit of a self-constituted little world of which the victim is the sole inhabitant. He interprets his environment in a light which reveals his neighbours in a false setting, though to him there is a rational explanation of his illusions, delusions and insane behaviour.

Distinct from this state of more or less complete alienation, though presenting with it some features in common, are those forms of neurosis in which there is

morbid preoccupation with self in so far as functions of bodily organs are concerned. Here, again, attention is directed towards and concentrated on feelings and sensations which, aggravated by fear, tend to interruption of normal contact and relations with the outside world, and to the creation of a state of persistent invalidity, not altogether isolated, for it depends for its preservation on the sympathy and attention of others as well. It is none the less on that account an example of morbid concentration of attention. It differs from the private adventure of the paranoiac in that it enlists where possible the co-operation of the social or domestic circle to which it makes an appeal.

Another and perhaps more dramatic form of excessive concentration of attention is that which finds expression in hypnotic or mesmeric states. The interest evoked by these strange phenomena in the middle and later decades of the last century was inspired largely by a curiosity about the unseen agencies of the supernatural world. It was the period of origin and growth of a variety of cults, each devising a nomenclature to signify its own peculiar beliefs regarding the nature and influence of these agencies. Some of them have survived in the form of corporate societies or institutions to meet the requirements of persons temperamentally adapted to what in some respects may be regarded as a special reaction to the materialistic and scientific doctrines which dominate modern thought. It must not be supposed however that these manifestations of special interest in supernatural matters are in themselves indications of mental aberration. Though they do not conform with average manifestations of spiritual tendency in Western peoples, they are quite different in kind from the pathological experience of the paranoiac or of the neurotic to which reference has been made. In no sense do they form part of the province with which Hippocratic medicine is concerned.

At the same time it would be misleading to overlook the part played by auto-suggestion and concentrated attention in the initiation of each individual into a new mystery. This is essentially a private adventure, no matter the extent to which it may depend on his own temperamental proclivity or on the emotional incitement of the group or crowd in which he may find himself. He at any rate accepts, and " lets himself go " in the new world which has been revealed to him through a fresh light. He makes his contribution to the building up and maintenance of this new world and shares with his fellows the inspiration and hopes which it provides. He is not isolated like the paranoic nor dependent on the support of sympathy like the neurotic. He has a freedom of his own which he enjoys in the practice of the creed he has adopted.

(2) *Defective attention.*—Attention in the lower forms of animal life is, as has been pointed out, involuntary or automatic. It is seen in the instinctive movements which characterize the behaviour of any species in the search for food or safety or for mates in the breeding season. There is a regularity and consistency in the way in which any particular animal attends to its surroundings. When evolution reached the human plane, and rational intelligence with creative

endeavour became factors in the struggle, attention took on a new and more complicated form. Not that it dispensed with the automatisms which it inherited, but on the basis of this heritage there appeared a new instrument in the form of voluntary attention which implied speculation and foresight, deliberate choice and striving. Even in the primitive stages of human existence and in the cruder forms of modern society, attention operates on a level where it is subject to a strain to which the denizens of the lower world are not subjected. When the plane of civilization has been reached, and education over years is necessary in order to survive in the battle of life, an entirely new set of conditions make fresh demands on voluntary attention. To meet these, reading, writing and counting are only an elementary preparation. Even in its higher stages the school education falls short of providing a solution to the problems that must inevitably arise. Apart altogether from the fundamental questions of food and shelter, there are others pertaining to religion and various social sentiments which will in due course demand an answer. The customs and inventions of a highly organized and self-respecting community impose a strain on voluntary attention, on discriminate thought, emotion and decision which only those who are well equipped in a constitutional as well as in an educational sense can bear.

The failures of voluntary attention may be noted under a variety of conditions. In children it may fail through congenital malformation of the brain or through the incidence of brain disease in early years. This involves the incapacity to acquire even the rudiments of education. Every school teacher who deals with children of this class recognizes that the difficulty is one of attention; it wanders from one thing to another, and even if it be secured it cannot be held along a directed path.

But this tendency to dispersion is not confined to the mentally defective. In conditions of nervous instability of all kinds, in neurasthenias, in states of morbid excitement and depression in various forms of organic brain degeneration and in toxic affections of the brain the mental phenomena may be described in terms of incapacity for ordinary attention.

This generalization may at first sight appear to be too broad to be of any value. It is suggested here, however, to emphasize the contrast between the two ways in which the process of attention may find pathological expression, between the excessive fixation on the one hand, and the purposeless diffusion on the other. It is in recognizing these aberrations of attention that it is possible to get a clear idea of the normal mode of activity. It is to be regarded as a process, animated by normal interest in surroundings, tending to voluntary movements in relation to such interest and preserving in the path of behaviour the solidarity of personality.

Viewed in the light of these considerations how are we to interpret the case which has been described? He is introduced in his average "tremulous and nervous" state, fairly well collected and capable of behaving and conversing

in an average way. His attention appears to be quite normal and there is no evidence of defective memory. In the course of an ordinary account of the events of the second battle of Gaza he describes what he recollects, devoting his attention to this purpose and meantime showing no change in his emotional reactions. Suddenly the events cease to be those of pictorial memory and become real. The situation is for him here and now. The emotional reactions change in accord with the new situation; the shaking state has gone and he steadies up, and acts with what would appear to be resolution and purpose. The story is no longer being told; he is now automatically part of its action. He may be said to be exhibiting a "second personality" but completely divorced from his surroundings. The attention which had previously directed his speech and behaviour has now all been canalized into an "imaginary" field, none the less real to him, though obviously quite false. And yet it must be assumed that a neural basis for the transformation lies in his nervous system: for his emotional reactions and behaviour correspond in detail with the world which he has rediscovered. The trail of ideas which seemed to mark the process of his thought continued, but at a critical point they became invested with the actual presence of the situation he was trying to describe, with the result that he lost contact with the immediate time and place of his existence.

While voluntary attention provides a convenient framework for analysing the course of his behaviour, it is well to examine further the underlying biological conditions of attention itself. Attention, it has been pointed out, is essentially motor. It involves activities or combinations of reflexes directed to special ends. In his classical work on the *Integrative Action of the Nervous System* Sherrington (3) refers to the succession, combination, interaction and mutual exclusion of reflexes which gain control of the motor mechanism (final common path) for specific purposes. "In the case of simple antagonistic muscles," he says, "and in the instances of simple spinal reflexes, the shifts of conductive pattern due to interaction at the mouths of final common paths are of but small extent. The co-ordination covers, for instance, one limb or a pair of limbs. But the same principle extended to the great arcs arising in the projicient receptor fibres in the head, e.g. the eye, which deal with wide tracts of musculature as a whole, operate with more multiplex shift and wider ambit. Releasing forces acting on the brain from moment to moment shut out from activity whole regions of the nervous system, as they conversely call vast other regions into play. *The resultant singleness of action from moment to moment is a keystone in the construction of the individual whose unity it is the specific office of the nervous system to perfect.* The interferences of unlike reflexes and the alliance of like reflexes on their action upon their common paths seem to lie at the very root of the great psychical process of 'attention'."

It is impossible to exaggerate the importance of the principle implied in these words setting forth the biological basis of attention. Referring to the observations which led to the conclusions, the great physiologist emphasizes the

difficulty which arises from " the high variability of reactions from experiment to experiment, and from observation to observation." " The variability," he suggests, " though often attributed to general conditions of construction, or to local blood supply, etc., seems far more often due to changes produced in the central nervous organ by *its own functional conductive activity* apart from fatigue. This functional activity itself causes from moment to moment the temporary opening of some connections and the closure of others. The chains of neurones, the conductive lines, have been, especially in recent years, by the methods of Golgi, Ehrlich, Apathy, Cajal and others, richly revealed to the microscope. Anatomical tracing of these may be likened, though more difficult to accomplish, to tracing the distribution of blood vessels, after Harvey's discovery had given them meaning, but before the vasomotor mechanism was discovered. The blood vessels of an organ may be turgid at one time, constricted almost to obliteration at another. With the conductive network of the nervous system the temporal variations are even greater, for they extend to *absolute withdrawal of nervous influence*. Under reflex inhibition a skeletal muscle is relaxed to its post-mortem length, i.e. there may be no longer evidence of even a tonic influence on it by its motor neurones. The final common path is handed over from some group of *plus* class of afferent arcs to some group of a *minus* class, or of a rhythmic class, and then back to one of the previous groups again and so on. The conductive web changes its pattern at the entrances to common paths. The changes in its pattern occur there in virtue of interaction between rival reflexes: occlusion, substitution of equivalence, inhibition, immediate induction, successive induction, fatigue, are factors. As a tap to a kaleidoscope, so a new stimulus that strikes the receptive surfaces causes in the central organ a shift of functional pattern of the linkage. The central organ is a vast network whose lines of conduction follow a certain scheme of pattern, but within that pattern the details of connection are, at the entrance to each common path, mutable. The grey matter may be compared with a telephone exchange where from moment to moment, though the end points of the system are fixed, the connection between starting points and terminal points are changed to suit passing requirements as the functional points are shifted at a great railway junction. In order to realize the exchange at work one must add to its purely spatial plan the temporal datum that, within certain limits, the connection of the lines shifts to and fro from minute to minute."

This concise and illuminating picture of the neural framework of nervous integration and its mode of operation suggests an interpretation in a biological setting of the case under review. It should be noted that in analysing the functions of the nervous system the term " impulse " is used to symbolize the events in the transmission of messages through nerve fibres from one part to another. All the stimuli that impinge on sense organs from the outside world, such as light, sound, touch, smell and taste, and all the stimuli evoked from within the organism, from the vestibular apparatus, from muscles, joints,

bones and tendons, as well as those from internal organs are converted at the receptor surfaces into "nerve impulses." Impulses are relayed singly along the nerve fibre at a particular rate and interval which is more or less constant for the same kind of nerve tract, but which varies for different paths. The individual impulses as detected by electrical experiment produce similar reactions even in tracts of differing function. The scheme of innervation may thus be regarded in the simple form of nerve tracts conveying impulses from sensory organs to centres of integration in the spinal cord and brain, from which they are relayed to other centres and finally to the entrance of the final common paths, where they find an exit to the motor mechanisms. The "messages" are all conveyed in the form of "impulses," and the whole organization has, as Sherrington pointed out, an analogy in the circulatory system. The impulses circulate in the nerve tracts just as does the blood in the vascular channels. It has been suggested that they originate in receptor surfaces, but this is only a part of their story. Fresh impulses arise of course in the centres of integration, and they, too, are regarded as subject to the conditions of transmission provided by the functional character of the nervous continium. Just as in the vascular system the structures of the vessels and heart, the vaso-motor mechanism and physico-chemical conditions provide for an equable distribution of the blood, so in the nervous system the impulses are distributed in accord with the biological properties of the system itself and the organic provision for its co-ordinate activities. Carrying this analogy a step further it may be suggested that each system is, in its own way, subject to considerable variations in the amount in which its content, blood in the one case and impulses in the other, is conveyed to its seats of distribution. In normal circumstances the supply to particular regions is dictated by the requirements of function, and is secured by the subtle provision of organic unity so as to provide for the natural course of events. On occasion there may be diversion of a proportionately large amount of blood to a special area, to the lungs in exertion or to the stomach and related organs in digestion, with a relative depletion in other parts. Similarly the exercise of special activity in particular parts of the motor mechanism, in the legs for example in running or in the hands in manipulation, is associated with a convergence of nerve impulses on the centres which regulate the movements. This "one thing at a time" implies a corresponding reduction of impulses in the paths not immediately involved. The normal changes of attention from this to that is thus associated with a co-ordinate redistribution of impulses appropriate to the purpose.

There is a further consideration in respect of the nervous mechanism which may throw some light on the problem under review. The conception of the biological basis of attention to which reference has been made derives mainly from the work of Sherrington on the spinal reflexes, though Sherrington himself, as has been pointed out, indicated the wider circuits through the brain as part of the neural framework for the "psychic process." It is only more recently

that, in the hands of Adrian and his collaborators, the higher planes of the nervous system have been subjected to the test of modern experimental methods. Still almost a century ago Laycock (5) suggested the extension of the doctrine of reflex action to processes which occur in the brain, and while the theories to which the idea gave rise have been mostly of a speculative character, the conception of *reflex action of the cerebrum* as set forth by Carpenter (6) and illustrated by numerous examples does indicate a line of thought that is now being followed with success.

When the doctrine of evolution was still in its infancy Carpenter recognized the importance of the expanded layer of cortical substance in defining the problems of comparative psychology. The characteristic behaviour of different animals in the phylogenetic scale was related to corresponding grades of development of cerebral centres. In the case of man, his unique position with his armamentarium of speech, creative dexterity and a world of ideas with a social heritage had been attained through the instrumentality of a brain of unusual dimensions and complexity. It was the source of his psychic faculties as well as the seat of control of his articulate movements. The hegemony of mind and motor activity was the secret of his predominance. " This reflex action of the cerebrum manifests itself not only in psychical change but also in muscular movements ; and these may either proceed from simple ideas, without any excitement of feeling, in which case they may be designated *ideo-motor* ; whilst if they are prompted by a passion or emotion, they are known as *emotional*. The nature of the response made by the reflex action of the cerebrum will depend upon the condition of that organ at the time when it receives the impression ; and the condition among the lower animals may be regarded as the *resultant*, in each individual, of the modification which its inherited constitution has undergone from the influence of external circumstances. But whilst the cerebrum of man, in common with that of the lower animals, has a reflex activity of its own—which in the first instance may be regarded as the direct resultant of his general constitution, modified by early training—an additional and most important influence comes into play ; namely, the directing and controlling of the ego's own *will*, in virtue of which he can to a great degree *direct* his own thoughts and *control* his feelings, and can rise superior to circumstances, make the most advantageous use of the faculties with which he may be endowed, and keep his appetites and passions under subordination to his higher nature. . . . Then each human ego, at any one moment, may be said to be the *general resultant* of his whole conscious life ; the direction of which has been determined in the first instance by his congenital constitution, secondly by the education he has received from the will of others or from the discipline of circumstances, and thirdly by the volitional power he has himself exercised."

This broad generalization, however vague from the point of view of the structure and function of the nervous system, contains the germ of a principle which underlies the relation of the human mind to the cerebral mantle. The

main distinctive features of the higher mentality have long been symbolized by psychologists in the terms "cognition," "emotion" and "will"; and while it is impossible to allocate these to special centres in the brain, there is abundant clinical evidence to demonstrate a connection between their disorder and brain disease. This assertion can provoke no dissent in reference to those cases in which organic brain disease is already well established. In arterial brain disease or in general paralysis of the insane, for example, there can be no surer test of the character and extent of deterioration than examination of the manner and degree in which these "components" of the mind are affected. Not that they are individually involved, for in the long run any hard and fast distinction between them is impossible just as their cerebral localization is not regionally defined. For even if there is some evidence to associate cognition or ideation with the association areas behind the central fissure, emotion with the thalamic and sub-thalamic regions and volition with the frontal lobes, these more or less general assumptions are not of much value in interpreting the average case of mental disorder.

The difficulty in finding, or in fact, the futility of searching for an anatomical basis of universal validity is obvious when the more intimate nature of a large proportion of mental disorders is borne in mind. One need reflect only for a moment on paranoia, hysteria, neurasthenia and *folie circulaire* to recognize the fatuity of looking for a pathological substratum in the anatomy of the brain, and this applies not merely to each of these syndromes, but to the specific clinical disorders, whether they be of emotion or of will, which characterize any one of them. Take for example *folie circulaire*, with its alternating phases of average health, exaltation and depression. In the course of a normal existence there suddenly supervenes a period of excitement, beginning with a mild flight of ideas going on to confusion and perhaps terminating in delirium. In the emotional field there is a corresponding excitement, while in the domain of will the trouble begins with spontaneity of action or freedom from control, and proceeds to impulse or even to violence. The period of depression exhibits reactions of an opposite character. Ideation is slow and attention defective, emotional reaction is dull and the will is impeded. It would seem as if the total activity of mind and body had been slowed down. Vitality once more begins to express itself, and there is a gradual rehabilitation of function with return to another normal course of events. Throughout all the varied scene there is no sign of organic nervous disease. Yet the disorder is profound and for practical purposes must so far be regarded as "functional" in character. It has its origin in the constitution and nervous proclivities of the patient.

Other nervous disturbances, running their own peculiar course, such as hysteria and neurasthenia, may be attributed to similar functional tendencies. Induced perhaps by environmental agencies they are nevertheless the expression of inherent instability. It is remarkable as well as fortunate that Nature should betray her weaknesses in this respect in a limited number of ways. It

might be expected that considering the incalculable potentialities of the nervous system it could not break down in forms which can be recognized and classified in some order. There must be some order in dissolution otherwise classification would be impossible.

The case which has been described certainly exhibits a more or less orderly sequence of events, so much so that it is possible to predict within limits what at some stages is likely to happen. With a knowledge of the history, and from observation of the episodes of " second personality," the question of a rational explanation naturally arises. When organic disease has been left out of account, there remains the problem of an abnormal distribution of " impulses " in the neural continuum.

It has been pointed out that experimental physiologists find that nerve impulses flow in the fibres like blood in the vascular channels, varying in concentration at particular centres according to local requirements, every changing movement implying the selection, for the time being, of particular routes, while others are dormant. Co-ordinate equilibrium over a period depends on an adequate supply of impulses and this in turn on the total reserve. It may happen that, as in the case of the vascular system, local engorgement or depletion interferes with equable distribution and so upsets the natural conditions of integrative action. This is believed with good reason to occur in epilepsy, in which in some instances the explosion of nervous energy commencing in a limited focus is associated with vascular change. There is also the well-known hypothesis elaborated by Janet and accepted by many neurologists that the phenomena of hysteria are due in one sense to the depletion of nerve " energy " in cerebral centres. This depletion, a feature of exhaustion to which hysterics are prone, is supposed to account for the massive anaesthesias and functional paralysis which constitute a feature of the hysteric's state.

Viewed in the light of these considerations Carpenter's idea of " reflex action of the cerebrum " may help to elucidate the problem. The " reflex action of the cerebrum " is, as Sherrington points out, an integral part of the whole system whose function it is to co-ordinate the activities and maintain the soliditary of the organism as a whole. The brain is the seat of the great projicient centres of the organs of special sense, and through it pass the wider circuits of sensori-motor activity related to skin, muscles, joints, tendons, etc. It is the central seat of organization. In the course of animal evolution it developed *pari passu* with the gradual expansion and diversity of interaction between the organism and environment. In this way it became the custodian of new acquisitions preserved by heredity and so made available for further progress. In the great expanse of the human neopallium the heritage has assumed proportions and acquired potentialities which separate man from the rest of the animal kingdom. Through its instrumentality he has built up a world peculiarly his own with thought and striving. But his conquest and reconstruction of nature to his own advantage is merely the material symbol

of his spirit. His success derives in the first instance from his *ideation*, from a mental economy represented in a simple form in counting, which has enabled him to *picture the world* in a way in which he can control it by his creative faculties.

What is meant by picturing the world in abstraction may be realized by noting some of the ways in which localized brain disease destroys the picture, for although there is no question of explaining mind as such in terms of brain, some of its attributes do undergo dissolution as a result of limited cerebral destruction. Take for example destruction of the peristriate area and angular gyrus especially on the left side or, if it be imagined, on both sides. Such a lesion might be accompanied, not by loss of vision, if the calcarine area were preserved, but by failure to understand the meaning of what is seen. Similarly a lesion localized in the temporal area might interfere with the interpretation of what is heard. While it is not suggested that clinical disorders of this type, of focal origin, throw any light on the anatomical substratum of the hallucinations or paranoiac states, they may have an important bearing on cases similar to that which has been described.

Human behaviour is essentially ideo-motor. Much of it may be engrained by habit and so become more or less automatic. Its normal course nevertheless depends on a recognition of the meaning of what is seen and heard and touched. Speech and manual dexterity are the final expression of a course of events, the passage of nerve impulses, from visual, auditory and tactile centres to the motor areas of the brain and thence to the motor apparatus. Interruption of the impulses, say in the area of psychic vision, leads to a confusion of ideation and so to an interference with the execution of appropriate movement.

If now it be supposed—and it is not too much to suppose—that this case, already under strain and exhaustion, was " shocked " by what he saw at Gaza, that at a particular moment *what appeared in his visual fields became indelibly impressed on the area of psychic vision*, there may be in this a clue to a clearer understanding of the position. That a recrudescence of the scene in its original reality took place there can be no doubt. That it went further than a mere hallucination is shown by the co-ordinate actions which it brought in its train, actions consistent with the picture, though quite foreign to his immediate surroundings. He was presumably, in the first instance, a person predisposed to " hysterical " dissociation and at the time suffering from exhaustion. A convergence of nerve impulses on the area of psychic vision, already sensitized by emotion, with a consequent depletion of the areas necessary to preserve self-consciousness and self-control left him the victim of automatism. His ideation became reduced through *morbid concentration of attention* to an isolated patch in which and from which his second personality found expression. It might in short be regarded as an instance of ideo-motor epilepsy.

This hypothesis is consistent with the repeated occurrence of attacks over years, with the incidence of an attack when the " idea " of the original scene

becomes a focus of abstracted attention to the exclusion of other and more immediate impressions. The facility with which suggestion induces the abstraction points to the abnormal tendency of the neural continuum involved becoming the seat of a morbid concentration of impulses, to the exclusion of an adequate supply for such other areas as would be necessary to preserve a stable personality.

The attempt to view dissolution of personality in a biological setting in which a physiological conception of attention is outlined may help to interpret another case of similar character on which there was engrafted a secondary syndrome of psychological origin, also the manifestation of morbid concentration, though in the first instance due to an accident.

Case 2.

This is a man now fifty-two years of age who also served in the last war. A school teacher by profession he joined the ranks, had a good record of service and retired in 1919 with the rank of Captain. He had not been wounded, but his right arm was crushed in 1917. The injury was not serious, though pain was severe. It was supported in a sling and he was well in a week.

For about a year prior to leaving the army he had been very sleepless and restless. From time to time he took " turns " when he wandered about looking for spies, but he was always able to keep control of himself, and he was never under medical care on this account.

When he came home he resumed his work as a teacher in the school he had left. But he never felt at ease. He was sleepless at night and troubled with nightmares. During the day he was restless and easily agitated, and by evening was quite exhausted. Though he felt that he was doing his work properly he had the suspicion that he was not giving satisfaction, and without any disagreeable interviews gave in his resignation at the end of the year and received from the headmaster an excellent testimonial.

He got another post as teacher, and though interested and, from all accounts, proficient in his work, and also on friendly terms with the staff, his nervous state made him uneasy and restless. His sleep continued to be disturbed and, tired by the end of the day, he was usually exhausted at the end of the week. He did not " take alcohol " in the sense in which that expression is commonly used. During the working week he did not touch it, but when on a Saturday he took one glass of whisky, it had a sudden and dramatic effect on his mentality and behaviour. He would on such occasions go into one of the " turns " to which reference has been made. The general suspicion by which he was haunted from day to day, without interference with his work, became more articulate. He would begin to look for spies, use language peculiar to army discipline, and French phrases relating to the military conditions in which he appeared to be living for the time being. Though in a state which on first

sight might have appeared to have been produced by alcohol he never became really "drunk." One glass of whisky produced the effect, and once the "turn" ensued he did not seek more alcohol. *The dissociated state occurred usually on a Saturday afternoon.* It would continue till he went to bed in the early hours of Sunday morning. On awakening on the Sunday it had passed off and on Monday he would resume his work.

On recovery he would have only a very faint recollection of what had occurred. Shadows of the suspicions continued to haunt him, but there was no such aberration as might interfere with the performance of his duties. The account of the "turns" given by his wife shows that they took precisely the same form on each occasion. The contrast in his behaviour in the normal and aberrant states was marked in itself and definitely limited by the periods during which each existed. When well he was kind and thoughtful and careful; when abnormal he was offensive, abusive and inconsiderate.

Persistence of the "turns" was accompanied by a growing discontent with the surroundings in the new appointment and he decided to resign. Again he got a good testimonial. The uncertain course of life led to domestic troubles, and on breaking up his home he went in 1925 to live on a farm where he worked as a labourer. He now felt more free from anxiety, and the farmer after some weeks realized his position and tried to help him. He arranged for him to be examined by a doctor, who sent him to a specialist. The history as detailed by the patient suggested that his disability could be traced to domestic trouble. He himself however was convinced that the domestic trouble was due to his nervous condition and the problem was not followed further from this point of view. After temporary separation from his wife, who had all along showed great patience, insight and sympathy, a home was again made and he resumed teaching. This was given up after three months, when they changed their residence to a large town in which, through good introductions, he made a living by "private coaching." This continued for some years, but the "turns" recurred at the usual intervals. Working hard during the week, Saturday arrived with its exhaustion and its usual sequel, a glass of whisky and transient aberration, with the usual automatic talk and performance, followed by a quiet Sunday and the resumption of teaching on Monday. There was never any sign of taking alcohol to excess. He would not touch it during the week, and in spite of resolution and promises all apparently in good faith he could not resist it when the time came. In this respect, of course, he has something in common with the dipsomaniac, although he differs in that he takes it in smaller amounts and at shorter intervals. The dipsomaniac does show evidence of dual personality, in that his whole character changes during a bout, but he takes alcohol over a period in sufficient quantity to become totally incapable. And moreover the weekly "turn" was not the customary "Saturday night" of the public-house habitué, but the habit of the hysteric automatically punctuated, as it often is, by time.

On April 6, 1935, he decided to go to a football match. This was on the Saturday, and having worked all week he was, as usual, very tired. He had lunch in a restaurant, took one whisky and soda and immediately realized that he had gone into one of his peculiar states. He went to an office, transacted some business, but feeling that he should not go to the match he went home to bed. He took a dose of hypnotic, went to sleep and awakened some hours later in a state of violent sickness. On rising out of bed to go to the bathroom he discovered to his horror that his right arm was swollen, inflamed and quite useless. The sickness continued and was accompanied by diarrhoea. He did not sleep during the night, and all the following day felt very ill and worried by the thought that he might not be able to continue his work. He was restless and sleepless on the Sunday night and on the Monday morning the arm, which was still swollen, now began to be very painful, and it could be raised only a very little and the hand was useless. On Monday morning he managed to dress with assistance and proceeded to his rooms to begin his teaching. He found, however, that this was impossible. He returned home utterly exhausted and went to bed. An X-ray was taken, and there was no evidence of fracture or abnormality in the joints. The pain had become more intense, so severe in fact that he says he was almost distracted. He remained in the house till the Thursday, that is till April 11, and on that date got up and managed to dress and return to his teaching. He continued this for a week, but the sleeplessness, which had been present all along, had proved so debilitating that he could not continue. On April 20, that is a fortnight after the accident, he went to the Western Infirmary, where he was seen by a surgeon, who thought that the condition might be one of elephantiasis. He refused to remain in hospital, but promised to return in two days. Meantime dressings of lead and opium lotion had been applied to the arm, which was placed in a sling. This gave some relief, and with the aid of an hypnotic he had the first satisfactory sleep since the accident occurred. In the following days the swelling gradually subsided, but the fingers tended to bend, although they straightened out when the arm was extended forwards. The pain having disappeared to a considerable extent the limb was massaged, but there was no return of power and he carried it in a support. When the hand was removed from the sling the fingers curled stiffly and became more difficult to straighten out. As the arm returned to more natural proportions the pain gradually faded both from the forearm and the fingers while the shape of the hand became more distorted.

Three months after the accident he was admitted to the Victoria Infirmary. By that time not only had pain completely disappeared from the arm, but sensation was very much diminished. It was completely absent on the ulnar side and in all the finger tips. In the palm and back of the hand it was much diminished, while on the outer aspect of the thumb and forearm reactions to pain and heat and cold were present, though sensory discrimination was

unreliable. Pain was induced by attempts to straighten the fingers, except in the case of the little finger, which was completely anaesthetic. The intrinsic muscles of the hand were atrophied and the hand was claw-shaped (Fig. 1). The skin had an unhealthy appearance. There was no evidence of vaso-motor disorder, and the radial pulse was as full on the right side as on the left. There was no tenderness on pressure over the course of the main nerve tracts on the forearm. The flexor muscles of the forearm were hard, and this appeared to be due to persistent contraction. Above the elbow sensation was normal and movements in the elbow and shoulder joints were normal. His general physical condition was satisfactory. His sleep remained disturbed.

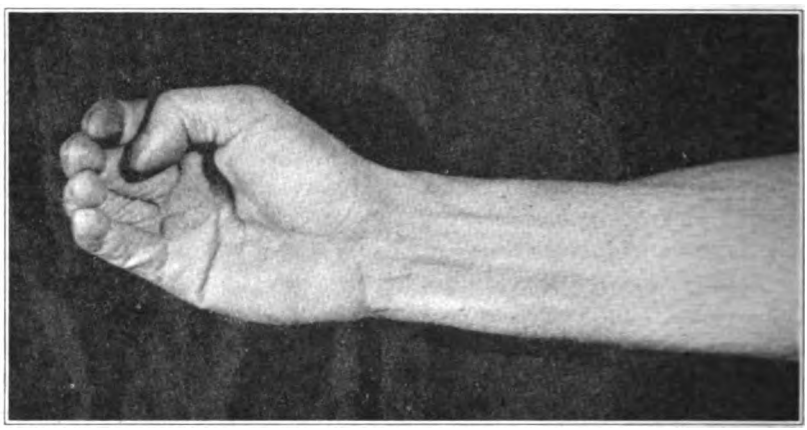

FIG. 1.—Case 2: Contracture of hand three months after accident.

The story of the onset and course of events in the disorder of the limb suggested that it was of the nature of an ischaemic paralysis, with consequent deformity due to tonic spasm of flexor muscles and loss of sensation which was possibly functional, but more likely to be due to involvement of the ulnar nerve as there was some evidence of wasting in the intrinsic muscles of the hand. It was decided in the first instance to try physical therapy. Under an anaesthetic the limb was manipulated and belladonna was given in the hope that it might induce relaxation. Massage was continued. This was followed by a return of sensation to the forearm and the skin of the limb took on a more healthy appearance. The tonic contraction of the muscles was markedly reduced and for a time he was able to extend the fingers (Fig. 2). This improvement was not however maintained, and after a month's treatment it was decided to expose the ulnar nerve. This was done and the nerve was found to be free from any adhesions, and presented, so far as naked-eye examination was concerned, a perfectly healthy appearance. The operation wound healed quickly and well and massage was again commenced. The operation was followed by a slight

improvement, more expecially in a gradual return of sensation which extended down to the fingers, although finer discrimination was still impossible at the finger-tips. Attempts to straighten the fingers or to move the wrist were accompanied by considerable pain. Sleeplessness was still the main difficulty, and although a variety of hypnotics were tried it was impossible to restore a natural state in this respect.

After three months' residence in hospital he went home and resumed his work once more. He reverted, however, to his former Saturday habits, and the sensation which had returned to the limb now acquired the form of distressing

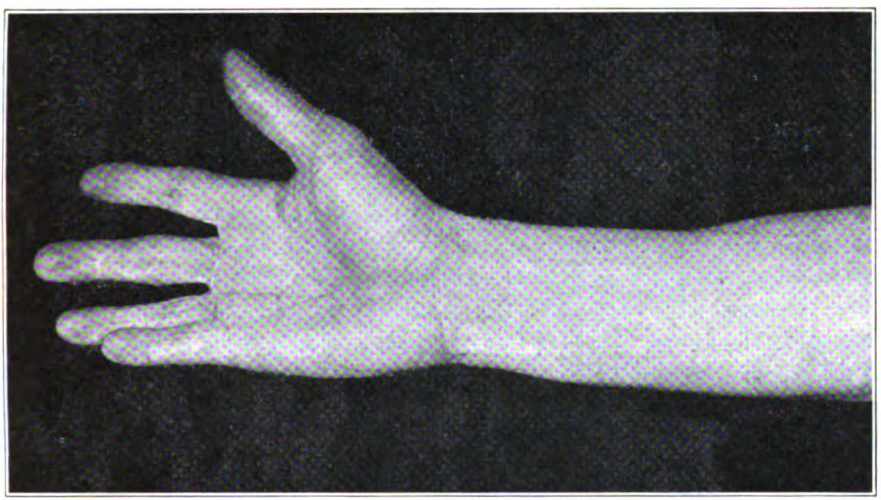

FIG. 2.—Case 2: Temporary extension of hand under the influence of atropine.

pains. These pains became so severe that he had to give up work and he was again admitted to hospital. On this occasion a more extensive exploration of the flexor aspect of the forearm was made and the median nerve was exposed in its course between the elbow and the wrist. Nothing abnormal was found. The muscles presented a healthy appearance, and minute portions examined microscopically showed no sign of degeneration. The wound healed well and quickly and the hand was put in plaster under extension. The plaster was removed after a week and the fingers were extended, but remained so only overnight and the following day both fingers and wrist were cramped and contracted as before. During the period in plaster the pains were severe and after removal of the plaster they continued. He went home and tried to continue his work, but his condition was worse than ever, as now, in addition to the sleeplessness and the "turns," he had the even more distressing disability of a useless and painful hand, which absorbed the attention of his waking hours.

In May, 1937, the hand had become even more stiff and more painful. He complained of a " strangle-like grip on his wrist." This became unbearable and he consulted a surgeon, who recommended amputation. The amputation was performed in November, 1937, and he says, " Since then I have never for a moment lost the sense of the bent position of the hand, the strangle-like grip on the wrist and severe pain which is sometimes replaced by a dreadful coldness and then by a fierce heat when I am in bed."

The amputation at the elbow brought no relief so far as the pain was concerned because he continued to have these even more disturbing sensations referred to the limb which was lost, and now, since the operation, there were added what he called the icy coldness and fiery feeling in the hand. The tissue round the stump was atrophied for about 3 in. and the skin had a glossy, blue appearance. The pain was so excruciating that he pleaded with the surgeon who had operated to try some further treatment. An operation severing the main trunks of the nerves relayed to the stump was performed, but this produced no relief. He gave up his teaching and went to rest in the country for two weeks and then went into a store to do clerical work. In spite of the continuance of the pains and other nervous disabilities he resumed his teaching. An attempt was made to relieve the pains by injections into the stump, but these produced only a temporary effect and when that had worn off the distress was worse than ever. He once more appealed for something to be done, and in April, 1939, a sympathetic ganglionectomy was performed. This operation resulted in greater relief than had followed either of the first two. He says he felt happier and more hopeful, and that though the sense of the hand was still present, there was a sensation of more normal "spread " of feeling in the fingers and the discomfort of the strangle-like grip in the wrist was less. This amelioration lasted only about two months, after which the pains recurred with their former severity. He has resumed work, and though very easily exhausted is able to continue during the week, but he is still, in August, 1939, subject to the weekly " turns," distracted by recurring pain in the hand that is lost and suffers, as before, from sleeplessness.

The main interest in this case lies not so much in the dissolution of personality as in the nervous disorder of the hand which it brought in its train. The recurrent " turns " of dissociation are not unlike those described in the former case, and may be regarded as examples of " ideo-motor " epilepsy. The alcoholic factor is incidental rather than causal, and a more satisfactory explanation lies in a constitutional tendency given rein by the experiences of war.

The relation of that tendency to the subsequent involvement of the hand is what attracts most interest and merits more detailed consideration. Does it also, and if so in what way does it, imply a morbid concentration of attention ?

Its mode of onset, occurring as it did during sleep, when he might have been lying in an abnormal position, associated with vomiting, pain and swelling of the arm and paralysis, suggests an ischaemic paralysis (Volkmann). This state

of paralysis or contracture is also known as retractile myositis. It is believed to occur most commonly in children of five to ten years, but has been described in adults when an arm has been fixed so tightly in a splint as to interfere with the circulation. It begins with acute pain and swelling of the limb with limitation of movement and subsequent "retraction" of muscles, those involved being usually the pronator and long flexors. The swollen limb is usually red in colour, and anaesthesia is extensive and segmentary in distribution. It may be of the "glove" type or extend as far as the elbow. When the swelling has gone down the retracted muscles are hard, and the pains tend to disappear. The hardness of the flexor muscles is supposed to be due to fibrosis. Ischaemia due to tightness of the splint is regarded as the cause and diminution in volume, or absence of the arterial pulse in the affected limb is the evidence for this conclusion.

There is no record in this case of the qualities of the radial pulse in the early stages. When he saw a surgeon at the infirmary a few days after the accident and when the arm was still swollen it may be assumed that in making the diagnosis of elephantiasis there was no abnormality in the radial pulse. Of course that diagnosis was merely a suggestion and the pain and colour of the limb did not support it. In any case, when he was examined three months later there was no difference in the volume of the radials on the two sides.

The course of events through the years following the accident cannot be explained by a simple obstruction of blood supply to the forearm. Even if it be supposed that pressure determining such obstruction or defective supply to the muscles and nerves involved fibrosis or adhesion, these complications would not account for the persistence of pain and vaso-motor discoloration of the stump. In addition there is the fact that in the earlier operations the main nerve trunks in the forearm were found to be normal, and the flexor muscles were not cicatrized as might have been supposed from their hardness. They were relaxed under the anaesthetic, and showed no sign of fibrosis either on naked-eye examination or under the microscope. Their hardness was due to spasm, or persistent rigor.

On the other hand, the condition presented many of the signs and symptoms of what has been described as "reflex contracture." This means that it could not be accounted for by lesions in the limb itself, but that the syndrome involved the participation of the *reflex mechanism of the central nervous system*. Simple destruction of muscle and nerve would be followed by paralysis and reduction of sensation, but it would not give rise to the excruciating pain, abnormal feelings of heat and cold and vaso-motor disorder which lasted over years.

"Reflex contracture" is a pathological reaction that became familiar to neurologists during the last war. It was described and analysed at length by Babinski and Froment in their volume "Hysteria and Pithiatism." The term "reflex" paralysis and contractures is applied, they explain, "because they resemble the amyotrophic or so-called reflex paralysis of which Charcot and

Vulpian have given such an excellent description." They point out also the similarity to the deformities which occur in osteo-arthritis, and which are due also to reflex action. The anaesthesia and vaso-motor disturbances are an additional evidence in their opinion of reflex pathogeny. They are satisfied that their researches prove that "there exists *a group of motor disorders of physiopathic nature*, which must be distinguished from organic phenomena properly so-called, and from hysterical and pithiatic phenomena."

Their main thesis, apart from a clear definition and description of the disorder, is the elaboration of a distinction between these "reflex" phenomena and organic disease on the one hand and hysteria on the other.

At a meeting of the French Neurological Society (8) on April 6, 1916, following a report on so-called functional motor disorders, the following resolutions were passed after discussion on the problem :

"*Regarding the matter exclusively from the standpoint of a medical board we have to distinguish among so-called functional motor disorders (i.e. motor disorders with none of the objective signs characteristic of organic affections of the brain, cord, or nerves, or of vascular lesions) :*

"1. *Hysterical or pithiatic disorders properly so called.*

"2. *Nervous disorders quite distinct from the preceding which are associated with real physiological disturbances of which the mechanism is still a matter of discussion, but which may be grouped with the reflex disorders observed after osteo-arthritic lesions.*"

This was followed by a number of publications all purporting to establish the validity of these conclusions. In an article by Gougerot and Charpentier (9) the authors summarize their observations as follows :

"To sum up, from the first we have been impressed by the contrast between the localization of the wound, with its apparently mild character, and the importance, diffusion and 'ascent' of the paralytic and very frequently trophic disorders ; by the frequency of ascending pain, which is sometimes intolerable ; by the distressing persistency of the pain, paralysis and trophic disorders ; their progressive aggravation many months after the wound ; in short, by the gravity of the prognosis . . ."

Our case certainly presented the paradoxical features of the syndrome thus described. It is impossible to be precise about the nature of the original injury, and it would probably be misleading to attach any importance to the damage to the same arm in 1917. The incident in 1935 occurred during sleep and it was neither a fracture nor a joint injury, and in itself, whether due to pressure on vessels or on nerves or on both, was certainly insignificant compared with the train of sequelae by which it was followed.

It might, with some plausibility, be argued that the oedema was due to vascular obstruction and the paralysis, initial anaesthesia, vasomotor and thermal disturbance and terminal pain, to localized damage to nerves. This, however, would be to leave out of account not merely the nature and

constitutional tendencies of the subject, but what is more obvious and more significant, namely the protracted and incurable nature of the malady, and the repeated failure of surgical attempts to isolate from the central nervous system the parts to which the distressing symptoms were referred.

Even if the initial manifestations of the disorder following the injury, the swelling, paralysis and sensory disorder could be explained in terms of local anatomy there was no reason to anticipate the subsequent course of events. In view of the common occurrence of serious injuries to the limb, experience is justified in regarding such a course as unique. Exposure of the ulnar and median nerves from the elbow to the wrist revealed in them no abnormality. Yet the paralysis was complete, while only the intrinsic muscles of the hand were atrophied and the initial anaesthesia extended at first to the elbow, though later it was complete only in the hand and on the inner side of the forearm. When to these signs of disorder is added the vasomotor disturbance, the clinical picture is certainly paradoxical. The paradox is continued and emphasized in the sequelae. No ordinary conception of the structure and functional integration of its parts provides a basis on which the successive stages of the disorder can be explained. This applies not only to the changes in the arm itself but more particularly to the disability after its removal. If it was the place of origin and continuation of the disability, its removal should have been followed by disappearance of the complaint. So far from that being the case the phantom of the arm remained the seat of excruciating pain, of disturbing sensations of heat and cold and of a strangle-like feeling in the wrist. Section of somatic and sympathetic nerves had no more than a transient effect on the whole array of symptoms and on the nutritional and vaso-motor abnormalities. An explanation of these phenomena must be sought in the wider circuit of innervation in relation to " the reflex action of the cerebrum."

Is it then the case that contrary to the conclusions of Babinski and Froment the reflex paralysis and contracture is after all associated with hysteria? The authors based their view largely on the belief that in their cases the will was not impaired. They no doubt differ greatly from those cases to which the conventional conception of hysteria, as elaborated by Charcot and Janet, applies. But if, to avoid controversy, the question of the will be left on one side, and the problem regarded from the point of view of morbid attention, it will be seen that in hysteria as well as in these cases of " reflex " disorder there is in respect of their defect a common substratum. The history of the case is in accord with the accounts of " reflex " paralysis in the literature, in respect of the morbid preoccupation with the injured part. A picture of the hand is constantly in the mind; the disturbing sensation which is repeatedly referred to it, even in its absence, are a real part of the content of conscious experience. The " reflex action of the cerebrum " has been adjusted in dissolution to fix attention on a focus which, though absent. is none the less there for the patient.

Taking up the line of thought followed in the previous case it is suggested

that the original injury to the arm, however slight or severe, produced on the sensorium related to the limb an impression of which it could not get rid. An exhausted and unstable nervous system, in this case amply demonstrated in his previous history, was exposed to "shock." The sensori-motor area of the limb was the seat of impact, and the focus of convergence of nerve impulses to an extent and in a manner which led to its dissociation from other regions indispensable to mental equilibrium. As in the other case the scenes of Gaza became the field of automatic attention, so here the arm when it had gone remained the *point d'appui* of morbidly concentrated interest. So a physiological interest was maintained not only in the supersensitive region of the cortex but in the whole circuit through the part of the arm that remained, thus accounting for its discolouration, atrophy and tenderness.

There had thus been engrafted on to his original aberration of spying "turns" a fresh expression of inherent instability in the form of a "reflex paralysis," characteristic not only in the paralysis, but in the sensory disorder which was the mainstay of its commanding effect. If in the first case there was justification for regarding it as an example of ideo-motor epilepsy, there are equally good grounds for seeing in this an example of ideo-sensory epilepsy.

The clinical features of Case 2 were seen to stand out in marked contrast with the usual course of events which follows injury to a limb whether it be contusion, laceration or fracture. Emphasis was laid on the psychic aberration antecedent to the accident, the tendency to "turns" of dissociated personality with morbid concentration of attention. There can be little doubt that the state of constitutional nervous instability was the groundwork on which the syndrome of reflex disorder evolved; and a recognition of this will be a clue to the interpretation of the other three cases which will be described.

Meanwhile, before proceeding to their description, it may be well to review shortly just how a "reflex disorder" marks a departure from what might be expected. In ordinary circumstances, after an accident, the degree of shock depends on the one hand on the severity of the injury, and on the other on the stability or resistence of the nervous system. In the average healthy person the reverberation in the higher centres quickly dies down and the course of recovery accords with the processes of repair in the region which has been damaged. This accounts for the simple mechanical principles which afford a reliable guide in the treatment of fractures and of other injuries to a limb. The scene of disorder remains localized, and even should recovery be associated with shortening or weakness, such disability is discounted in an otherwise healthy subject; the defect is accepted in the light of a sensible appreciation of what has happened, its degree remaining in proportion to the extent of local default.

This "acceptance" obviously involves participation of the wider circuit of innervation which connects the limbs with the brain through the spinal cord, and the preservation of integrity of function compatible with loss of

structure from the injury. The use of the term "acceptance" implies a *mental* element in the situation, unconscious though it may be in the majority of cases. In Case 2 it may be said that a determining factor in the disorder was inability through morbid distraction of attention to accept the situation.

It is well to recognize however that occasionally there may occur during the treatment of injuries to a limb unexpected complications which cannot be explained in terms of aberration of mentality. This applies to such intercurrent incidents as quadriceps paralysis in the lower, or ulnar paralysis in the upper limb, in which there has been a fracture, or in the case of the lower limb, arthritis of the knee. Such paralysis is usually supposed to be due to atrophy from disuse of the muscles involved. But its comparative rarity, and the selection of particular muscles when all limb muscles are out of use, points rather to a temporary dislocation of neural energy whereby certain muscles are deprived of the nerve impulses adequate to healthy preservation. Disuse is unlikely, of itself, to produce rapid atrophy, and far less likely to make a selection which is fairly constant. An explanation is to be sought not in the limb alone, but in its relations with the spinal centres on which it depends for its vital nerve supply. The transient character of these atrophies suggests that the shock of the accident in some cases suffices to induce a temporary aberration or impediment of impulses in the spinal centres of the peripheral motor paths. It may be that the muscles involved are concerned with highly specialized functions which render their neural centres particularly sensitive to the disturbances involved in shock, a sensitivity which would be naturally exaggerated in persons with an unstable nervous system. In this connection it is to be noted that the knee joint, placed in the axis of erect posture, is one of the most complicated articular instruments in the body, while the ulnar nerve subserves the refined activities of manual dexterity.

Simple complications of this kind arise and recede, leaving to speculation a theory of their origin. That they cannot be explained by the conventional conception of sensori-motor nerve supply to the limb is obvious. Atrophy of an isolated muscle like the quadriceps in one instance when there is only a fracture of the femur, or in another where there is simply arthritis of the knee joint, implies that the injury or disease has brought in its train nervous derangement beyond the immediate site of the lesion, a derangement in which it may be assumed that the corresponding centres of integration in the cord, at least, are involved. This does not mean involvement in the ordinary pathological sense, with degeneration of neurones, but it does suggest an interference with the average course of nerve impulses through the usual channels. It may be assumed that the circuit of innervation between the limb and the cord, of which the supply to the quadriceps forms a part, is but a portion of an intricate system related to other muscles, tendons and fascia, to the skin, and more especially to the knee joint. To the muscle itself both efferent and afferent fibres are relayed, but the atrophy cannot be due to destruction of afferent

supply, for locomotor ataxia shows that destruction of afferent fibres is not followed by atrophic change in the muscles; nor is there any evidence that the sympathetic system contributes to the process. It is therefore in some defect in motor innervation that an explanation must be sought. Motor neurones are indispensable for the *nutrition* of somatic muscle.

A normal supply of motor impulses depends in the last resort on an adequate and equable distribution in the motor centres in the cord of impulses which converge there from a variety of sources: from the cortex through the pyramidal tracts, from subsidiary centres in the extrapyramidal system, from other regions in the cord related to other limbs and from those structures in the limb itself to which reference has been made. It is not unreasonable to suggest that a spinal centre of motor co-ordination may be thrown out of gear by excessive irritation in a diseased limb. This, as has been pointed out, would be more likely to occur with disease of the knee joint, which has a highly complicated afferent supply, and which surgeons have long recognized to be more readily accompanied by shock following excision than any other joint in the body. Atrophy of the quadriceps, in such a case, may thus be regarded as an example of "reflex nervous disorder" the ambit of which does not extend beyond the spinal centres, although it is probable that it occurs only when the nervous system is unstable as a whole.

Ulnar paralysis is a fairly common occurrence and is attributed to a variety of causes, including fractures, pressure on the palm or elbow, or by cervical rib. Its obscure aetiology in many cases suggests a functional dissolution in the spinal centres. One of the cases to be described (Case 4) had an ulnar paralysis following a fracture in which there was no evidence of mechanical interference with the nerve trunk. The possibility of a psychic element in her case is discussed later. The paralysis followed a simple fracture of the radius about two inches below the elbow joint. No damage was done to the joint, or as far as could be seen to the soft structures of the arm. The fracture healed rapidly in good alignment, but was followed by intense pain and sleeplessness and by paralysis of the intrinsic muscles of the hand supplied by the ulnar nerve (Figs, 7, 8, 9 ,10). The flexor carpi ulnaris and inner half of the flexor profundus digitorum muscles of the forearm supplied by the ulnar remained normal. Cutaneous sensation was not impaired. The patient was a highly excitable young woman, and a pianist by profession. After the accident she was sleepless and complained greatly of pain. Movement was restored in three months.

These selective atrophies of quadriceps and of refined ulnar musculature indicate in the first instance a dissolution of neural integration in spinal centres. In the case of the quadriceps it was suggested that the dissolution did not likely extend beyond these centres. With regard to the ulnar paralysis the clinical phenomena were different in that they suggested a wider sphere of participation. The sleeplessness and severity of pain in the initial stages implied

the reaction of a "nervous temperament" in a young woman with the prospects of a career in playing the piano. The consequencies involved in an injury to the upper limb were possibly the source of morbid reflection and concentration of attention on the prejudice to her future. Should such an assumption be justified it would mean that the disorder in the spinal centre had been aggravated by the disturbance in higher centres in the brain.

Reverting to Case 2, let us examine how the reactions differed from those which usually follow on injury to the limb. The course of events suggested a tentative diagnosis of "ischaemic paralysis." Whether or not this represented an accurate estimate of what had happened, there remained as an essential factor in the syndrome the constitutional or hysterical instability represented in a tendency to phases of "second personality," in which a recurrence of war experience held the field of attention to the practical exclusion of other matters of immediate interest and importance. What actually took place at the time of the accident fades into the background in the light of the peculiar reactions in the limb and in the patient, and of the futile attempts to excise the source of intolerable sensations. So far from removing the "cause," surgical measures would seem to have consolidated its mechanism, the essential parts of which lay beyond the region to which the symptoms were referred. Even after amputation of the limb, the phantom arm remained the seat of painful cramp and the locus of distressing thermal feelings. The skin of the stump was glossy and blue, always cold to the touch and often tender. Transection of the main branches of sensory nerves and later cervical sympathectomy, while giving transient relief, were followed by return of the symptoms severe as ever. That the conditions of the persistence of the disorder were in the higher levels of the nervous system seems perfectly plain.

To appreciate in this case the significance of the problem which it raises it had to be stated in a wider context. Assuming that there may have been an "ischaemic paralysis," what does this mean? As the term implies, "ischaemic paralysis" is the result of vascular obliteration. It may follow arterial thrombosis or ligature or compression by too tight bandaging of such large arteries as the subclavian, axillary, brachial, femoral or popliteal. It is only very rarely however that complete obstruction is followed by more than a transient anaemia of the limb. There may be only a fleeting ischaemia of the hand or foot and no paralysis after occlusion of the axillary or femoral artery. Occasionally however there is swelling, cyanosis and cooling, with pain and paralysis of the affected limb. There is thus a great variation in the character and extent of the disturbances from case to case. These disturbances are difficult to explain. It has been suggested that they depend on the condition of the arteries, the presence or absence of disease in their coats, or on the character of the collateral circulation. The possibility of involvement of nerves and of secondary influence of nervous disorder has been noted.

When this complication does occur its history and manifestations have

certain characteristic features: (1) It begins with swelling of the affected limb, which is usually though not always painful. Discoloration is usually blue but may be mottled; as a rule it is cold and sensitive to changes of temperature: the distal pulse, radial or dorsalis pedis may be imperceptible or relatively reduced in volume. (2) Even when pain is not severe at the onset it may come on with great intensity after some days. There is a feeling of tension, as if the limb would burst. The skin of the distal parts may then become anaesthetic while the deep pain remains. As time goes on, the swollen tissue becomes harder and gives the impression of fibrous transformation. This applies to muscle and other subcutaneous structure, including, it is suggested (Tinel), tendons, fascia and nerves. Trophic changes are seen in glossy skin, curved and cracked nails and in decalcification of bone. Electrical reactions are varied; in one case they are diminished, in another they are those of degeneration, and in a third they may be normal; muscular contraction may be induced by strong currents only, but without inversion of polarity; and again stimulation of the nerve at a distance may induce reaction more readily than direct excitation of the muscle itself.

Ischaemic paralysis is thus a complicated disorder of sensori-motor and nutritional activities the pathogeny of which remains obscure. That it is not due simply to deprivation of blood supply is generally accepted. On the other hand the disorder has a segmentary distribution; most intense in the distal parts of the extremities, it fades away towards the middle reaches of the limb; it has no relation to the peripheral topography of the nerves. Its anomalous character is illustrated in a case described by Bonamy and Verchère (10), and cited by Tinel (11), in which "ischaemia of the hand, resulting from lesion of the axillary, was accompanied by gangrene of the hand and fingers in the region of the musculo-spiral which was itself slightly injured." Even more dramatic is another case, also quoted by Tinel, in which obliteration of the radial artery in the "anatomical snuff-box" was followed by ischaemia of the hand and fingers.

The problem of ischaemic paralysis is further complicated, as has been pointed out by the resemblance of its clinical features to those which sometimes follow "nerve irritation" *apart from arterial occlusion.* The clinical material which has been the source and subject matter of the question of nerve irritation had, as was pointed out, a very prominent place in the literature of neurology of the last war. Ischaemic paralysis was a rare event in comparison with the incidence of anomalies attributed to the "irritation" of nerves. They had however this in common, that they defied explanation in terms of the ordinary conceptions of anatomy and physiology which obtain in analysing the functions of a limb.

The phenomena of "irritation" following nerve injury were seen to comprise a variety of disorders, expressed in symptoms and signs which are sufficiently characteristic on the whole to justify the use of the term "syndrome"

for their course. Motility, sensation and nutrition are involved in different ways and in varying degrees. Muscles may be atrophied, hypotonic or hypertonic ; anaesthesia, paraesthesia, neuralgia or thermal hyperaesthesia represent the abnormal sensations, which with atrophy or hypertrophy of the skin and nails, vasomotor irregularity and excessive sweating are manifestations of vegetative disorder. These morbid reactions have been described at length and interpreted from different points of view in the publications by Tinel and by Babinski and Froment which have been quoted. It would be superfluous and in any case irrelevant to the purpose of this thesis to deal at length with the observations of these authors ; for while no study of the problem can afford to overlook them, it should be sufficient for the present to emphasize some general conclusions which they suggest :

(1) In the first place, it is remarkable that a single limb or the distal half of a limb should become the seat of such profound disorder as the result of what at first sight is frequently a trivial accident. Local damage, say a wound of the inner part of the hand, might destroy a portion of tissue including skin, nerves, vessels, muscles, tendons and bones, but would be expected to heal quickly and leave little defect. Should there be no sepsis the wound would be repaired with resultant interference with function in proportion to the structure which had disappeared, and to the capacity of the remaining structures to compensate functionally for the loss thus sustained. Even in the event of local infection, and the irritation and extension of destruction thereby involved, no more disability might be expected than would accrue from the total amount of tissue that had degenerated. So far from this being the case, the incidence of " irritation " involves development of the far-reaching complications to which reference has been made, and which in their *progress* tend not only to ablation of the function of the limb, but to persistent discomfiture and total disability of patient.

(2) In the second place, the progressive course of events, even after structural repair in the narrower anatomical sense has taken place, points to a state of disorder in the vital conditions, a disturbance of equilibrium in physiological relations, not only in the parts immediately involved in the original injury, but step after step in other structures to which these are biologically related. The paths by which the disorder spreads are the nerve fibres. The neural continuum is the basis of integration, and though the vascular system is one and universally pervading, and vasomotor disturbances are a feature in " irritation," it is through the neural channels that the disintegration spreads. A lesion in the ulnar region, and a trivial one at that, may be, according to Tinel, a local focus of " irritation," and set up a conflagration which extends to the whole forearm with spasm, immobilization, anaesthesia, acute pain or thermal discomfort, and concomitant changes in the skin and derangement of blood supply as the more superficial evidence of organic dissolution. This spread has been attributed to " neuritis." It must not be supposed however that neuritis,

in the generally accepted pathological sense, is a factor in the irritation syndrome. Genuine neuritis is said to occur occasionally, but only as a complication, and that, of course, a serious one. Its gradual ascent and appearance in due course in the other limb, in a reported case, indicate that it may be an independent affection on which the irritation has been engrafted with prejudicial results. Tinel however suggests that it may originate in the infected injury, and be due to the toxic by-products either of infection or of metabolic change in the degenerating tissue. On the whole, however, infective agents and neuritis may be ruled out as determining factors in the general class of "irritation syndrome."

(3) In the third place, the question arises as to whether the accepted physiological principles of innervation throw light on these extraordinary reactions. If, as has been pointed out, innervation consists in the flow of nerve impulses in adequate supply to appropriate terminals and centres, then it might be expected that interference with that supply by interruption, or increase by excessive excitation, would disturb the balance of organic equilibrium. Interruption of motor fibres should be followed by reduction in motility, while destruction of sensory tracts would lead to anaesthesia in the parts to which they were relayed. Partial interruption of a trunk would in that case be followed by corresponding diminution of function in the structures to which the fibres involved were distributed.

In what might be called "a normal case of complete interruption" there is fixity of signs and symptoms, a constant limitation of (*a*) paralysis, (*b*) anaesthesia, (*c*) reaction of degeneration, and (*d*) area of formication according to the nerve involved. A partial interruption might be expected to interfere with function to an extent which could be estimated by calculation if only the number and function of degenerate fibres were known. So far from that being even theoretically possible in cases of "irritation" or "reflex disorder," the reaction is out of all proportion to what might be expected from the original lesion. Not only so, but the nature of the reaction itself may be so extraordinary as to defy explanation in terms of the structure and function of the tissues ultimately involved. A partial lesion of the median or of the ulnar nerve may result, after a time, in immobilization of the whole hand and forearm accompanied by sensory and vasomotor disorder of corresponding extent, and continue in that morbid state while the original "cause" is merely a fibrosis of a number of nerve fibres. These so-called paradoxical reactions are supposed in some cases to have their origin in "adhesions" at the site of nerve injury, and surgical liberation of the nerve trunk has been found occasionally to be followed by cessation of the symptoms. Be that as it may, successful therapeutic procedure does not reveal the course of events whereby a simple local defect leads to such disastrous consequences. Neither defect nor simple adhesions could be expected to originate a conflagration of so great dimensions unless the whole material were highly inflammable. The most striking impressions received

on reviewing the literature dealing with these cases is just the insignificance of the original cause when compared with the magnitude and variety of the effects.

We are then forced to the conclusion that the conventional concepts of physiology do not apply in these cases; that the nervous system is to some extent, or in some of its parts, in a state of chaos, that the natural co-ordination of its reactions is partially in functional dissolution, and that in this dissolution the higher cortical centres play a determining role. The designation of "reflex nervous disorders" applied by Babinski and Froment to these phenomena implies an extension of the field involved to the centres in the spinal cord. They deliberately place the limit there, and no attempt is made by them to find evidence of participation of the high levels of cerebral association. Their thesis purports to establish a distinction between these disorders and hysteria, on the one hand, and organic brain disease on the other. "Objective signs which were independent of the will had thus been discovered, and consequently we felt convinced that these disorders were not due to hysteria." The present analysis of reflex disorder is designed to show that in its more dramatic forms it is associated with mental aberration.

Case 3.

M. L—, a married woman, aged 34, with no children, was working in a paper factory when her right hand was caught at the wrist in the machinery. The pressure of the grip of the machine was strong; ten minutes, she says, elapsed before it was freed, and during this period she suffered torture and was greatly alarmed. The back of the wrist appeared to be the part most severely bruised, and there the skin was lacerated. The limb was quite useless, and she could not close her hand, the fingers being movable only to a slight extent. Within an hour after the accident it was cleaned, dressed and bandaged. The pain however was excruciating, and although she was given a hypodermic she passed a restless and sleepless night. On the following morning the limb was red, swollen, stiff and completely paralysed. She went to an infirmary, where an X-ray photograph was taken. There was no evidence of broken bone or of dislocation. Moist dressings were applied with a view to easing the pain, and massage was prescribed. The pain from manipulation or even from light massage was so great that these remedial measures had to be stopped. In four or five days it disappeared from the skin over the whole hand, but remained in the deeper structures when any attempt was made to move them. The arm was now placed in a splint and sling, and she was given medicine with a view to restoring sleep and easing the discomfort. When after two months the tenderness had abated and the swelling had gone down massage was resumed. The skin, which was still insensitive, had a mottled appearance; blue, red and white patches could be seen on the back of the hand and forearm. The broken skin at the seat of injury was replaced by a smooth white scar.

Massage itself was not uncomfortable, but passive movements of the joints were very painful. The limb was still paralysed.

Massage was continued at intervals for two years. During this period she remained nervous, excitable and restless in her sleep. She had also been worried by dispute about compensation for the injury. The hand was useless, and while there were slight voluntary movements of the fingers, the wrist was stiff. It was painful at times, and especially at night was the seat of sensations of heat and of cold. Anaesthesia of the skin extended about 2 in. above the wrist; that is, just above the scar of the original injury. The skin of the whole hand had a glossy appearance.

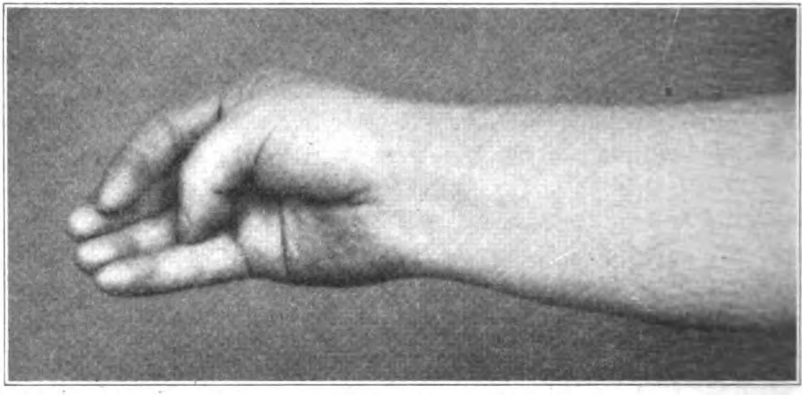

FIG. 3.—Case 3: Contracture of hand (accoucheur's hand) two years after accident.

Figs. 3 and 4 illustrate the posture of the hand when she was admitted to the Victoria Infirmary of Glasgow two years after the accident. It is typical of one of the forms of contracture associated with "reflex disorder." It resembles what occurs during spasms of tetany, and has been described by Trousseau as the "accoucheur's hand": "In the upper limb the thumb is forcibly and violently adducted, the fingers are pressed close together and semi-flexed on the thumb, the movement of flexion taking place only at the metacarpo-phalangeal joint; the palm then being made hollow by the approximation of its inner and outer borders, the hand assumes the shape of a cone, or rather the shape given it by the accoucheur when he introduces it into the vagina."

The manner in which the hand had been an object of concern and of morbid attention cannot be better described than in her own words after she had recovered its use: "I carried it about with me and nursed it as if it was a baby." From time to time in the interval since the accident she said she had had "fainting turns." She did not lose consciousness completely, but felt

giddy, had a sensation as if things round her were far away, and she felt compelled to sit down. More annoying than the bursting feelings which sometimes came into the hand were the sensations of heat and cold. She had taken her food well and had not lost weight. When she entered the infirmary for treatment she weighed just over 12 st. She appeared nervous and apprehensive and slightly tremulous. Her internal organs were healthy and the menses had been normal.

After a preliminary rest of a few days, when the diet and alimentary functions were regulated, she was given at short intervals small doses of belladonna

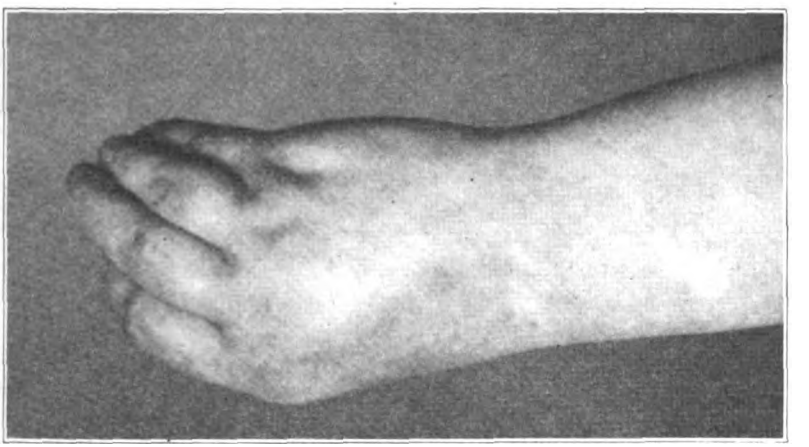

FIG. 4.—Case 3: Contracture of hand two years after accident (dorsal view).

and hyoscine. This was done as in Case 2 to induce distraction of attention. On the fourth day there was a definite return of power to move the hand, and she said she felt the movements at the joints between the fingers and the palm. This appeared to give her confidence, and under the influence of the drug, while slightly confused, she was much more cheerful, and the anxious, tremulous condition had abated. On the following day capacity to move the fingers had increased and there was a return of some movement in the wrist. While prior to the treatment supination and pronation of the hand by rotation at the elbow produced slight involuntary flexion of the fingers, this had now disappeared. She was much pleased with what had happened, devoted her attention to active movements as much as possible and said that she now felt it was "more like a hand." By that time sensation had returned to the skin. Following an interruption of two days the medication was continued in smaller doses for a further two days. Massage and passive movements were commenced and in six weeks she was sent to a convalescent home. Sleep had returned to a comfortable degree, her nervousness had gone and she was cheerful and hopeful.

She was able to use her hand to a limited extent, for example in knitting. The main defect seemed to lie in a weakness of the extension of the wrist and fingers ;

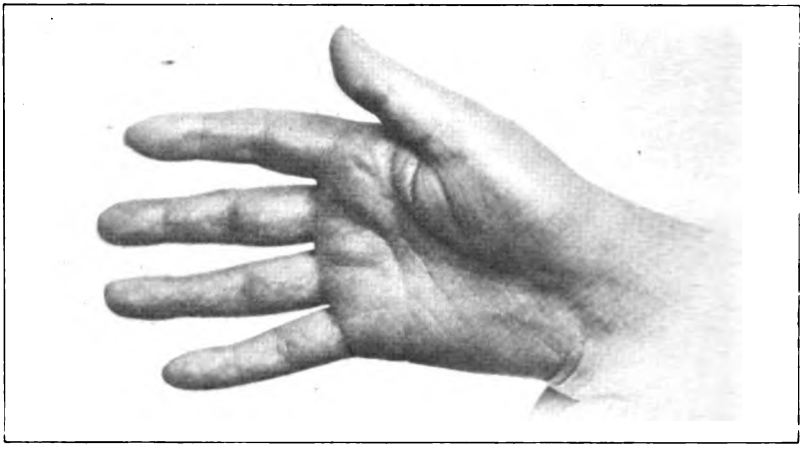

FIG. 5.—Case 3 : Hand in extension two months after commencement of treatment.

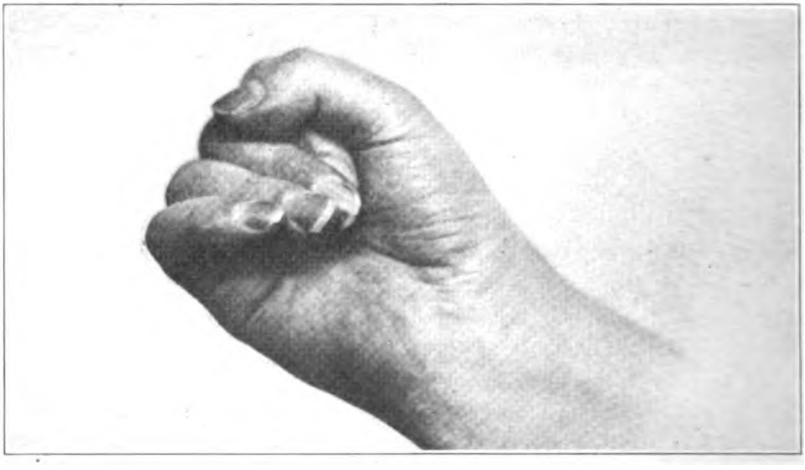

FIG. 6.—Case 3 : Hand in flexion two months after commencement of treatment.

the extensor tendons had probably been damaged more severely than other parts in the accident.

Figs. 5 and 6 indicate the extent of recovery at the end of two months. By this time she could extend and spread the fingers, though abduction of the

thumb remained slightly impeded. She could close the hand, though still imperfectly, for power was defective on the ulnar side. In the succeeding six months improvement continued. Pain and thermal disorders had gone and nervousness diminished. She was able to do her ordinary household work and could knit, though some of the finer manipulations were still impaired.

There can be little doubt that this case also comes within the category of reflex disorder or irritation syndrome. The nature of the injury, compression at the wrist, might suggest a temporary occlusion of blood vessels and consequent ischaemic paralysis. The similarity of Fig. 3 to Fig. 1 in Case 2, in which the possibility of ischaemia was raised also, might be taken as evidence. But the considerations put forward in criticism of this interpretation in that case apply here also. In addition there is the fact that in this case the course of events was towards a resolution of the disorder incompatible with the wasting and fibrosis of muscle and the hopeless prognosis in genuine ischaemic paralysis. In any event the clinical evidence in both cases is that which has been accepted by the authority of Tinel, Babinski, Froment and others as justifying a diagnosis of reflex disorder.

It is obvious that a simple obstruction of blood supply to the hand could not of itself have given rise to such widespread reactions unless the centres of integration in the cord at least had become involved. The hypertonicity of muscle localized to the affected limb is of itself proof of morbid reaction on part of the spinal mechanism to which it was related.

But there is evidence also of participation of a wider circuit of innervation which includes the higher centres in the cerebral cortex. In the first place there were "fainting turns" which recurred over the period of disability of two years. These, as described by herself, suggest a temporary diminution of self-control associated with feelings of sensory aberration and "loss of grip" in a minor degree. In the second place the glove anaesthesia pointed to a psychic defect which is usually termed "hysterical." In the third place, her own attitude to the injured limb, as defined in her nursing it as if it were a baby, betrays her bondage to morbid attention; and the insight which she thus showed on recovery is an indication of the extent to which the faculties of her higher cortical centres had been laid under restraint.

There is in this case no indication, as there was in Case 2, of nervous instability prior to the accident. The earlier history is not accurately known. The nature of the accident however was such as to produce severe shock. There was not only the crush of the wrist, but the period of ten minutes (even though that be an exaggeration) which elapsed before it was set free, must have been the occasion of profound disorder in the central nervous system. When to these reactions are added the reflections on a probable loss of use of the hand, the *morbid attention* paid to it, and the anxieties arising from compensation, the picture of her disability is seen to include the wider circuit of cortical innervation which underlies personality.

Case 4.

M. D—, a girl, aged 21, fell from a ladder and fractured her left radius 2 in. below the elbow joint. There was practically no displacement and very little swelling. There was no evidence of bruising or of injury to the arm apart from that immediately related to the fracture. She sustained no injury to any other part of the body but got a severe shock. The arm was placed in a splint and sling. On the night following the accident she did not sleep. She said she suffered more from discomfort than from pain and that she could not find an easy position for rest. Next day she was exhausted and restless, and felt nervous and frightened. At night she was given an injection of morphia sulphate, gr. $\frac{1}{8}$. Any little sleep she had was disturbed by dreams. On the following day, that is on the second day after the accident, there were shooting pains in the arm. These increased in intensity until the whole arm down to the fingers had a feeling as if it would burst. On the third day the splint was removed. The arm was in good position. There was some swelling at the site of fracture but no redness or visible evidence of inflammation. The whole limb below the elbow was tender. She was very nervous and inclined to weep. Lotions were applied and she was given a sedative.

The pain subsided gradually but she remained nervous and disturbed in her sleep. A fortnight after the accident atrophy was noticed in the hand. She could move her elbow and wrist quite well, but movements of the fingers were defective. Pain and swelling had gone but there was tenderness on pressure of the tissues in the region of fracture and also tenderness on pressing the palm of the hand.

Three weeks after the accident she was still nervous and morbidly emotional and sleep had not been restored. She was inclined to weep, and was worried about the possibility of interference with her prospects as a pianist.

The condition of the hand at this date is illustrated in Figs. 7, 8, 9 and 10. They are typical for paralysis of the intrinsic muscles of the hand supplied by the ulnar nerve.

Fig. 7 shows atrophy of the thenar and hypothenar eminences with slight flexion of the ring and little fingers; Fig. 8 atrophy of the dorsal interossei and slight flexion of the ring and little finger; Fig. 9 failure to extend the ring and little fingers when the fingers are flexed at right angles to the palm, thus showing paralysis of the inner lumbricals (supplied by the ulnar); Fig. 10 voluntary semi-flexion of all the finger joints, showing that the ulnar supply to the flexor profundus digitorum was not involved.

The ulnar branch to the flexor carpi ulnaris had also escaped and there was no anaesthesia.

The paralysis was thus confined to a group of small muscles concerned in the highly specialized functions of manual dexterity. It was only a selection of the fibres of the ulnar that were concerned in the defect. The fibres relayed

to the larger muscles, the flexor carpi ulnaris and the flexor profundus digitorum, in the forearm, as well as the cutaneous fibres were functioning normally.

The electrical reactions of the muscles involved showed a reduction to faradism, a normal reaction to galvanism and no inversion of polarity. This in

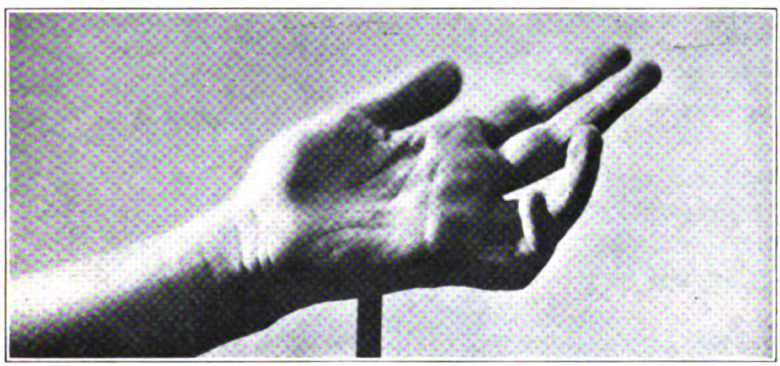

FIG. 7.—Case 4 : Palmar view of ulnar paralysis three weeks after accident.

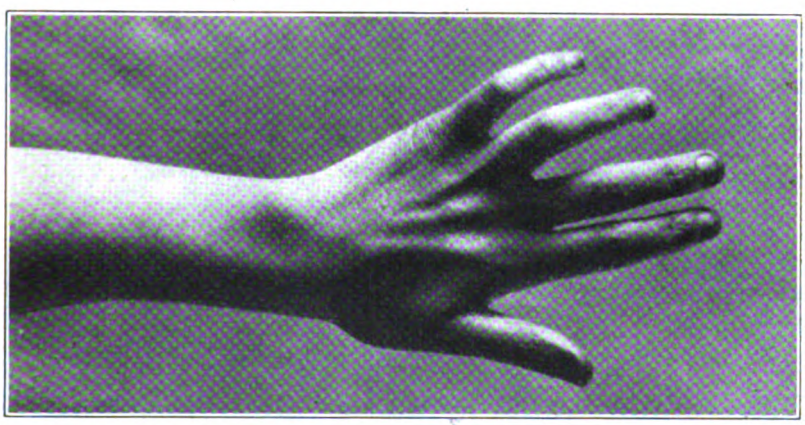

FIG. 8.—Case 4 : Dorsal view of ulnar paralysis three weeks after accident.

itself is significant, for the external appearances and defect in function as shown in the photographs point to a state which cannot be distinguished from that due to organic paralysis of the muscles, yet the reactions were not those which are characteristic for organic degeneration.

Should it be suggested, in spite of this, that the ulnar nerve might have been involved at the elbow, either by extension of the reaction from the seat of fracture, or by some independent trauma or pressure at the time of the

accident, the answer to that is this: while the nerves to the larger muscles may have already been separated from the main trunk, it is not likely that they

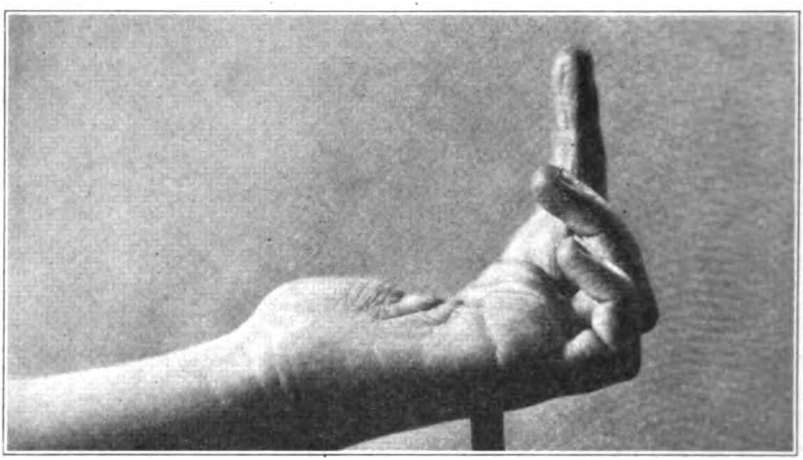

FIG. 9.—Case 4: Posture of hand showing paralysis of inner lumbricals three weeks after accident.

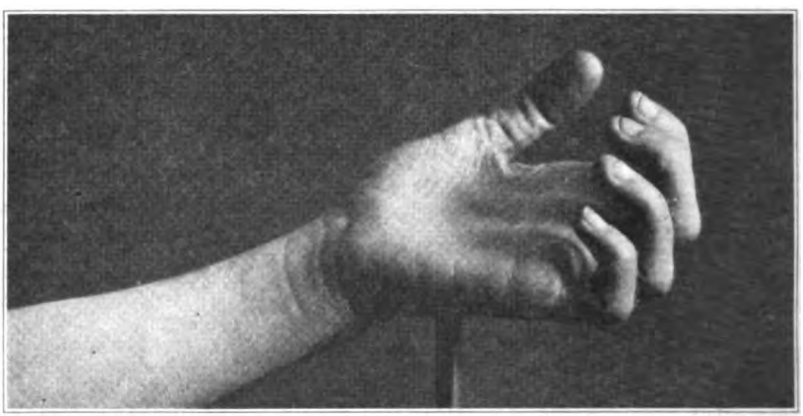

FIG. 10.—Case 4: Posture of hand showing retained function of inner parts of flexor profundus digitorum three weeks after accident.

would escape the local pressure or damage, and still less likely that the sensory nerve should escape. In any case the electrical reactions point to a paralysis of the hypotonic type, recognized in reflex disorder, and distinguishable from the form of paralysis due to organic nervous disease. She was given assurance that the tests had shown that no serious damage had been done by the accident. She had electrical treatment and massage, and was encouraged to practise

active movements. In four months the hand had regained its form and its functional activity had returned to a large extent.

In this case, while there was no history of mental abnormality prior to the accident or evidence of aberration, or indication of dissociation of personality after it, she obviously got a severe shock. The emotional reaction was profound, and it is significant that it should have reached a climax only some days after the fall. So far from contributing to recovery by a hopeful acceptance of the situation she began to ruminate on the prejudicial effects on her professional career as a pianist.

The outstanding features of the case are :

(1) A dissociated ulnar paralysis which cannot readily be explained by mechanical effects on the nerve trunk from the fracture of the radius.

(2) The absence of electrical reactions characteristic for organic paralysis.

(3) The incidence of excessive emotional reaction and anxiety about the use of the hand after the shock of the accident.

(4) Gradual recovery when she became more assured of the future and was able with confidence to co-operate in the treatment.

There is reason to believe that here, as in the previous cases, the cortical centres of manual dexterity were involved in the dissolution of nervous integration. These psycho-motor areas were the source of currents of nerve impulses which contributed to disorder in centres of the cervical enlargement, already deranged by shock from the injury to limb. In this physiological setting the psychic processes of morbid attention may be said to have been a determining factor in the disorder of function.

Case 5.

J. G—, aged 28, a miner, had the little finger of the left hand crushed by the fall of a stone. The tissues were contused, the skin broken and the wound became septic. From the start he suffered acute pain, and though the inflammation did not spread to the rest of the hand, three months elapsed before healing took place. He was restless and sleepless, and the pain, which was at first confined to the damaged finger, became referred to the whole hand. A fortnight after the accident the middle and ring fingers became fixed in flexion and the pain disappeared at the same time. He could move the thumb and index finger, but said he had "no feeling" in the other parts of the hand (Fig. 11).

The hand was fixed in extension, but immediately on removal of the splint it resumed its former posture. There was no pain during the extension and the skin was insensitive over the inner half of the hand and on the inner side of the forearm in its distal part. There was thus a complete ulnar anaesthesia. There was no muscular atrophy. Repeated attempts by splinting and by manipulation failed to restore movement or sensation.

Six months after the accident the hand was still in the condition indicated in Fig. 11. The little finger was stiff in extension, remaining immobile from damage to its structures. The middle and ring fingers which were not immediately affected by the injury were in a state of hypertonic contraction. These fingers as well as the associated area of the hand were anaesthetic except for a disturbing feeling of coldness. The skin was blue and he always wore a glove. The other two fingers were mobile and had feeling. He was sleepless, nervous and depressed. He was anxious about the settlement of his compensation claim, and was convinced that the hand would never be of any use to him.

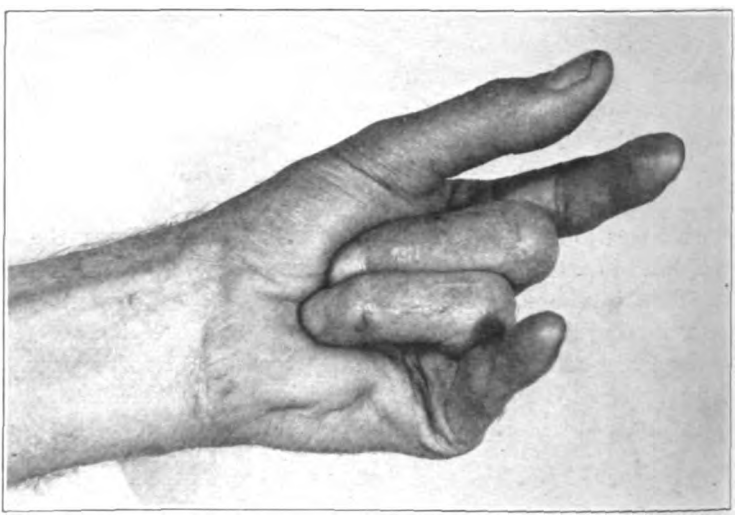

FIG. 11.—Case 5: Posture of hand six months after accident. Thumb and index finger were mobile.

He was given atropine and hyoscine in small doses at short intervals with a view to reducing his tension, and to induce if possible distraction of attention from concentration on his state. On the fourth day he was slightly confused and the fingers were manipulated frequently. This could be done easily on account of the anaesthesia. On the sixth day he said he had feeling in the metacarpo-phalangeal joints of the two contracted fingers. Two days later it returned to the proximal and on the following day to the distal interphalangeal joints. Return of sensation in the joints was accompanied by progressive restoration of cutaneous sensation with the exception of that to the little finger.

Massage and manipulation were continued, and he was encouraged to do active and passive movements himself. The change that took place, especially the return of sensation, proved interesting and even exciting to him, and there was no difficulty in securing his full co-operation in the treatment.

Meanwhile he had been assured that his compensation claim would be settled. His sleep gradually improved and the restless nervous anxiety disappeared. Six weeks after the commencement of the treatment he was able to extend the fingers fully (Fig. 12) and to shut the hand (Fig. 13). It will be seen from the illustration in extension that the proximal interphalangeal joints of the ring finger and little finger are swollen. This arthritic condition is interesting as manifesting a special reaction in the reflex disorder confined to the ulnar area. The illustration of the closed hand (Fig. 13) is misleading in that it shows the little finger in flexion. This flexion is artificially produced by

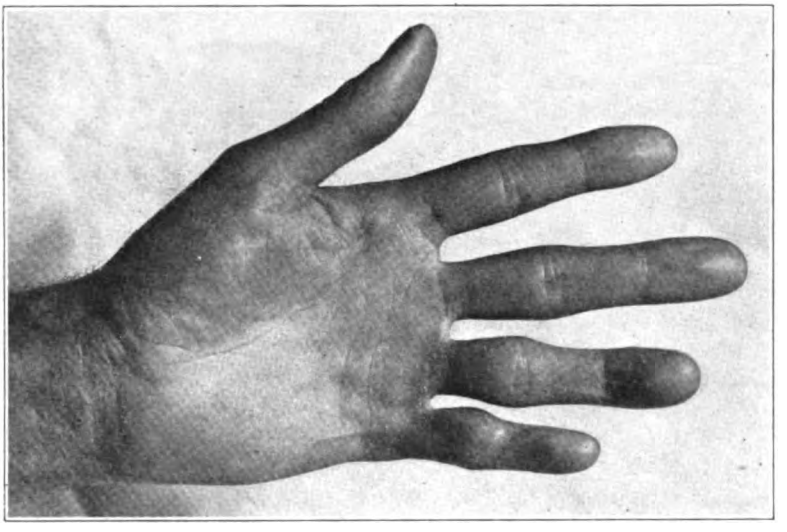

FIG. 12.—Case 5: Extension of hand after six weeks' treatment. Swelling of proximal interphalangeal joints of ring and little finger.

pressure from the ring finger holding down the little finger, for the little finger was so damaged by the injury that the interphalangeal joints remained fixed, and he was never able to flex it more than 45° to the palm as depicted in Fig. 11.

By practice the hand became quite useful, though even at the end of a year it was blue and uncomfortably cold in cold weather, so that he continued to wear a glove in these conditions. His general health improved without interruption and he returned to work.

There is no difficulty in recognizing features which the case had in common with the others which have been described. A local injury admittedly severe, though confined to the little finger, was followed by reactions which spread to other parts of the hand. This spread was not due to inflammation but to an anomalous circulation of nerve impulses in the region supplied by the trunk of the ulnar nerve, of which only small terminal branches had been involved

in the injury. There was no muscular atrophy or atony; on the contrary there was hypertonic contraction of the flexors of the fingers adjacent to the injured one, and in addition, throughout the parts supplied by the nerve, a loss of sensation with the curious exception of abnormal feeling of cold. In addition there was vasomotor disturbance. These morbid reactions point to a reflex disorder due to dissolution of integration in the centres in the cord. An excess of motor impulses and a deficiency in sensory impulses imply an infringement of the physiological laws of reflex action, a process which can be explained, if it can be explained, only in terms of pathological physiology. This derangement

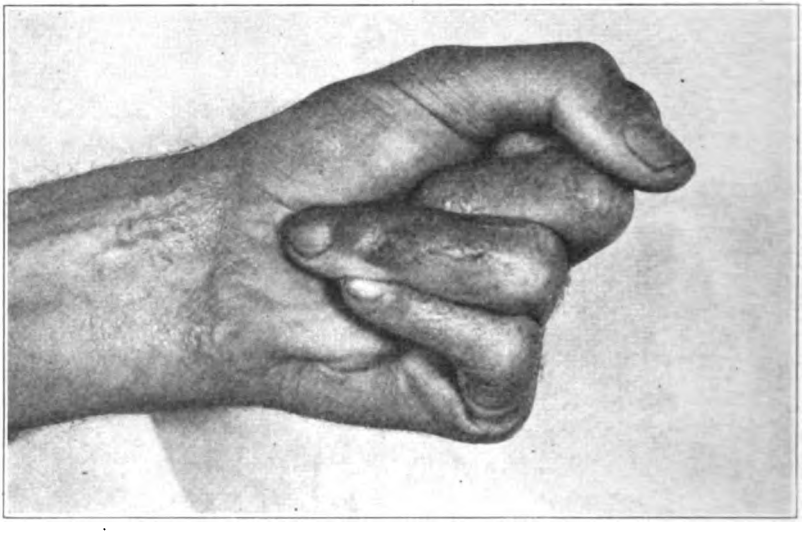

FIG. 13.—Case 5: Flexion of hand after six weeks' treatment. Little finger held down artificially by flexion of ring finger.

of the nervous economy by excessive production and faulty distribution might be the subject of investigation by modern methods of electrical physiology, but so far, it may best be conceived as suggesting an analogy to the "breakdowns" that occur in the economics of industry when production and distribution get out of control.

The evidence of a cortical or psychic element in the case is not difficult to find. He was a simple, rather poorly developed man. Nervousness, sleeplessness, anxiety and preoccupation with his hand were obvious. It was not only that it was useless, but its uselessness was the measure of the compensation which he estimated as his due. It was the object of morbid concentration of attention which impeded any attempt to contribute to recovery. When measures were adopted to distract the morbid attention and he was enabled to take a personal interest in the restoration of function, improvement went

on to a stage which conformed with the destruction of tissue due to the injury. The anaesthesia in the hand was typical for what is usually regarded as a functional or hysterical reaction. Its mode of recession, with gradual return of sensation from proximal to distal joints, indicated a process of redintegration in which psycho-motor activity played a part. There can thus be little doubt that in this case also the reflex contracture was the expression of a widespread disorder of the nervous system in which the psycho-motor area as well as the cervical enlargement were involved, and that morbid concentration of attention was a determining factor in the syndrome.

Summary.

Cases have been selected and described with a view to illustrating the part that may be played by morbid attention in nervous disorder. It was suggested, to begin with, that the classical theories devised to explain the relations between mind and body do not provide a suitable framework for clinical reference. The history of medicine however bears testimony to the manner in which disease itself may reveal the secrets of average biological processes. The psychic process of morbid attention was chosen as a clue to elucidate certain so-called "reflex disorders" in a limb, a condition which came into prominence during the last war and which was the subject of a special study by Babinski and Froment. These authors maintained that the condition was distinct on the one hand from hysteria, according either to the older or later conception, and on the other from organic nervous disease as commonly understood. They regarded it as a peculiar phenomenon, not easily explained, somehow associated with derangement of spinal reflexes, but "not due to hysteria" because "objective signs independent of the will had been discovered." The present study challenges that view, and evidence is produced to show that the higher cortical centres related to mental activity are involved in the morbid reactions.

The mental activity of attention is regarded as being essentially motor, spontaneous in some respects and voluntary in others. Its physiological basis, as set forth by Sherrington, is described shortly, and this is supplemented by references to the conception of innervation as a circulation of nerve impulses adjusted under average conditions to the co-ordinate movements of the body. Failure or derangement of this circulation by abnormal "drainage" may give rise to anomalous reactions which cannot be explained on physiological principles. The incidence, character and course of reflex disorder can be understood only in the light of pathological physiology.

Morbid concentration of attention is something more or other than suggestion, though suggestion may be a factor in its incidence. It implies a sustained deviation of nerve impulses to aberrant ends, and these ends may involve behaviour as a whole in relation to surroundings, as in paranoia, hypnotism, mesmerism, or dual personality; or it may be directed to particular ends as in

reflex disorders. The biological processes of nature, instead of tending to accommodation, end in chaos.

Case 1 illustrates the conversion of memory images, through morbid concentration of attention, into aberrant trains of psycho-motor activity which found expression in dissociation of personality.

Case 2. already the subject of dual personality, meets with an accident to an arm and his tendency to dissociation is expressed, through morbid concentration on the limb, in reflex contracture with associated pain and vaso-motor disorder. Ischaemic paralysis and the features it has in common with reflex disorder are discussed.

Cases 3, 4 and 5 are typical instances of reflex disorder in which there was no history of mental instability prior to the accidents. The reactions were not what should have been expected. They were paradoxical in character and out of all proportion to the injury. Though all depended on dissolution of spinal integration each had its own distinctive features. In Case 3 the whole hand was immobilized by hypertonic contraction of muscles with no atrophy. In Case 4 there was hypotonic atrophy (not organic) of the intrinsic muscles of the hand supplied by the ulnar, whose sensory branches as well as those to the muscles of the forearm retained their function. Case 5 showed a fantastic deformity of the hand due to hypertonic contraction of flexors of the middle and ring fingers, with no involvement of muscles which moved the thumb and index finger and the wrist. Though there was no history of mental abnormality prior to the accident, each case showed signs of nervous instability during the syndrome. There was morbid concentration of attention on the limb, and on what it was supposed to mean. Distraction of this concentration was accompanied by an interest in recovery and the co-operation necessary to secure that end.

The sensory aspect of reflex disorder has not been examined in detail, though pain, thermal disturbance and vasomotor irregularities have been mentioned in the clinical descriptions. The psychic process of attention has been viewed as motor, and this for the simple reason that the teaching of Sherrington affords the most reliable approach by which a solution of the problem could be attempted. That motility and sensibility are but different aspects of the same process is fundamental, and the relation of sensation to attention is a guiding principle in clinical medicine. John Hunter, among the greatest of biologists and clinicians, said that one of the best ways of relieving pain in a gouty toe was to concentrate attention on a finger. Referring to his own sufferings from angina, he writes: "When I had the spasm in my heart upon the smallest exertion of the body, as in walking up a small ascent, or upon the least anxiety about an event, such as bees swarming, yet I could tell a story that called up the finer feelings, which I could not tell without crying, obliging me to stop several times in the narration, yet the spasm did not in the least take place (then). Therefore those feelings of the mind we have for other

people are totally different operations of the mind from the anxiety about events, whether of our own or of others ; *because its effects on our bodies are very different*" (12).

We are indebted to the records at the Victoria Infirmary, Glasgow, for many of the details used in the descriptions.

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THE MODERN TREATMENT OF EPILEPSY:

A CRITICAL SURVEY, WITH SPECIAL REFERENCE TO SODIUM DIPHENYL HYDANTOINATE AND A COMPARISON OF ITS EFFECTS WITH THOSE OF OTHER ANTICONVULSANTS.

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EPILEPSY is as old as history. To the ancients it was a sacred disease, each convulsion signifying a visitation of its victim by one of the gods. Hippocrates first seriously attributed epilepsy to material causes, but the light of scientific approach which he momentarily kindled was soon extinguished, and for centuries the mysteries of epilepsy remained shrouded in a cloud of mysticism and religious cult, and if treatment was administered at all it usually consisted of incantations and spirit-exorcising rituals. In the modern era of medicine scientific battle has been joined with this disease in common with all others, and since the epileptic, like most other sufferers, is liable to an exacerbation of his disease in times of mental and physical stress, the present human warfare cannot but render more important than ever successes in the therapeutic field against epilepsy.

One of the main difficulties in the treatment of idiopathic epilepsy has been our comparative ignorance of its aetiology and pathology. Thus, although attention has been paid to such general treatment as diet, exercise, psychotherapy, etc., the chief line of attack has been through the use of anti-convulsant drugs, whose criterion of success has been entirely empirical.

The use of anticonvulsant drugs in treating epilepsy has developed in three phases: (1) the use of bromides, (2) the use of barbiturates (luminal and prominal), (3) the recent introduction of sodium diphenyl hydantoinate (epanutin, dilantin sodium).*

The reported successes of the latter drug, which was put on the market less than two years ago, appear in many respects epoch-making. The verdict is not yet final, however, and, as a warning against premature conclusions, it is

* For the purposes of this article it is important to realize that the following terms are used synonymously (B.P. = British Pharmacopoeia; prop. name = proprietary name):

1. 5-Phenyl-5-ethyl barbituric acid = phenobarbitone (B.P.), luminal (prop. name).
   Gardenal is another prop. name in use.
   Phenobarbital is the American synonym.
2. Sodium-diphenyl hydantoinate = epanutin (prop. name).
   Dilantin or dilantin sodium are the American synonyms.
3. N methyl-ethyl-phenyl barbituric acid = prominal (prop. name).

well to remember the excessive claims and enthusiasms with which modern treatments for certain other psychiatric diseases have been hailed. Before the potentialities of this drug can be finally assessed further observations of two different types are required :

(1) Clinical observations of its anticonvulsant and toxic properties in many patients over a prolonged period.

(2) Experimental work throwing light on its pharmacological actions.

This paper is written with the object, firstly of presenting personal work along both these lines, and secondly, of combining my own findings with those reported in the literature in an endeavour to reach accurate conclusions regarding the drug as far as present knowledge extends. With this object in view the material will be dealt with under the following headings :

(*a*) The scope, method and results of my personal investigations.

(*b*) A review of the literature published regarding it.

(*c*) A comparison of its properties with those of other anticonvulsants.

(*d*) A discussion of its true place in the treatment of epilepsy.

PART A1.

Personal Observations on Cases Treated with Epanutin for over a Year.

I first started using epanutin in the treatment of epilepsy early in 1939. For one reason or another many of the patients who originally received the drug are no longer doing so, so that whereas originally 29 male and 7 female patients were put on it, only 13 male and 7 female have received a full year's treatment. These patients have been submitted to various routine tests at the end of this period. The results of the whole investigation are presented forthwith.

Clinical Observations.

The cases comprising the present series were all chronic epileptic psychotics who had mostly been resident in Cane Hill Mental Hospital for many years, and who all remained there throughout the period of the present investigation. Consequently, although they had the disadvantage of chronicity and a high average age, they had the advantage of continuous observation throughout treatment. The latter fact was particularly useful from the point of view of accurate observation of the frequency of fits, change in weight, etc.

The ages of the 29 male patients varied from 28 to 69, with an average of 42·8 years. The female limits were 26 to 60, with an average of 37·8 years. The fact that all seven females remained on treatment throughout the year, whereas there was such a large reduction in the number of males who survived the full year on epanutin, is probably accounted for by the fact that the female cases were carefully selected individually as having responded badly to other

treatments, whereas for purposes of research all male epileptics, except the very feeble patients (no matter what their previous treatment), were changed to epanutin. Consequently, when serious toxic symptoms developed in the latter it was frequently considered unwarranted, owing to their age and chronicity, to try epanutin again once they had recovered.

The reasons for cessation of epanutin treatment in 16 patients were as follows:

Acute exacerbation of fits		2
Toxic symptoms:		
Severe and prolonged confusion	4	
Ataxia	2	
Psycho-somatic delusions	2	
Psycho-pathological depression	2	10
Deaths (not proven as due to the drug)		4

Of the patients who remained on the treatment several had at one time or another experienced complications, as follows:

Acute exacerbation	1
Severe and prolonged confusion	2
Ataxia	2

Thus, of the total 36 patients 21 developed severe nervous toxic symptoms (i.e. 58·3 per cent.), but none developed skin eruptions, hyperplasia of the gums or any other toxic manifestations.

Dosage, Tolerance and Toxicity.

Dosage was regulated according to previous medication, one capsule of epanutin being considered equivalent to 1½ gr. of luminal or 15 gr. of pot. brom. Thus, some cases commenced on two capsules *per diem*. Even on this dosage three cases developed toxic symptoms. Most of the cases were symptom-free on three capsules *per diem*. However, one female patient, whose fits were reasonably well controlled on two capsules *per diem*, developed a rolling ataxia as soon as she was tried on three capsules; another patient who had complained of various subjective sensations on two capsules became much worse on three capsules, and two patients developed confusion (one after several weeks and the other after several months) on three capsules a day.

The majority of toxic manifestations occurred when an increase was made from three to four capsules a day. Of the nine patients put on to four capsules a day seven developed severe toxic symptoms. Three tried on five capsules a day all developed a very marked ataxia. One of the cases showing toxic symptoms on four capsules tolerated a re-introduction later on, and one of the cases ataxic on five capsules subsequently had his fits reasonably well controlled on four capsules, on which he was free from toxic symptoms.

It is of importance to note here that symptoms that are definitely due to

the toxic action of the drug occur soon after the change-over to epanutin, or an increase in its dosage. They are to be differentiated from exacerbations of fits and confusion occurring later on in the therapy (see below). Many cases seem to acquire an increasing tolerance, so that some patients who have developed toxic symptoms may remain symptom-free on a re-introduction of epanutin in the same dose or one capsule less.

It was soon found that the controlling dose of epanutin did not necessarily bear any relation to the previous dose of luminal. One case, for instance, who had been free from fits for many years on mist. sodii luminal, gr. 1 *nocte*, had several fits during his three months on epanutin, two capsules per *diem*, which culminated in a bout of seven fits in three days. During these, epanutin was increased to three capsules a day, and since then (nine months ago) the patient has had no further fits. This case is of great importance as an example of an exacerbation following an increase of fits during epanutin treatment as opposed to those occurring during previous medication (luminal, etc.). The right treatment is to increase the dosage. This is in contrast to the treatment of exacerbations following a complete freedom from fits during epanutin treatment (see below), in which case complete withholding of the drug is indicated.

Exacerbations of Fits and Symptoms.

There occurred four cases of a marked exacerbation of fits following a long period free from fits (or with a marked reduction in fits), due to epanutin therapy. It might be thought that the correct treatment on these occasions would be an increase of epanutin, but this was tried in each case and was found to lead to an increase of fits. In one case which I have already published (Blair, 1940) an associated hemiplegia occurred. Reduction of epanutin, on the other hand, led to a reduction of fits. It is obvious that if the fits become very frequent appropriate treatment with other sedatives (luminal, etc.) will be required.

Another symptom which occurred following a prolonged period free from fits was continuous confusion. In one case free from fits for a consecutive period of two months (where they had been frequent before transference to epanutin) confusion set in and continued in gradually increasing severity for four weeks until a reduction of dosage, from four to three capsules a day, led to a recurrence of fits twelve days later and a cessation of confusion. Four other cases of severe and continuous confusion occurred as long as 9, 11, and 12 weeks after the introduction of epanutin, during which time they had a reduction of fits compared with previous medication. These cases took as long as two weeks to clear up after epanutin had been withdrawn.

It seems probable that this type of confusion, occurring a considerable time after epanutin has been introduced, is due to a damming-up of the epileptic process by a raising of the threshold for fits, and is to be distinguished from the type which occurs immediately following the change to epanutin or an increase

of dosage and which is probably toxic in origin. Exactly why an increase of dosage should be so detrimental in such cases is not clear.

The Change-over.

This was effected in the males, broadly speaking, by replacing one dose of previous anticonvulsant by one capsule of epanutin every five days. An early increase of fits occurred in nearly all of these cases. It is now my practice to introduce epanutin gradually while retaining full doses of previous medication, and then gradually reduce the latter in stages, as was done with success in all the female cases.

Fatalities.

As has been noted, four cases died during the last year. It can be said straight away that no death was proven due to epanutin. In one case epanutin had been withdrawn long before death, which had no association with it. The circumstances of the other three cases are as follows :

CASE 1.—The patient was an old epileptic, aged 69, when he was transferred from mist. tribrom. *b.d.* to epanutin *b.d.* This was insufficient to control fits, and dosage was increased to *t.d.s.* He had only had few fits on mist. tribrom. (15 during the previous year), but on epanutin he was fit-free for eleven months on end, during which he had no untoward symptoms. At the end of this time he suddenly collapsed and died. He was known to have marked cardio-vascular degeneration before he was put on epanutin, and this was confirmed as the cause of death at post-mortem. This case may be considered as a vindication of epanutin rather than a condemnation, as witness no ill-effects in such an old and feeble person one during year's treatment.

CASE 2.—This was a dull and deteriorated schizophrenic, aged 42, who had developed epileptic fits six years previously. Epanutin (one capsule *t.d.s.*) did not control his fits better than phenobarbitone, gr. 1 *b.d.*, had done. After seven months on epanutin he suddenly had a bout of seven fits in a row. Following them he remained confused and restless, and after two further fits died. Post-mortem showed myocardial degeneration and congestion of the lungs, and nothing suggestive of epanutin's responsibility for death could be found. The fact that he developed no toxic symptoms during epanutin medication further exonerates the drug.

CASE 3.—This patient had been in hospital for 25 years previous to epanutin treatment. He was aged 59 at the time of being changed from luminal, gr. 2 *b.d.*, to epanutin, one capsule *t.d.s.* He had only had 20 fits during the year immediately prior to epanutin, and although he had a typical epileptic temperament, he had been well behaved and quite a good worker for some time. Three weeks after being solely on epanutin he had a bout of confusion following a fit. This was accompanied by religious delusions, which he had never exhibited before. He kept wandering round the room, saying "Spare us all," a thing he had never done previously. A week later he complained of being gassed, having no use in his arm, lockjaw of the face and inability to see. He was taken off epanutin and put back on luminal. The following day he had two strong major fits, during the second of which he died. Post-mortem revealed some cardio-vascular disease.

In the last case it must be admitted that there is some doubt as to the exact part played by epanutin. This, and the fact that other cases who have had

psycho-somatic delusions have seemed to fare badly on epanutin and nearly all had to be put back on their previous medication, indicate the following precautions:

(1) When a bout of fits occurs during epanutin treatment withdraw the epanutin and replace by luminal or bromides. The fact that these may require some days of accumulation before they act to their full may necessitate the concomitant use of other sedatives, such as paraldehyde, etc., in the early stages.

(2) Psychosomatic symptoms (of lockjaw, uselessness of an arm, etc.) must be considered very serious, and temporary or permanent withdrawal of epanutin and substitution of alternatives instituted in the manner suggested above.

Other Toxic Symptoms of the Central Nervous System.

Psychosomatic symptoms developed in other cases; personality of the patients soon became upset and they complained of an unpleasant "feeling of difference" from their usual selves. The best simile that can be given is the feelings frequently complained of by patients having cardiazol therapy when an injection fails to produce a fit.

One patient, who had two years previously attempted suicide, soon had a revival of such inclinations when put on epanutin, although he had been absolutely free from them for three years on luminal treatment. This patient was subject to very few fits.

Toxic Symptoms of Other Systems.

In none of the present series did gastro-intestinal or cutaneous symptoms occur. Hyperplasia of the gums did not occur in a single case and no case developed a hyperpyrexia.

Anticonvulsant Effects.

The fact that the male patients were so old and chronic made results, such as some of those already enthusiastically published, extremely unlikely. The prognosis in the females was more favourable and the effect of the epanutin more beneficial.

Table I represents the state of affairs in the 20 cases which have been on epanutin for not less than a year. The number of fits occurring while on epanutin for twelve months is contrasted with those occurring in the three years immediately prior to its use. The temporary increase in fits occurring in some cases immediately after complete substitution of epanutin is omitted in these figures, otherwise all fits are included.

TABLE I.—*Frequency of Fits in 20 Patients during a Year on Epanutin as Opposed to those Occurring in these Patients on Other Treatments in Previous Years.*

Case No.	Age.	Fits.			Epanutin.		Grading.
		1936.	1937.	1938.	12 months on epanutin.	Longest period free from fits.	
				Males:			
1	53	27	35	34	6	11 months	CR.
2	40	76	69	59	16	3 ,,	GD.
3	38	112	83	86	19	2 ,,	,,
4	42	69	68	52	24	3 ,,	MD.
5	36	65	58	59	28	..	,,
6	45	56	31	42	21	..	,,
7	36	Admitted 1938	..	79 (9 months)	35	..	,,
8	67	69	39	22	16	..	SD.
9	65	24	26	26	24	..	NC.
10	45	0	0	0	2	..	,,
11	38	0	0	12	6	..	,,
12	60	24	20	12	19	..	,,
13	49	9	3	4	14	..	W.
				Females:			
14	60	92	83	69	7	7 months	GD.
15	46	65	35	30	11	3 ,,	,,
16	33	49	22	16	5	9 ,,	,,
17	35	62	45	40	9	8 ,,	,,
18	32	62	68	22	22	3 ,,	,,
19	26	95	141	135	85	..	SD.
20	33	94	85	105	99	..	NC.

CR = Complete relief; GD = great decrease (75 per cent.); MD = moderate decrease (50 per cent.); SD = slight decrease (25 per cent.) (see text); NC = no change; W = increase.

If we use the following definitions of gradings the meaning of the results will be obvious.

Complete relief: No fits during the last six months.
Great decrease: A reduction by more than 75 per cent.
Moderate decrease: Any reduction of between 50 and 75 per cent.
Slight decrease: A reduction of between 25 and 50 per cent.
No change: No increase or decrease of less than 25 per cent.
Worse: An increase of over 25 per cent.

The reason for making "complete relief" apply to the last six months only was to allow all cases six months for trial *re* dosage, etc. Of the 20 cases only one (5 per cent.) was "completely relieved"; six (30 per cent.) showed great decrease, and of these one had had a consecutive period of nine months free from fits, one eight months, one seven months and three three months, after which one or two fits had recurred in each case; five (25 per cent.) cases

showed moderate decrease; two (10 per cent.) slight decrease; five (25 per cent.) no change and one (5 per cent.) was worse. Comparison is made with the average number of fits for the previous three years.

The contrast between the male and female results is obvious. Of the seven females, four were "greatly decreased," one moderately, one slightly, and the case with "no change" would have ranked in the "greatly decreased" group had it not been for an exacerbation of over 50 fits in a few days. Judging from these figures one may conclude that the outlook is better in younger and not too chronic cases, but that, providing adequate care is taken of the indications for abandoning treatment, excellent results are sometimes obtained in old patients (over 60) as well.

In every case except one reduction in fits refers to *grand mal* seizures In the exceptional case the fits were of an equivalent type (Case 17). Minor fits in all cases prior to treatment were so infrequent as not to warrant special consideration. In one case (No. 19) following a reduction in *grand mal* fits minor ones were more frequent. In another (No. 14) with a marked reduction in major fits, myoclonic jerkings without any loss of consciousness were found to develop, but these were not of a disabling nature.

Effects on Mentality.

Here, again, owing to the chronicity of the cases, comparatively little change was to be hoped for. This was especially so because they had all been well standardized on their previous treatment and none of them exhibited the drowsiness, etc., so often attributed to other drugs. Nevertheless, I am of the opinion that several patients benefited considerably, being more alert and amiable and less querulous, quarrelsome and egotistical. None of these 20 patients was rendered noticeably worse mentally.

Weight.

Comparatively little has been said regarding changes in weight during epanutin therapy. Since some practitioners complain of the reduction of weight produced by this treatment, the following findings seem of particular significance:

In considering changes of weight during epanutin therapy, certain factors must be borne in mind. Before any change can be considered due to epanutin one must rule out the usual fluctuations common to all patients. This is best done by comparison of changes in monthly weighing during the previous three years. This was done with all the 20 patients who had received treatment for over 12 months (see Table II).

Having established an unusual change of weight during epanutin therapy one has to consider whether the change is beneficial or harmful, and whether it can be considered as an indication of prognosis during epanutin therapy or

TABLE II.—*Change of Weights (expressed in stones and pounds).*

Case No.	Age.	1936.	1937.	1938.	Commencement of treatment.	Present weight.	Lowest weight during treatment.	Gain or loss.
1	53	9·5 – 9·0	9·5 – 9·1	9·8 – 9·2	9·0	8·0	7·11	– 4
2	40	8·3 – 8·0	8·0 – 7·11	7·11– 7·7	7·5	7·2	6·9	– 3
3	38	9·2 – 8·12	9·2 – 9·0	9·1 – 8·12	9·0	8·9	8·6	– 5
4	42	10·1 – 9·9	10·0 – 9·6	10·0 – 9·9	9·11	9·6	9·6	– 5
5	36	9·8 – 9·2	9·11– 9·7	9·8 – 9·4	9·6	8·10	8·9	– 13
6	45	9·7 – 9·1	9·5 – 8·13	9·4 – 8·13	8·11	8·3	8·3	– 10
7	36	..	..	8·2 – 7·7	7·13	7·3	7·0	– 10
8	67	9·8 – 9·4	9·8 – 8·13	9·5 – 9·0	8·13	8·7	8·2	– 6
9	65	10·3 – 9·10	10·5 – 9·8	10·8 –10·2	10·2	9·11	9·10	– 5
10	45	9·2 – 8·12	9·3 – 8·11	9·2 – 8·11	8·12	8·5	8·5	– 7
11	38	10·3 –10·0	10·0 – 9·7	10·3 – 9·11	9·13	9·4	9·4	– 9
12	60	10·1 – 9·10	10·1 – 9·13	9·12– 9·6	9·5	8·8	8·2	– 11
13	49	9·6 – 8·12	9·5 – 9·0	9·1 – 8·10	8·7	7·10	7·10	– 11
14	60	6·13– 7·2	7·4 – 6·12	7·13– 7·4	8·0	7·8	7·5	– 6
15	46	..	8·4 – 8·3	8·8 – 8·3	8·0	8·5	7·9	– 5
16	33	8·0 – 6·13	8·0 – 6·13	7·4 – 6·11	7·7	8·1	7·4	– 8
17	35	8·4 – 7·10	8·2 – 7·9	8·1 – 7·8	7·3	8·1	7·3	+ 12
18	32	7·4 – 6·12	7·0 – 6·11	7·11– 6·12	7·0	8·4	6·13	+ 18
19	26	..	6·12– 6·5	6·6 – 6·2	6·4	6·13	7·8	– 9
20	33	7·0 – 6·11	7·7 – 6·12	7·9 – 7·2	7·6	7·4	6·9	– 2

merely an incidental occurrence. For purposes of control comparison with epileptics on other drugs during the same period was resorted to.

The results of the 20 patients are recorded in Table II. It is seen that of these all the males lost weight and all the females, except two, gained weight. At first sight the state of affairs on the male side appears somewhat startling. One has to admit that, of the 13 cases, 11 were lower in weight than at any time during the previous three years. In 4 of these the weight had been decreasing before treatment started, so that the process might have occurred apart from the present treatment.

A point of importance is that in no case was the loss of weight sudden (after the introduction of epanutin). These patients were put on epanutin in March, 1939. The interesting fact is that by September none of them had lost more than a few pounds. The steady loss which continued in several cases may have been in some way influenced by war-time diet. This possibility is supported by the fact that in at least five control cases an exactly comparable drop of weight of 12, 10, 10, 9 and 7 lb. occurred. All the cases, both on epanutin and in the control group, seem to be gaining again now.

Case 1 is an illustrating example. He was put on epanutin in March, 1939 By September he had only lost 2 lb., but by January, 1940, he had lost a further 16 lb. During the last two months he has gained 3 lb. His loss may have been associated with a concomitant fall of blood pressure (see below).

A comparison of variation in weight with frequency of fits and complications produces no absolute correlation. However, it may broadly be said that a gain of weight is a favourable sign, and a persistent loss of weight is to be valued according to general physical condition, etc.

It is obvious that a minor reduction in weight may occur in association with mental improvement. The fact that many patients are more alert and active may produce this. This is not so in all cases, however, and sometimes, as in most of the female cases, increased vitality went with an increase of weight and general physical well-being.

No correlation was established between changes in weight and change in blood pressure, blood count, sedimentation tests, etc.

Changes in Blood Pressure.

These remained remarkably constant throughout treatment in the male cases. Unfortunately the female cases were not under my care in the early days of treatment, and since no record of blood pressure was kept, comparison was not possible. In the male cases it will be seen that variations of blood pressure were negligible except in two cases (see Table III). In Case 1, who was completely relieved of fits, there occurred a marked drop of blood pressure. The nature of this is, however, obscure and cannot, as yet, be in any way attributed to epanutin. In Case 9 there was an increase of blood pressure, but here again the patient was aged 65, had experienced no toxic symptoms and only a small loss of weight (5 lb.), and the rise in blood pressure is almost certainly due to progressive cardio-vascular degeneration and not epanutin. In the female cases all recordings are normal, except Case 15. Here the blood pressure is low, but again it cannot definitely be blamed on epanutin. It is more likely associated with her state of depression. This has been the most marked feature of her psychosis during her ten years in hospital, and she is on a suicidal caution ticket.

Laboratory Investigations and Their Relation to Clinical Progress.

Urine.

Examination of urines was made at the beginning of epanutin treatment, after a year's treatment on it, when serious complications arose, and at the time of the usual routine physical examinations. At no time was any significant abnormality found. At times there was an alkaline reaction which may have been associated with the alkaline nature of the drug, but on repetition of examination this was always found to disappear in a short time and in each case to be an occasional rather than a frequent occurrence.

In the female cases the same factors governed the times of examination as in the instance of blood pressures.

TABLE III.—*Blood Pressures and Blood Counts in 20 Cases Treated for One Year with Epanutin.*

		At the beginning.								After one year's treatment with epanutin.							
Case No.	Age	Blood pressure.	Total R.B.C. in millions.	Total W.B.C. in thousands.	Neutrophils.	Basophils.	Eosinophils.	Lymphocytes.	Mononuclears.	Blood pressure.	Total R.B.C. in millions.	Total W.B.C. in thousands.	Neutrophils.	Basophils.	Eosinophils.	Lymphocytes.	Mononuclears.
1	53	128/9	4·9	6·4	62	..	3	35	0	88/72	4·6	5·7	72	0	4	23	1
2	40	125/88	5·0	7·0	65	0	2	33	0	124/82	4·8	6·5	72	0	0	28	0
3	38	122/85	4·8	6·6	61	0	0	39	0	188/87	6·0	4·6	51	0	4	45	0
4	42	132/92	4·7	4·6	65	0	0	34	1	124/92	5·0	7·4	66	0	6	24	4
5	36	100/70	4·8	6·6	61	0	0	39	0	122/88	6·0	4·6	51	0	4	45	0
6	45	125/92	4·9	7·4	65	0	1	33	1	132/86	5·5	4·7	76	0	5	19	0
7	36	126/82	4·9	5·6	55	0	0	44	1	133/82	5·3	6·0	44	0	3	52	1
8	67	137/88	4·9	7·0	63	0	1	36	0	126/88	4·5	9·0	64	0	0	35	1
9	65	172/88	4·8	6·6	58	0	2	38	2	118/84	5·2	7·0	60	0	3	37	0
10	45	172/92	4·9	7·0	54	0	1	45	0	118/84	4·1	6·9	51	0	9	39	1
11	38	148/100	..	..	..	..	..	..	..	142/97	4·3	8·4	52	0	12	34	2
12	60	145/108	4·9	7·7	80	0	0	20	0	122/92	3·0	6·2	66	0	3	31	0
13	49	118/72	4·3	6·7	70	2	1	27	0	112/78	3·8	8·6	62	0	2	34	2
14	60	..	..	..	..	..	..	..	..	122/82	5·2	9·6	54	2	3	38	3
15	46	..	..	..	..	..	..	..	..	90/68	4·4	8·8	72	0	1	27	..
16	33	..	..	..	..	..	..	..	..	129/88	3·6	6·4	58	0	7	33	2
17	35	..	..	..	..	..	..	..	..	138/96	5·1	4·1	49	0	2	39	10
18	32	..	..	..	..	..	..	..	..	115/72	5·4	10·3	62	0	1	33	4
19	26	..	..	..	..	..	..	..	..	112/66	4·2	5·3	72	2	0	22	4
20	33	..	..	..	..	..	..	..	..	122/82	5·1	7·7	67	0	0	33	0

Blood Counts.

Owing to limitations of time it was not possible to perform regular fortnightly or monthly examinations as has been done by some authors. Counts were taken from the male patients at the beginning of the treatment, after a year on it, and at the times of serious complications. The same provisos apply to the female patients as in the blood pressure and urine recordings.

Table III represents the findings at the beginning of treatment and after a year. An examination of this shows at once that there is no gross abnormality that can be associated with epanutin. The only thing in the nature of a consistent change is an eosinophilia. Even this is not constant, and although nine cases have an eosinophilia of over 4 per cent., of these only four have one of over five cells per cent. Case 12 and 11 have a low red count. They have both lost considerable weight, the reason for which is not clear. The blood changes are probably of the nature of a secondary anaemia, which is not uncommon in epileptics not being treated with anticonvulsants.

Blood counts taken during severe toxic symptoms showed no change of note.

Blood Sedimentation Tests.

These were done on patients whose progress seemed particularly unfavourable (of Case 1 and Case 12, etc.). The rate was invariably found to be normal.

Summary.

The above investigation of 36 patients suffering from chronic psychotic epilepsy on epanutin treatment, of whom 20 remained on treatment for more than one year, emphasizes the following points :

(1) Toxic symptoms of the nervous system were frequent and usually severe. Of particularly ominous nature seemed psychosomatic delusions, revival of such psychotic symptoms as severe depression, etc. Toxic symptoms were not correlated with age and appeared more a matter of individual idiosyncrasy of the nervous system than other constitutional factors. No toxic symptoms of severity occurred in any other system.

(2) The reduction in fits in the 20 patients treated for a year was absolute in one case, over 75 per cent. in six cases ; between 50 and 75 per cent. in five cases and between 25 and 50 per cent. in two cases ; one case had a slight increase.

(3) Loss of weight was frequent, occurring in 15 out of 20 patients. Observations of a control group suggested that other factors, such as diet, were responsible for this rather than epanutin. Nevertheless, gain in weight seemed to be prognostically favourable and any considerable loss unfavourable.

(4) No change of blood pressure or composition of urine could be attributed to epanutin.

(5) Blood counts showed no evidence of agranulocytosis or severe blood changes. An eosinophilia of between 4 and 12 per cent. occurred in a few cases, and in two cases a reduction of red blood cells occurred.

(6) Toxic symptoms always occurred soon after introduction of epanutin or an increase in dosage.

(7) The nature of exacerbation of fits and confusion and their correct treatment is worthy of note (see text).

PART A2.

Some Observations on the Contrasting Effects of Sodium Diphenyl Hydantoinate (Epanutin) and Phenobarbitone (Luminal) on Cardiazol Convulsions in Human Beings.

The fact that the clinical trial of epanutin soon proved that, broadly speaking, some patients do far better on the first drug, some on the second, and others still on a combination of two, lends probability to the suggestion that the two drugs act in fundamentally different ways on the nervous system. From the early days of my experience with epanutin I have been on the look-out for observations that might confirm this experimentally, and thus devised the following experiment for comparing the effect of the two drugs on cardiazol fits in human beings :

Method.

This experiment originated in an attempt to combat the fear and agitation so often arising during cardiazol therapy. Luminal had been tried with little success and it was decided to try epanutin. At first, owing to its well-vaunted toxic complications, it was given in small doses which had little effect. Experience of its use in the treatment of chronic epileptics led to subsequent use of much larger doses. Failure of epanutin to produce any ostensible anticonvulsant effect on the cardiazol fits, even in large doses, prompted me to try the controlling effects of luminal, and the following plan was evolved and, as far as possible, adhered to :

(1) Each case treated was standardized on cardiazol to the extent of having had at least as many as four consecutive fits on the same dosage of cardiazol. (The usual method of inducing a fit every three days was employed.)

(2) The drug was then administered until it had produced failure of a fit to materialize on the same dose of cardiazol on four successive occasions.

(3) The anticonvulsant was then withdrawn and the same dose of cardiazol continued. If this now caused fits once more (on four successive occasions) it was considered as absolute proof of the anti-convulsant effect of the drug concerned.

Unfortunately the following limiting factors usually prevented the plan from being carried out in full :

(*a*) The difficulty of getting the type of case that remained standardized on a constant dose of cardiazol.

(*b*) The fact that even when this was done the governing criterion to the number of fits that were induced had to be the patient's therapeutic reaction to cardiazol and not that to the anticonvulsants.

(*c*) The very toxic effects of epanutin on certain epileptics, when given in high doses, made one wary of using more than four capsules a day. Thus five capsules were given for only three days (one injection) and six capsules for only a week (two injections).

(*d*) In some cases the experiment was only begun comparatively late in the course of cardiazol treatment.

Results.

These are expressed in Table IV.

Details of the individual cases are discussed below:

CASE 1.—Up to the tenth injection epanutin was given solely with the object of trying to relieve the patient's antipathy and fear of the injections. It failed to do so, and, after the 14th injection, the patient was put on to triazol. On this his subjective symptoms were not so marked and it was possible to complete the treatment. Epanutin in large doses was started after the 23rd injection, by which time the patient had started to complain again. It had very little effect, and by the 29th injection it was considered necessary to terminate the treatment in the near future owing to the patient's protestations and failure to benefit therapeutically. In view of the fact that epanutin had failed to produce any anticonvulsant effect in doses of even six capsules *per diem*, a change to luminal, gr. 1½ *b.d.*, was made in the hope of observing an immediate contrasting effect—a hope which did not materialize.

CASE 2.—Epanutin was given in large doses only. The remarks regarding luminal in the first case apply in this case also. The fact that the 26th injection failed to produce a fit cannot in itself be considered significant, especially as the second injection of luminal (28th) failed to do so as well. Treatment had to be stopped for the same reasons as in the first case.

CASE 3.—This was the best case of all. Owing to the patient's continuous, if slight, improvement and his indifference to the fits, it was possible to continue the treatment without any setbacks. The contrast between the failure of epanutin (in doses of up to six capsules *per diem*) to have any effect on the cardiazol fits, and the complete arrest of fits on luminal (gr. 1½ *b.d.*) under the fully stipulated conditions, speaks for itself.

The subsequent prevention of three fits out of four injections on prominal (two tablets *per diem*) is also noteworthy. Unfortunately this is the only case where the opportunity to use prominal under the desired conditions arose.

CASE 4.—Epanutin in large doses had no anticonvulsant effect. Luminal was sporadic in its action, but the fact that in doses of gr. 1½ *t.d.s.* it prevented fits in two out of five injections, and in two out of three injections when the dose was increased to four times a day (i.e. gr. 1½ *q.d.s.*), showed that it did at least have some definite effect.

CASE 5.—In this case epanutin had no anticonvulsant effect in a dose of four capsules *per diem*. The method already mentioned had not been fully devised when this case was treated, so that the fact that the increased dosage of epanutin to five and six capsules led to an increase of the amount of cardiazol necessary to produce a fit is not conclusive. This may have been a chance occurrence, as shown by the further rise in dosage (at the 22nd injection) after epanutin had been withdrawn. The persistently sporadic reaction of luminal 1½ gr. *b.d.* gave place to a complete cessation on gr. 1½ *t.d.s.* The fact that this was due to luminal was substantiated by the occurrence of another fit on the same dose of cardiazol when the luminal was withheld (39th injection).

CASE 6.—The inhibiting effect of the luminal on four successive injections of cardiazol is seen. The absence of anticonvulsant effect of epanutin gr. 1½ *b.d.*, i.e. one capsule twice a day, is also demonstrated. It is a pity that the dislike of the

TABLE IV.—*Showing the Varying Effect of*

Number of injections	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Case 1:																		
Convulsant	C4	4	4 + 5	5·5	5·5	5·5	5·5	5·5 + 6·5	6·5	6·5	6·5	6·5	7·5	7·5 + 7·5	T1·6	1·8	1·8	1·9
Result	+	+	+	+	+	+	+	+	+	o	+	+	+	+	o	−	o	−
Anticonvulsant	..	..	E1	1	1	1	2	2	2	..	..	..	..	..	..	..	..	..
Case 2:																		
Convulsant	C4	5	5	5	5	5	5	6	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Case 3:																		
Convulsant	C6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	E4	4	4	4	5	6
Case 4:																		
Convulsant	C5	6	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	E4	4
Case 5:																		
Convulsant	C5	6	6·5	6·5	6·5	6·5	6·5	6·5	6·5 + 6·5	6·5	6·5	6·5 + 6·5	7	7	7	7	7	7
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	E4	4	4	4	4	5
Case 6:																		
Convulsant	C5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	o	o	o	o	−
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	..	L2	2	2	2	..
Case 7:																		
Convulsant	C4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	−	−
Anticonvulsant	..	..	..	..	..	L2	2	..	..	..	3	3	3	3	3	4	4	4
Case 8:																		
Convulsant	C4·5	4·5	4·5 + 4·5	5 + 4	6	6 + 4·5	6·5	6·5	6·5	6·5	6·5	6·5 + 6·0	7	7	7	7	5	5
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	o	D	o	−	+
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	..	L2	2	2	..	..
Case 9:																		
Convulsant	C 5 + 5	6	6	6 + 5	7	7	7	7	7	7	7	7	7	7	7	5	5 + 6	6
Result	+	+	+	+	+	+	+	+	+	+	+	+	o	o	o	+	+	−
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	L2	2	2	..	..	..
Case 10:																		
Convulsant	C5	5	5	6	6	6	6	6	6	6	6	6	6	6	6	6	..	..
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	..	..
Anticonvulsant	..	..	..	..	..	..	E1	1	1	1	1	1	2	2	2	2	..	..
Case 11.																		
Convulsant	C5	5	5	5	5	5 + 5	5 + 5	6	6	7	7	7·5	7·5	7·5	7·5	7·5	7·5	7·5
Result	+	+	+	+	+	+	o	+	+	+	o	+	+	+	+	−	−	−
Anticonvulsant	..	..	..	..	..	..	..	..	..	..	..	..	..	E1	1	1	1	1
Case 12:																		
Convulsant	C5	5	5	5	5 + 4·5	5 + 4·5	5 + 6	6 + 7	7 + 8	8	8	8	8	8	8	..	..	..
Result	+	+	+	+	+	+	+	+	+	+	+	+	+	+	o	..	..	..
Anticonvulsant	E	..	..	..	..	..	..	..	..	1	1	1	1	2	2	..	..	..

C = Cardiazol (in c.c.). E = Epanutin expressed in number of capsules *per diem*.
T = Triazol (in c.c.). L = Luminal „ „ gr. 1½ tablets *per diem*.

Epanutin and Luminal on Cardiazol Fits.

19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41
2·25	2·25	2·25	2·25	2·25	2·25	2·25	2·25	2·25	2·25	2·25	2·25	2·25	..	..	..	..	..	..	..	..	..	..
+	+	+	+	+	+	+	+	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..
..	..	..	..	E4	4	4	4	5	6	6	L2	2	..	..	..	..	..	..	..	..	..	..
6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	..	..	..	..	..	..	..	..	..	..	..	..	..
+	+	+	+	+	+	+	o	+	o	..	..	..	..	..	..	..	..	..	..	..	..	..
..	E4	4	4	4	5	6	6	L2	2	..	..	..	..	..	..	..	..	..	..	..	..	..
6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	..	..	..
+	+	+	+	+	+	+	+	o	o	o	o	+	+	+	+	o	+	o	o	..	..	..
6	..	..	..	..	..	..	..	L2	2	2	2	..	..	..	P2	P2	2	2	2	..	..	..
6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5	6·5
+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	o	+	+	+	o	o	o	+
4	4	5	6	6	..	..	..	..	..	..	L2	2	2	2	3	3	3	3	3	4	4	4
7·5	7·5	7·5	7·5 + 6·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	8·5	..	..
+	o	+	+	+	+	o	+	+	o	o	+	o	o	+	o	o	o	o	o	+	..	..
6	6	..	..	..	..	L2	2	2	2	2	2	2	2	2	2	3	3	3	3	..	..	..
5 + 5	5	5 + 5	6	6	6	6	6	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
+	+	+	+	+	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	E3	3	3	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
5 + 4·5	6	6	6	6	6	6	6	6	..	..	..	..	..	..	..	..	..	..	..	..	..	..
+	o	+	o	+	+	o	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	E3	3	3	3	3	3	3	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..
7	7	7	7	7	7	7	7	7	7	..	..	..	..	..	..	..	..	..	..	..	..	..
+	+	o	+	+	+	o	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..
E3	3	3	3	3	3	4	4	4	4	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
7·5	7·5	7·5	7·5	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
+	+	+	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
2	2	2	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..

D = Delay of over 120 seconds.
+ = Good fit. o = No fit occurred.
| = Interruption of treatment at the beginning of the war.

patient for the treatment, combined with the fact that he was not improving clinically, made it necessary to terminate the treatment.

CASES 7, 8 and 9.—In all these treatment was temporarily suspended at the beginning of the war and this rather spoilt their value as well-standardized cases. In Case 7 the failure of epanutin to stop fits is well established. In No. 8, luminal stopped fits in two out of three cardiazol injections and delayed the fit for over two minutes in the third, but, in view of the fact that it could not be shown that this was not associated with an incidental increase of dosage, some of the significance is detracted. The same applies to Case 9, in which three successive fits were apparently prevented by luminal. Sporadic omissions of fits in these two cases, when on epanutin, cannot be considered of real significance in themselves, especially in the former where the standardization was obviously not very satisfactory.

CASES 10, 11 and 12.—Although epanutin was given in these cases only with the idea of combating the patients' fear of the cardiazol treatment, they demonstrate further the inability of epanutin in small doses to prevent cardiazol fits.

In all the above cases cardiazol injections were given at 11 a.m. The anticonvulsants were given at the same times as they would have been given to epileptics. This meant that the dose in the mornings was given at 7.30 a.m.—before breakfast—a total of 3½ hours before the cardiazol. In order to make sure that it was not rapid excretion that was rendering the epanutin ineffectual this dose was also tried later, firstly at 9 a.m., then at 10 a.m. The cases in which this was done are not specified, but it was done so frequently as to establish beyond doubt that this factor did not enter into the causation of epanutin's failure to prevent the cardiazol fits.

SUMMARY.

Twelve cases which had been well standardized on a convulsive dose of cardiazol were treated with epanutin. The maximum dose reached was six capsules *per diem* in 5 cases, four capsules a day in 3 cases, three capsules a day in a further 3, and two capsules a day in the remaining 2. In none of these cases could epanutin be considered to have a definite anticonvulsant effect on cardiazol fits.

In three cases which had been having as many as six capsules a day it was possible to carry out adequate control experiments with luminal. In two out of the three, cardiazol fits were completely arrested on gr. 1½ *b.d.* and gr. 1½ *t.d.s.* respectively. In the third they were frequently but not successively prevented. In another case who only received three capsules of epanutin a day before the treatment had to be terminated, complete cessation of fits was produced by luminal gr. 1½ *b.d.* In two further cases in which epanutin had no anticonvulsant effect luminal appeared to have one, although owing to the interruption of treatment at the beginning of the war this was not so definitely established as in the previous cases.

Although these observations cannot in themselves be considered final, they suggest strongly that epanutin and luminal differ in their ability to prevent cardiazol fits, probably due to some fundamental difference in the way they affect the nervous sytem.

N.B.– Frost (1939) noted the failure of epanutin to raise the threshold of cardiazol in three well-standardized cases, but epanutin was only given in small

doses and he did not make any comparison with luminal. The present work was under way before Frost's paper had been read (July, 1939).

PART B.

A Survey of the Literature on Sodium Diphenyl Hydantoinate.

Following the work of Krasnogorski (1935) and Spiegel (1937), Merritt and Putnam (1937 and 1938) used the method of producing epileptic convulsions in animals by electric stimulation (with the skull intact) to investigate the properties of various anticonvulsants. They found that sodium diphenyl hydantoinate stood out pre-eminent. Clinical trial substantiated this, while revealing that it had very definite toxic reactions.

(*a*) *Composition.*

For formula see p. 916. It is a white powder with a bitter taste and a pH of 11·7.

(*b*) *Dosage.*

At present epanutin is made up in 0·1 gm. (1½ gr.) capsules. The dosage for adults consists of from two to six of these per day (gr. 3 to gr. 9), and Merritt and Putnam (1939) describe the use of 0·2 gm. (3 gr.) at a time. This large dose is particularly useful at night in nocturnal cases or at times when exacerbations are most common (of menstruation). The dosage bears no relation to that of luminal or bromide pre-medication.

For children above six years of age the maximum dose is 0·4 gm. (6 gr.) and below four years old 0·12 gm. (4 gr.). For use in small doses capsules of 0·05 gm. (¾ gr.) are supplied.

(*c*) *Change-over.*

In order to minimize an increase of fits and other complications many authors have emphasized the desirability of gradual substitution and withdrawal. No one method has been yet agreed on. Personally I have found no evil effects in adding epanutin 0·1 gm. (gr. 1½) *t.d.s.* to any medication of bromides or phenobarbitone, etc. (starting by one capsule of epanutin and increasing the dosage every five days until the patient is having epanutin one capsule *t.d.s.*), and then reducing the previous medication at about the same rate (i.e. withdrawing one dose every five days). Even if this is carefully done in cases which have been on luminal or bromides for a very long time, a temporary increase of fits is to be looked for. In some cases the withdrawal of the sedative effect of the latter leads to a reactivation of psychosis.

(*d*) *Anticonvulsant Effects.*

Numerous articles have established the anticonvulsant power of this drug beyond all doubt. Nevertheless it is difficult to synthesize the results published owing to a lack of uniformity of approach to the subject and gradation of results. Merritt and Putnam (1938), in their original article dealing with 198 cases treated for periods varying from two to eleven months, give the following results:

	Grand mal.	*Petit mal.*	Psychomotor equivalents.
Completely relieved . .	68 (58%) .	26 (35%) .	4
Greatly decreased . .	32 (27%) .	36 (49%) .	2
Moderately decreased .	6 (5%) .	3 (4%) .	..
No change . . .	12 (10%) .	9 (12%) .	..
	118 .	74 .	6

No definition of " moderately " and " greatly decreased " is given.

Kimball (1939) treated 129 children for over three months and found that seizures were " entirely controlled " in 62·7 per cent. of cases, alleviated in 14·7 per cent. and not benefited in 22·5 per cent.

Blair, Bailey and MacGregor (1939) in 58 cases of chronic psychotic epilepsy with *grand mal* seizures, treated for over three months, found 39·6 per cent. completely relieved, 20·6 per cent. greatly decreased, 8·6 per cent. moderately decreased and 24·1 per cent. increased. Of all the articles published up to date they alone define what they mean by the gradations:

Completely relieved = No fits for six weeks.
Great decrease = Reduction by more than 50 per cent.
Moderate decrease = Any reduction less than 50 per cent.

McCartan and Carson (1939), in 20 cases treated for over three months found complete relief in 79 per cent. and " marked decrease " in 10·5 per cent.

Steel and Smith (1939) treating 20 mentally defective epileptics found " considerable diminution " in six cases and " slight diminution " in six cases. No change in five cases and increase in three cases.

Williams, D. (1939), treated 91 cases of chronic epilepsy of a non-psychotic nature who had failed to respond satisfactorily to other drugs. He found that after 1½ to 10 months' treatment (average 4·1 months) in 79 per cent. of *grand mal* and 63 per cent. of *petit mal* the frequency of fits was decreased. In 19 per cent. improvement was dramatic and retained for five months.

Hodgson, E. R., and Reese (1939) found that of 88 epileptics receiving dilantin sodium (epanutin), 66 per cent. were definitely benefited and 34 per cent. received no benefit.

Hawke, W. A. (1939), reported 60 per cent. improvement in *grand mal* and 8 per cent. in *petit mal* in 24 epileptic children transferred to epanutin.

Fetterman (1940), in treating 28 cases at a clinic and in private practice, found epanutin to be of "marked" anticonvulsant value in 10 cases, "moderate" in 7 cases, "slight" in 3 cases, "mild" in 4 cases, "doubtful" in 1, "questionable" in 1 and none in 2. No definition of the terms are given.

Kimball and Horan (1939) found seizures "entirely controlled" in 55 per cent. of cases, modified or partially controlled in 20 per cent. of cases and not improved in 25 per cent.

The American Medical Association's Committee on Pharmacy and Chemistry (1939) published an article compiled from several different sources showing the overwhelming superiority of dilantin sodium over other anticonvulsants and officially recognizing its potentialities.

Merritt and Putnam (1939), in describing treatment of cases treated by other methods who had not been relieved of their attacks (for the majority of cases luminal sometimes in large but often in small and inadequate doses had been the means of treatment), give a comparison of epanutin's efficacy thus:

	Percentage.
Sodium diphenyl hydantoinate more effective	79%
Previous therapy more effective	2%
No form of therapy of value	13%
Attacks too irregular for evaluation	6%
	100%

Butter (1940) in 43 non-psychotic cases treated for one year found "great improvement" in 46·5 per cent., "improvement" in 16 per cent., "no change" in 13 per cent. and "worse" in 2 per cent.

Frankel (1940) in 48 cases treated from 3 to 18 months found entire control in 39 per cent., alleviation in 21 per cent. and no benefit in 39 per cent.

Other articles deal with less than 20 cases, and are therefore not considered worthy of note from a statistical point of view.

All the above figures are truly remarkable in their claims for epanutin, but it is very questionable whether they represent the true contrast of the effect of epanutin as opposed to luminal. The reason for this is that it is doubtful whether the cases have been previously treated with the maximum efficiency on luminal (see p. 917).

Grounds for this belief are forthcoming in the works of Pratt (1939), and Cohen, Showstack and Myerson (1940).

Pratt selected 52 cases which had not shown any marked response to, or had not been controlled by, phenobarbitone and other barbiturates up to or

near the limits of tolerance (as advocated by Lynch). The cases were treated on epanutin for two to ten months and he found the following results:

Seizure occurrence.	Number of cases.	Percentage.
Controlled for past two months or longer	6	11·5%
Markedly reduced	11	21·2%
Little or no reduction	35	67·3%
Total	52	100%

Cohen *et al.* (1940) consider that "dilantin sodium is an inadequate substitute for adequate phenobarbital."

In combination with other drugs.—Several authors have found that certain cases have less fits on a combination of epanutin with luminal. Pratt (1939) reports some such cases. Cohen *et al.* (1940) found that "in many cases a synergistic combination of the two (i.e. luminal and epanutin) is the most effective proceeding." Williams (1939) also claims that some cases do better on a combination of epanutin with luminal, or in a few cases with luminal and bromides. I have observed one or two cases that seem to do better on the combination with luminal.

The criticism may be levelled against all these observations that they have been conducted over a comparatively short period, and to gauge the real potentialities of this combined method further investigation is required. However, it seems indicated definitely that at least a few cases do better on a combination of epanutin with luminal than on either alone.

(*e*) *Individual Cases.*

Even if there is considerable doubt regarding statistical comparisons between the anticonvulsant properties of epanutin and luminal, the records of individual cases prove beyond all doubt the great value of epanutin in certain patients not benefited to an appreciable extent by any other anticonvulsant.

Williams, D. (1939), Coope (1939), Coope and Burrows (1939) and Pickles (1939) present very impressive cases, and many other authors have also instanced similar successes.

(*f*) *Mental Effects.*

The almost complete absence of hypnotic effect claimed by Merritt and Putnam has been confirmed by most authors. There has also been almost universal emphasis on a marked improvement of the temperament and personality as a whole. The patients have been more alert, more cheerful and amiable, less quarrelsome and querulous and generally more easily managed

by relatives or nurses. Several individual results have proved almost miraculous.

Here, again, a word of warning is necessary. Most cases treated have admittedly not done very well on luminal or other medications. The improvement in such cases on epanutin is undoubted and vindicates beyond doubt the place of epanutin in the treatment of epilepsy, but when considering the matter as a whole one must remember that, *vice versa*, many cases who do well on luminal without mental impairment (see below) might not fare so well on epanutin.

(*g*) *Toxic Effects.*

From the beginning these have been recognized as frequent. Merritt and Putnam (1938) described toxic effects of a minor type in 15 per cent. of their 198 cases and of a serious type in 5 per cent. of cases. Other authors have found them more frequent in their occurrence and more tardy in their development. A synthesized summary is given forthwith commencing with effects on the nervous system which are far the most common.

(i) *Nervous system.*—(*a*) Subjective neurological symptoms: It is frequent for cases in the early stages of treatment to feel uncomfortably different from their usual selves. They will complain that they "feel different" or of being "jittery," uncomfortable, restless, and the like. They may exhibit subjective sensations seen in neurosis and sometimes in early psychosis, e.g. consciousness of their heart beating, etc. They may feel tremulous, clumsy or unsteady in their movements and experience difficulty in walking, eating, writing, sewing, etc. Sometimes they complain of loss of power in a limb, anaesthesia, loss of taste, blurring of vision, giddiness, drowsiness and headache, etc.

(*b*) Objective signs:

Tremors of a generalized or localized type.

Ataxia of a gross type so that the patient frequently cannot walk.

Slurring of speech.

Eye signs, nystagmus, squint, diplopia, ptosis.

(*c*) Psychological symptoms: The patients may become irritable and overactive and suffer from insomnia. Some become suspicious and quarrelsome; others develop definite paranoid psychoses (Fetterman (1940), Merritt and Putnam (1939). One case in the present series did so); others still develop delusions and hallucinations and confusion. The activation of depressive psychosis has occurred in the present group of 30 cases. Frankel suggested that in his five cases with psychosis this may have been due to withdrawal of sedative rather than the toxic effect of epanutin.

The evaluation of psychic symptoms is obviously very difficult because of their occurrence in epilepsy untreated by anticonvulsants.

Nervous symptoms usually occur early in treatment, when they tend to be of a mild nature and soon pass away, sometimes without a reduction of dosage. However, severe ataxia, confusion and psychotic symptoms may occur as late as three months or more on the same dose of epanutin. An increase in dosage may lead immediately to any of these symptoms.

(ii) *Pyrexia* usually associated with a skin eruption—but occasionally of sporadic origin—may occur.

(iii) *Skin rashes* of several types, namely erythema, scarlatiniform, morbilliform, rubeoliform, urticarial acneiform, and in one case exfoliative dermatitis have been described.

(iv) *Hyperplasia of the gums* has been given considerable prominence since Kimball first described it. It was attributed by him to deficiency of ascorbic acid in the blood. Gruhzit (1939) experimenting on animals is said to have disproved this, but rats and dogs may react in a different way from humans (for instance, dogs tolerate colossal doses of epanutin). The nature of the hyperplasia, which is a pale, serrated swelling at the root margin, and which has not been known to bleed, is not typical of vitamin C deficiency.

A point of striking contrast is the frequency of this complication in the U.S.A. compared with its rarity here. Kimball (1939) described it in 62·7 per cent. of 127 cases. Frankel found it in a severe form in 30 (62 per cent.) and in moderate form in a further 6 (12 per cent.) of 48 cases. Hawke describes it in children, and even Merritt and Putnam (1939) admit it in 6 per cent. of cases. Fetterman (1940) found it in 7 out of 28 cases (25 per cent.). On the other hand, in this country Blair, Bailey and MacGregor (1939) in 75 cases, Williams in 91 and Coope and Burrows in 69 cases found no case of hyperplasia. McCartan and Carson (1938) found it in one case out of 20 and Butters (1940) in one case out of 48.

One thing that would seem of great importance is careful attention to sepsis of the teeth, etc., prior to commencing treatment.

(v) *Gastro-intestinal symptoms.*—Nausea, vomiting and heaviness of the stomach have been described as due to the alkalinity of the drug, but if the drug is taken with meals or just after instead of before, as is usually described, this is rare. Merritt and Putnam (1939) advise administration of 15 minims of HCl (dilute) with meals in persistent cases.

(vi) *Cardiovascular system.*—Blood pressure: A rise in blood pressure with consequent epistaxis has been described in two cases (Frost, 1939). The present observation and those of other authors have failed to find any change in blood pressure definitely due to epanutin. Further observations are required.

Cardiac: Denis Williams describes "changes in cardiac rate during toxic symptoms." No one else has reported cardiac changes.

(vii) *Haemopoietic system.*—As a prelude to an examination of the changes in this system, it is well to consider changes taking place in epileptics not on drugs. This has been thoroughly reviewed by Patterson and Weingrow (1929). They point out how conflicting opinions on this subject are. They record a leucocytosis with relative lymphocytosis as the most frequent change, a leucopenia or secondary anaemia as quite common (see two cases in the present series, Nos. 12 and 13), and remark on the inconsistency of the picture as a whole. It is therefore necessary that blood counts should be taken before treatment as well as during it, to establish the relationship of any change to epanutin.

Blood changes of a minor type have been frequently recorded during epanutin treatment, but no case of agranulocytosis has been observed. Merritt and Putnam, in over 300 cases, found a few cases of secondary anaemia, a mild leucocytosis in many cases and an eosinophilia of over 5 per cent. in six cases. A mild leucopenia with relative lymphocytosis has been described by several authors. Pratt records a case of a drop of 700,000 red cells during six weeks' treatment in a child. The present article confirms the production of a mild eosinophilia (in one case 12 per cent.) and secondary anaemia, but these seem the only changes in any way constant. Blood changes cannot be correlated with other complications.

McCartan and Carson (1939) record constant and progressive fall in sedimentation rate. No one else seems to have paid attention to this interesting aspect. Personally I have not been able to confirm a fall in sedimentation rate during or at the end of one year's treatment (present article).

Obviously it is in children that one might expect most frequent and severe haemopoietic changes and one awaits reliable information on this subject.

(viii) *Genito-urinary system.*—No changes in urine have been observed except by Pratt (1939), who found a mild albuminuria in some cases. MacGregor described one case of cystitis which was probably directly due to the drug (see Blair, Bailey and MacGregor (1939)) and Coope and Burrows (1940) another. Merritt and Putnam (1939) describe three cases of increase of sexual libido, one so excessive as to necessitate cessation of treatment.

(*h*) *Loss of Weight.*

Apart from the present article little has been said about this. Pratt (1939) records some gains and some losses of little import and Fetterman (1940)

several "losses." From the present work it would seem that prognostically gain in weight is favourable, and loss of more than a few pounds unfavourable and grounds for special care.

(*i*) *Fatalities.*

Few have been recorded. None can be absolutely definitely labelled as due to epanutin. Merritt and Putnam (1939) describe two deaths during treatment—one due to miliary tuberculosis. Williams recorded two patients who died in *status epilepticus* while on epanutin and bromides (see discussion under pharmacology). Coope and Burrows (1940) had two fatalities due to bronchopneumonia following an acute exacerbation of fits. One death which may have been due to epanutin occurred in the present series.

Finally, a word regarding the frequency of the various toxic symptoms. As already stated, Merritt and Putnam (1938) found them in only 15 per cent. of cases in a mild form and 5 per cent. in a serious form. Other authors have found these more frequent. Pratt found them in as many as 73 per cent. of his 52 cases. The present author found them in 60 per cent. of 36 cases. Davidson and Sutherland (1938) found them in 8 out of 12 psychotics, McCartan and Carson (1939) in 40 per cent. of 20 cases. Williams found them in 36 per cent. of 83 patients, Coope and Burrows (1940) in 12 (20 per cent.) of 60 cases. Hawke found them in 38 per cent. of 20 children, and Frankel (1940) remarks that in a miscellaneous group of 48 cases toxic symptoms were most frequent in children.

The most frequent toxic symptoms are those of the nervous system. Apart from these, occasional pyrexia, skin rashes and mild blood changes are the most common toxic manifestations.

It seems probable that toxic symptoms are most frequent in old and chronic cases and in children (as one would expect from experience with luminal, etc.).

It has been noted that luminal may act anticonvulsively in a few hours, or only after several days' administration, and it seems probable that this is true of epanutin also. This is one reason for reducing the luminal dose very gradually when a change-over to epanutin is being effected. Butters (1940) has noted the disastrous effect of withdrawing epanutin suddenly—an action in which it again resembles luminal (phenobarbitone). Williams (1939) pointed out that when severe toxic symptoms were present fits never occurred. I have confirmed this in my observations, and also noted on these occasions (ataxia, etc.) that withdrawal of the drug does not lead to fits even if it is not replaced by other anticonvulsants. The rapidity with which the fits may be expected to recur following such a withdrawal varies from one patient to another, but I have found that usually no fit occurs for two or three days, or more, in the absence of any anticonvulsant therapy.

Mode of Action.

Very little is known regarding the way in which epanutin acts in such an efficacious anticonvulsant manner. This is, of course, not surprising in view of our poor knowledge of the aetiology of epilepsy. One thing is absolutely certain, and that is that it has extremely little, if any, sedative or hypnotic action. To assume, however, as Williams (1939) suggests, that its mode of action is fundamentally different from luminal is not yet warranted, since Cohen *et al.* (1940) have proved almost conclusively that the hypnotic effect plays no part in the anticonvulsant action of luminal (phenobarbitone).

Many authors have reported that some cases do better on a combination of epanutin and luminal than on either singly. Cohen *et al.* consider that the synergistic action is definitely superior in nearly all cases. If this is so one wonders whether this is due to the well-known additional reinforcement effect of the combination of two drugs that work in the same way or whether they work in a different method altogether.

The latter suggestion would seem to be supported by my work described in the early part of this article contrasting the effects of luminal (phenobarbitone) and epanutin on the incidence of cardiazol fits. The definite anticonvulsant effect of luminal in this respect and apparently complete absence on the part of epanutin is the opposite to what one would have expected if the two drugs acted in the same way.

However, the interesting and conflicting fact that Goldstein *et al.* (1940) found that in epileptics who had cardiazol injected subcutaneously the bouts of fits which usually resulted therefrom were controlled by both drugs, but considerably more efficiently by epanutin (dilantin sodium) than luminal (phenobarbitone), makes things more doubtful. One wonders whether this apparent contradiction may be because my work was done on non-epileptics (schizophrenics), whereas the latter was done on epileptics, and again I injected cardiazol intravenously, whereas the other workers injected subcutaneously.

It has been suggested by some that epanutin has a directly stimulating effect on the cerebral cortex. This remains to be *proven*. That it is possible is shown by the fact that by combining benzedrine (a cortical stimulant) with luminal the latter's anticonvulsant effects are enhanced (see Cohen *et al* (1940)). It is further suggested to a certain extent by the reported personality changes (increase of alertness and efficiency, etc.), but reserve is required in this respect, since a similar state of affairs was described as due to luminal in the early days of its use, and it is quite possible that these apparent changes are associated with a reduction of fits more than with anything else.

One may also point out that epanutin is, like luminal, more effective on *grand mal* fits than on *petit mal* ones, that it occasionally decreases *grand mal* fits at the expense of an increase of *petit mal* ones (Butters, 1940, etc.) or the occurrence of myoclonic movements, etc. (present article). Moreover, in a few cases

at least the fits, although less common, are more severe, as I have observed previously (Blair, 1940), and as has been remarked on by Williams (1939) and Pratt (1939).

Finally, as I have suggested early in this article, it is questionable whether complete cessation of fits for long periods is desirable in all epileptics. I personally believe that mental confusion and exacerbation of fits after a prolonged period of relief from seizures is due to complete absence of fits being undesirable in these cases.

There remains a tremendous amount of work to be done on the pharmacology of this drug, and it is only when this has been scientifically worked out that the best results will be obtained from its use.

PART C.

A Comparison of the Effects of other Anticonvulsants, etc.

(*a*) Bromides.

Bromides were first introduced for the treatment of epilepsy about 1850 by Locock, who did not, however, publish any article on their effects. For 50 years bromides reigned supreme in the treatment of epilepsy until luminal was synthesized in 1903.

Although bromides were used so extensively, it is difficult to find literature dealing with their anticonvulsant power from a statistical point of view.

Anticonvulsant Effects.

Binz is quoted by Sollman (1936) as finding total relief from fits in 12 per cent. of cases, a diminution in frequency and violence of attacks in 83 per cent., no influence in 2½ per cent. of cases and an increase in 2½ per cent. Boshes (1936) treated 72 cases and obtained complete prevention of fits in 31 (43 per cent.), a persistence of *grand mal* in 19 (26·4 per cent.) and of *petit mal* in 22 (30·6 per cent.) of cases. Regarding the group free from fits he says that the period varies from many months to several years. Diethelm (1925) vindicates the use of bromides in preference to phenobarbitone. He says: "Phenobarbitone is considered anticonvulsive but not anti-epileptic. It checks the convulsions, but cannot cure the patient or clear up mental symptoms. Bromide, on the other hand, has an influence on the whole epileptic picture. The attacks as well as mental symptoms clear up."

Mental Effects.

Bromides have a depressing effect on the nervous cells, and in non toxic doses may be beneficial to certain unstable mentalities.

Toxic Symptoms.

These are now well recognized. Barbour, Pilkington and Sargant (1936) divide them into three types: (1) *Fatal intoxication:* This occurs with a chloride replacement of 40 per cent. or thereabouts and a blood bromide usually of 450 to 500 mgm. (2) *Severe intoxication:* Mental symptoms consist usually of a confusional state or delirium with disorientation, amnesia and hallucinations prevailing. In patients already psychotic a mixed atypical picture may be produced. Physical symptoms consist of a dry skin, furred tongue and such nervous symptoms as slurred speech, ataxia, tremor, etc. Reflexes tend to be diminished or lost. (3) *Mild intoxication:* In this group the patients exhibit mild psychic changes. They become irritable, tired or weak and may suffer from insomnia or lethargy; frequently their memory is impaired. Skin rashes are more rare than is usually indicated in text-books, as also are the irritation and secretion from mucous membrane.

The liability to toxic manifestations varies from one case to another accord- to individual idiosyncrasy. Under 100 mgm. of blood bromide rarely produces effects, from 100 to 200 mgm. not often, whereas over 200 mgm. usually does. Some cases have a tolerance of over 300 mgm. As would be expected from remarks on excretion, patients with cardio-vascular disease, renal disease and anaemia are most liable to symptoms and, therefore, liability increases with age.

Owing to these now well-known toxic symptoms bromides have largely fallen into disrepute, especially as they have erroneously been blamed as the cause of dementia in epilepsy. Properly used this should not happen (see Paskind, 1934). It is interesting to note that Boshes (1936) found that his patients completely controlled required less bromide and had less toxic reactions than the cases which did not respond so well.

Pharmacology.

Bromides depress the activities of the cells of the central nervous system. Dixon (1936) states, "Bromides have a specific action on the nervous system which they depress. This depression does not show an evolutionary progress as after alcohol. On the contrary all cells psychical, motor area, medulla, and cord are affected at the same time." There is a great diminution in the excitability of the motor area and blunting of sensation. A general diminution of superficial reflexes may occur.

Bromides will accumulate for weeks until an eventual equilibrium is established between intake and output. Chloride intake has an important influence. A low chloride diet favours the action of bromides, and a high one tends to reduce the accumulative deposit and decrease the effects of bromides. Bromides are excreted by the kidneys and intestinal tract (per the gastric juice). Therefore

impairment of kidney function or constipation, etc., increase the liability to toxic symptoms.

The manner in which bromides act on the nervous system is not perfectly understood. It has been shown in animal experiments (Boshes) that even when rabbits are completely bromized the brain bromide concentration is very low and bears no constant relationship to the blood concentrations. Nevertheless, for each individual there is usually a particular blood bromide level which will control fits, and the success or failure of bromide treatment depends on whether this is lower than the toxic level in the individual concerned.

(*b*) Luminal (Phenobarbitone).

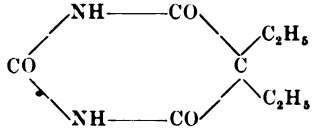
This was introduced as an anticonvulsant by Hauptmann in 1912 and gradually obtained wider recognition and more extensive use until, following the revelation of bromide toxicity, it almost completely replaced bromide therapy.

Again it is difficult to obtain statistics on its anticonvulsant effects, but one outstanding article of the greatest importance has recently been written (Lynch, 1939).

Table V.—*The Chemical Formulae of Certain Barbiturates and Hydantoinates.*

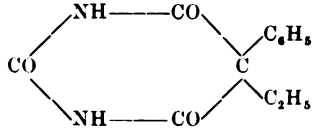
Barbitone (*veronal*).

5 : 5-*di-ethyl-barbituric acid.*



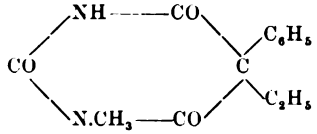
Phenobarbitone (*luminal*).

5-*phenyl*-5-*ethyl-barbituric acid.*



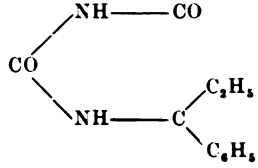
Prominal.

N. methyl-ethyl-phenyl-barbituric acid.

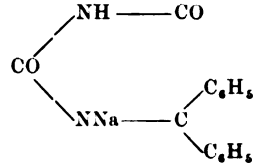


Nirvanol.

Phenyl-ethyl-hydantoin.



Epanutin (*sodium diphenyl hydantoinate*).



Anticonvulsant Effects.

Grinker (1920 and 1922) had emphasized that to obtain its best results luminal must be used in large doses. Pratt (1928), using this method, had found it successful in reducing the fits and improving the mentalities of the patients thus treated. Lynch (1939), using this method, gave doses as large as 10½ gr. per day. He found that of 469 cases admitted to Woodstock Hospital for epilepsy during five years, 314 were discharged, of whom 140 (or 44·5 per cent.) were recovered in the sense of being symptom- and fit-free for one year or more.

In the early days of luminal treatment, figures were almost as remarkable as those claimed for epanutin. Kirk (1921) treated 212 cases for five months, of whom "61 (28·7 per cent.) were completely free from fits since treatment began, and 106 (58 per cent.) had less than five fits during treatment." The first cases treated were those whose fits were the most frequent and most severe and many of whom were bedridden. He says, "We felt that if luminal would improve the condition of these patients we would then be justified in proceeding in the treatment of milder cases. The results in certain cases were so startling and so remarkable that within 30 days all cases of idiopathic treatment were placed under treatment." Golla (1921) found improvement in 89 (71·2 per cent.) out of 125 cases transferred from bromides to luminal.

Watkins (1920) treated 22 cases for three months and found a reduction of 70 per cent. in the total number of fits occurring. He found that despite this one or two had more fits (two of over 100 per cent. increase). Some developed toxic nervous symptoms.

Greenwald (1922), treating 105 miscellaneous epileptics at New Jersey State Village for epilepsy, found complete arrest of fits in 24 per cent. of cases, partial cessation in 40 per cent. and no change in 36 per cent.

Patterson, Damon and Levi (1926), treating 300 patients for from one to four years, found that, by giving gr. 1½ in the evening and occasionally in the morning, a 45 per cent. reduction was obtained in the number of fits.

Finally Cohen, Showstack and Myerson (1940) have shown a reduction of 68 per cent. of fits where dosage of phenobarbitone was raised to an average of 3 gr. per day per person, as opposed to a previous much lower average dosage.

Effects on the Mentality and Personality.

The detrimental drowsy effect produced by luminal is much emphasized, but this is comparatively rare. It is interesting to note the remarks of various authors on this aspect of luminal treatment.

Grinker (1922) says: "The convulsive variety of epilepsy almost always yields to phenobarbitone in correct dosage and it is mostly the wrong dose which is responsible for unsatisfactory results and toxic symptoms. . . .

There has been no mental deterioration from administration of phenobarbitone ; on the contrary, patients have become more alert and keen and have lost their unnatural reticence."

Patterson, Damon and Levi (1926) say : " Dull, surly and irritable epileptics frequently become more cheerful and co-operative. Altercations among the patients lessened, and the attendants reported that the luminal cases were much easier to handle than previously. In some instances effects of this kind were the only ones noted."

Greenwald (1922) says : " The feeling of well-being was very well marked."

Toxic Effects.

The effects on the nervous system bear a marked resemblance to those occurring in bromides and epanutin. Apart from cases whose treatment was started on a relatively high dose and those with some other physical disease (goitre, etc.,) these are rare except for drowsiness and lethargy. Even this is not so frequent as many physicians believe.

Tyler Fox (1927) says : " Of 167 patients it was only to be expected that luminal would make the patient a little more sleepy and dull than usual. Such an effect was noted in a small portion of patients. It was never very marked and, as a rule, it passed off in a few days. In no case was it serious enough to necessitate cessation of treatment."

Nervous system.—Subjective : The patient usually feels drowsy, and may feel different from his usual self. Psychosomatic symptoms are not described, but presumably may occur.

Objective : Squint, diplopia, nystagmus, facial weakness, difficulty in protruding the tongue, swallowing and speaking (the latter being thick and indistinct) ; vertigo and gross ataxia resembling alcoholic or cerebellar disease may occur.

Psychological changes : Psychopathological depression is sometimes present. The patient may become confused and disorientated. Amnesia and hullucinations and delusions are not infrequent in severe cases.

Cutaneous system.— Rashes of erythematous, morbilliform, rubeoliform or scarlatiniform character have been recorded. Urticaria and oedema of the face have been reported as a rarity.

Cardio-vascular system.—Wilcox has reported cases with an alarming fall of blood pressure which he thinks may be due to the effect of luminal on the myocardium.

Haemopoeitic system.—No changes of any consequence have been noted.

Genito-urinary system.—Albuminuria is sometimes present and nephritis has been ascribed to this drug.

Wilcox (1927) says : " There are recorded cases of idiosyncrasy to even small doses of drugs of this group, but the majority of cases of poisoning

following small (0·2 gm.) doses have been reported, either in elderly patients or in those patients in whom other factors are present (thyrotoxicosis, etc.)"

In view of similar remarks regarding epanutin it is interesting to note that Harman (1927) says: "It has generally been found that the effective dose of luminal is very near the toxic dose, more than three grains daily producing ataxia."

Pharmacology.

It is a very slightly alkaline powder. The sodium salt is freely soluble.

It is absorbed easily and excreted per the kidneys, although it is mostly oxidized in the body. The small fraction which remains not oxidized is excreted rather slowly. Its action is slower and more prolonged than medinal (barbitone), and a single large dose may protect against fits for three or four days. Owing to this action it is usually possible to give adequate doses in the early mornings and evenings only, and an increase of the dosage at particularly susceptible times, such as night, at the time of menses, etc., may be particularly efficacious.

The speed of excretion and amount recovered from the urine vary greatly and this is responsible for a varying duration of action. It may become active in a few hours or only after several days' administration. Similarly, when it is withdrawn from treatment its activity may cease almost immediately or gradually over several days. In either case the results in epilepsy are usually disastrous if further sedatives are not given.

Seat of action.—In large doses the drug may be found in every part of the nervous system in equal portions. In smaller amounts (*cf.* therapeutically) it is recovered mostly from the diencephalon and to a lesser extent from the cortex, hence the hypnotic effect (Keeser and Keeser, 1928). The bulbospinal reflexes are comparatively little affected.

The exact manner in which this drug affects epileptic convulsions is unknown, but from the recent observations of Cohen *et al.* (1940), who abolished its drowsy effect by the use of benzedrine and found that they thereby reduced fits still further, it is apparently not related to its hypnotic action.

These workers also produce valuable and well-controlled proof that there is for each patient an optimal dose beyond which no benefit is obtained by increasing the dosage, and that toxic symptoms are due to idiosyncrasy and bear no definite relationship to dosage.

(*c*) PROMINAL.

This is a proprietary barbiturate. As will be seen by reference to Table V, the formula is related to that for luminal, the difference being the addition of a methyl group. The addition of this radical is said to produce a substance equally anticonvulsant but less hypnotic than luminal. Only a few reports dealing with small numbers of patients have appeared in this country.

Anticonvulsant Effects.

Page (1936) found that of ten patients treated for a year, a reduction of over 50 per cent. of fits was obtained as compared with luminal. Millman (1937) found a reduction of 66 per cent. of fits in 39 mental defectives (as opposed to luminal), and Henderson (1937) a reduction of 67·3 per cent. in 13 cases treated for twelve months with prominal compared to a similar period on luminal. Sands (1937) found that in 14 out of 26 cases it reduced fits compared with the bromides and luminal. Hughes (1936) found a reduction of 50 per cent. in the fits of 14 cases as opposed to those on phenobarbitone. Davies (1937) found no improvement in 27 cases previously treated with phenobarbitone.

Mental Effects.

Most authors comment on the improvement in mentality when patients are changed over to this drug. The drug is said to be less hypnotic than luminal. Its best effects are obtained in cases with mild mental symptoms, and luminal or bromides are considered preferable in the mentally more acute cases.

Toxic Effects.

These were rare among the cases observed. Some developed drowsiness at the beginning of treatment which soon passed off. Others showed signs of a weakness of limbs and ataxia. Millman (1939) found albuminuria in some cases, and even attributed possible renal damage to this drug in cases with the slightest deficiency in renal activity prior to its use.

It has been noted that some cases did worse on prominal than they had done on luminal, and that others benefited more from the combination of prominal with luminal or bromides than from any of them individually.

Pharmacology.

Dosage: 3 to 6 gr. daily (one tablet equals 3 gr.). The drug is apparently fairly rapidly absorbed. Page notes that its effects last for some time after withdrawal and suggests it is, therefore, slowly excreted. It has no cumulative effect.

(*d*) NIRVANOL.

This has not been used as an anticonvulsant, but as it is a hydantoin and it has been suggested that epanutin might mimic its toxic action, a word or two seems desirable.

It is interesting to note that nirvanol was originally used with success as a sedative and hypnotic (Curschmann (1918)). Mild toxic symptoms were found in certain cases, but these nearly all had some physical debility or other (thyrotoxicosis, etc.). Later it was used in massive doses in the treatment of

chorea in children. In these doses toxic complications were invariable and often serious. Their nature was as follows:

General: Pyrexia of up to 103° F. or more and a generalized reaction.

Skin: Erythematous, morbilliform, rubeoliform, or scarlatiniform rashes.

Haemopoietic system: The most frequent changes consist of a mild anaemia, leucopenia with a relative lymphocytosis and eosinophilia. No case of agranulocytosis was reported, but Leichentritt, Lansfeld and Silberberg (1929) produced it in animals by prolonged administration.

Nervous system: No complications are described (in large doses), presumably because any confusion, delirium, etc., was attributed to the pyrexia.

Genito-urinary system: Frequent irritations of urinary tract (Balanitis, vaginitis, cystitis and even nephritis may occur).

Respiratory: Irritation of the mucous membranes with increased secretion is described and pulmonary oedema occurred more than once.

Discussion.— In the early days of epanutin treatment, Schlesinger (1938) suggested that dangerous toxic complications would occur (inference from the resemblance in constitution between epanutin and nirvanol). Lennox (1939) controverted this by pointing out that the two substances are really, chemically, clearly differentiated, and that in Merritt's and Putnam's experimental work results with nirvanol differed from those with epanutin.

My observations above make it clear that epanutin is being used in a manner altogether different from that in which nirvanol was used in chorea when it produced such markedly toxic actions. In small doses nirvanol is not nearly so toxic, and it seems almost certain that in many cases epanutin in large doses would produce similar toxic reactions to those attributed to nirvanol. Similar cases have occurred when luminal has been given in large doses (see Phillips (1922)).

One point is of great importance, and that is that both drugs have some effect on the blood picture. So far only changes of a minor nature have been found, but it is essential to rule out more serious complications in patients having an idiosyncrasy, and desirable that work should be done to eliminate the possibility of harm to the bone marrow during prolonged use of epanutin in children.

PART D.

The Place of Epanutin in Modern Therapy.

The treatment of epilepsy has in the past been handicapped by almost complete ignorance of the nature of the abnormal processes occurring. Recently electro-encephalography has thrown an entirely new light on the subject.

As a result of researches along this line Lennox (1940) has now defined epilepsy thus: "Epilepsy is a symptom of a disturbance in the electrochemical activity of the discharging cells of the brain; it is a paroxysmal cerebral dysrhythmia. In epilepsy the dysrhythmia of the brain is analogous to those disordered rhythms of the heart which interfere with cardiac function." He points out that the dysrhythmia varies according to the type of seizure prevailing. In some cases dysrhythmia may occur although the patient is quite free from fits. In such a person, however, the liability to fits when an excessive strain is put on the body or mind is always present.

Modern treatment of epilepsy must, therefore, be directed towards (1) the control of the fits and (2) the abolition or diminution of the dysrhythmia. It is obvious that for experimental and therapeutic purposes electroencephalographic observations are desirable, and it is only when the clinical effects of various drugs have been correlated with these readings that the best results will be obtained.

It is not the purpose of this article to deal with the numerous details of successful treatment of the individual case. It is hoped, however, that some light will have been thrown on the part played by various anticonvulsant drugs in this respect. In epanutin we have a new and powerful anticonvulsant drug, but its true potentialities can only be gauged by patient and careful investigations. The best results will only be obtained when we have a full knowledge of its pharmacological actions. A comparison of the claims made for epanutin when compared with those put forward in the early days of other anticonvulsants should act as a warning against excessive enthusiasm.

There seems little doubt that the ideal treatment for any individual patient will vary according to his idiosyncrasy for the various anticonvulsant drugs and to the localization of origin of his epileptic dysrhythmia. No hard and fast rule for treatment can be laid down, each case being a problem unto itself.

In determining the line of treatment to be adopted the following points regarding the various anticonvulsants should be borne in mind:

Epanutin is a powerful anticonvulsant with little if any sedative or hypnotic effects. It is a drug that produces comparatively frequent and severe toxic symptoms, but these are with few exceptions confined to the nervous system, and if treated properly are seldom really dangerous or cause for alarm. For practical purposes they may be divided into two groups:

(*a*) Early manifestations occurring within a week or two of the introduction of epanutin therapy or an increase in its dosage. (For details of their characteristics see text.)

(*b*) Late manifestations occurring many weeks or even months after the patient has been on epanutin treatment, more often than not with marked benefit to the patient. Whether these symptoms are really of a toxic origin or due to an excessive reduction of fits in a patient whose dysrhythmia is still very marked is not yet clear. They take one of the following forms: A severe

mental confusion ; the onset of such psychotic symptoms as delusions, hallucinations, etc. ; gross ataxia ; an acute exacerbation of fits.

The treatment of all the above symptoms, early or late, is a temporary or permanent, complete withholding of the drug. This step in itself will nearly always lead to a diminution and gradual cessation of the complication concerned, but various other sedative and hypnotic drugs may be required according to the degree of severity of the symptoms present and the rapidity with which they respond to the cessation of the epanutin.

Bromides.—Although these have fallen into comparative disrepute they are probably still of definite use in certain cases. They quite often produce mild and pernicious toxic symptoms and sometimes severe ones. In cases in which there is the slightest doubt blood bromide estimations should be done.

Luminal (phenobarbitone).—This is probably the most useful of the anticonvulsants. To get its best effects, however, it is necessary in many cases to use massive doses even up to 10 gr. *per diem.* Toxic symptoms are comparatively rare even in large doses, provided these have been attained by very gradual increases in the recognized manner. The greatest disadvantage of this drug is the hypnotic effect it often produces. Sometimes this wears off with time, but at others it persists even when only small doses are being given. Moreover there are certain cases in which luminal in adequate dosage does not have such a good anticonvulsant effect as epanutin or one of the other drugs.

Prominal.—This drug should, in my opinion, be reserved for cases that do not do well on one of the other anticonvulsants. It is seldom toxic and in certain cases its anticonvulsant effects may prove superior to those of the other drugs.

Combination of these drugs.—There is no doubt that a few cases will do better on a combination of two of these drugs than on either alone. This probably applies especially to luminal and epanutin, but may apply also to luminal and bromides or prominal and bromides, etc. In the case of epanutin and luminal combination, I have found the most convenient way of giving the drugs is to give one capsule of the former (gr. $1\frac{1}{2}$ = ·1 gm.) five minutes before meals three times a day, and one tablet of the latter (gr. $\frac{1}{2}$ or gr. 1) at the end of the same meals.

When confronted with a case of epilepsy which has not been previously treated with anticonvulsants the order in which these drugs may be most advantageously tried out would seem to be, broadly speaking, (1) luminal, (2) epanutin, (3) a combination of luminal and epanutin, (4) bromides alone or in combination with one of the others, (5) prominal. The circumstances of the individual case may of course call for variation of this plan. In any case already not doing as well as might be expected on one or a combination of the other anticonvulsants epanutin is undoubtedly worthy of a trial. In view of the time, patience, and specialized knowledge required to obtain the best results from the above methods of treatment, it is desirable that each individual

epileptic should primarily be treated by a neurologist or psychiatrist until the most efficient drug therapy for the case concerned has been determined, and in this respect electro-encephalography should receive much wider and more frequent use.

Finally I should like to join with Lennox (1940) in condemnation of the defeatist attitude of certain practitioners towards this disease. Hope should never be abandoned until the above treatments have each been patiently and efficiently tried out. If this is done there are few epileptics who cannot now expect reasonable control of their fits. It is to be hoped that even cases of traumatic epilepsy, whose incidence will undoubtedly rapidly increase as the result of the present bellicose state of the world, may obtain relief not hitherto anticipated.

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PSYCHOTHERAPY IN MENTAL HOSPITAL PRACTICE.*

(BEING THE PRELIMINARY REPORT OF A FULL-TIME PSYCHOTHERAPIST IN A PUBLIC MENTAL HOSPITAL.)

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INTRODUCTION.

IN no other branch of medicine have doctors appeared so nihilistic or so defeatist as in the domain of psychiatry. It seems to me questionable whether this is due to the disparity in the therapeutic results between psychiatry on the one hand and general medicine on the other. In general medicine it is frequently forgotten that the really specific remedies at our disposal are so few that they can be counted on the fingers of one hand. If, on the other hand, we remember that as late as the time of the French Revolution mental patients were kept in chains, and that to-day in modern hospitals we see impressive results with such specific treatments as malarial therapy, then it must be admitted that the psychiatrist is not the only nihilist ; but that this also applies to representatives of other branches of general medicine.

If, however, the psychiatrist appears to be the greater nihilist, this is, in my opinion, due to the fact that in each of us there is the unconscious conviction that in our relationship with our patients, behind our hypodermic syringe lies something else, something personal and individual, which we believe we are unable to grasp.

It is now nearly half a century since Freud published his first book. There is no doubt that his productions, like those of Adler, Jung, Meyer, etc., have caused a revolution ; or at least have profoundly influenced scientific thought. How much, however, have they influenced the nihilism of the psychiatrist ? I am afraid not much. No doubt they have on the one hand contributed a great deal to our understanding of mental patients ; but on the other hand they have stimulated false hopes of cure which often were transformed into bitter disappointments. The fact that in the majority of mental hospitals in England there is no full-time psychotherapist tells its own story.

This leads to the question : Can psychotherapy be applied in mental hospitals in a systematic and economical manner, and be productive of favourable results ? If so, what is the system ? At the instigation of Dr. R. Ström-Olsen, Physician-Superintendent, I have tried to give an answer to this question after my

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activities extending over a year, during which more than 70 patients have been treated.

The work includes both in- and out-patients. As we run two out-patient departments once weekly, it has been necessary on several occasions to ask the patients to attend at Runwell for more frequent treatment and interviews. As this was coupled with financial difficulties on account of travelling expenses, it was not often possible to do it. In the out-patient department the patients were first diagnosed by another psychiatrist ; or, if admitted to hospital, by the psychiatrist in charge of the particular ward, as well as by the Superintendent. Apart from obviously organic cases, practically all forms of neuroses and psychoses were referred to me ; and no case has been refused by me as unsuitable. In general the bulk of cases treated were recent ones ; but I have also dealt with a number of chronic cases whose psychoses or neuroses have lasted a number of years.

Method.

When I see a patient for the first time I usually have a few facts to go by from the clinical notes of another psychiatrist ; or, if an in-patient, I have at my disposal a detailed mental examination, though as a rule the social service report does not come, for technical reasons, until a few days later. The first impression that a patient makes on me I regard as very significant. This is obtained from expression, attitude, movement, language, behaviour, and also from small movements like those of the legs, feet, etc.

It appears to me very important that the doctor should at once obtain a general view of the situation and what the case is about. This is not only to shorten the treatment, but also because I believe that the threshold of sensitivity of neurotics and borderline cases, just as with children, is much higher, and the attitude of the doctor unconsciously affects the patient very strongly. For this purpose I obtain from the patient his earliest recollections and dreams from childhood, as well as those of the present time. These are written down by the patient and are given to me after a few days, or posted to me from an out-patient. Next I try to obtain either a verbal or a written answer to the following questions : Aim and ambition in life ? Likes and dislikes ? Disappointments ? In the case of children the parents are brought into the domain of treatment ; and in sex problems this applies also to the partner. In most cases some modification of the environment is necessary.

Childhood recollections play a very important role in modern psychotherapy. It is, however, unfortunate that a whole mass of problems in connection with this remains unclarified. We assume that the events we remember must be more important than the events which we do not, an assumption for which there is good support. The question still remains whether the recollections are remembered primarily from the point of view of childhood or of our present life, or whether from the standpoint of our general attitude. Of importance

also is whether the type of recollections differs at different times during our life, or whether it remains essentially the same in form and general character. If they are capable of differing, can psychotherapy itself influence them in any way ?

In another work which I am undertaking with two of my colleagues we are investigating in greater detail the importance of recollections. As the general impression which one obtains through the reading of the childhood's recollections is not satisfactory, and also because comparisons are very difficult to make, I have tried to devise an objective system for dealing with them. This consists of taking a certain number of recollections, the total expressed as 100 per cent., and the various characteristics expressed as a percentage of the total number. I employ written recollections from children whom I have never seen. Subsequently the head-mistress of the school was interviewed, together with the various teachers, in order that they might give their opinion on the character of the various children whose recollections had been investigated, and to see whether their opinion agreed with the forecast given by myself. To avoid the suspicion of any suggestion, the teacher was asked to give her results on certain days, and particularly on the day on which I had agreed to send my results of the recollections to her.

I have been able to demonstrate that the results were congruous in 80 per cent. of cases. With a patient actually present I am able to amplify a picture which I have already obtained, and thus in the shortest time construct a picture of the patient's "general attitude." What is meant by "general attitude" ? "General attitude" is not the sum of single attitudes which arise in each case at the moment of the event (this will be behaviour), but is generally a previously fixed, and therefore anticipated, attitude towards all things that we meet. It is formed in the first years of childhood, and later it is only modified. It can be so changed by intensive psychotherapy that it will not cause any further trouble to the individual. The congenital factors undoubtedly participate ; but they are not decisive in the formation of the general attitude.

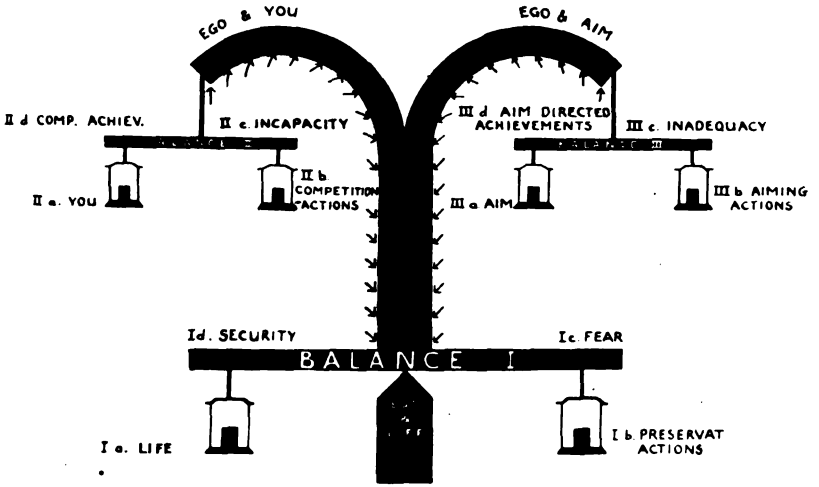
The general attitude is inexplicable unless we recognize the principle of the totality of man. Totality is not used here in the sense of unity between mind and body, and therefore I do not propose to touch upon the various theories of the mind-body problem ; it is here used in the sense of a teleological unity. On the principle of *panta-rei* one is inclined to say that living matter is distinguished from dead matter in that it has purpose and goal. If the living substance is purposive then we arrive at the logical conclusion that it is a totality, because attempts by part of the whole to strive at the same time from one point to a certain goal must of necessity coincide.

We can approach the problem of life scientifically in two ways : either by investigating the life of others, for which we have only our own senses to help us, or by experiencing our own life. It is, however, without doubt recognized

that the experience of one's own life from the philosophical point of view is a fact.

If my life is a fact, then I can construct the following proposition in accordance with the laws of logic. Life is not life, or cannot be life, if certain actions are not undertaken, e.g. a human being cannot remain alive for any length of time unless certain actions, active or passive, for his nourishment are undertaken. These actions I would call preservation actions.

If we place on a balance (see diagram) life on the one scale (Ia) and preservation actions on the other scale (Ib), then the relationships Ia : Ib will indicate how strong or how weak a person is in his Balance I relationship. All persons who have experienced that the scale Ia began to sink as a result of trauma,



D. Elliot.

illness, etc., will have a more sensitive ratio of Ia : Ib. The sinking of the scale Ia as a rule liberates a mechanism which stimulates forces, and this is usually fear. If now the preservation actions are so strong that the mechanism, fear, has lost its effect, then we find ourselves in the field of the opposite mechanism Id security.

We may distinguish between various preservation actions :

I.—Primitive : (*a*) Automatic preservation actions, e.g. sexual instinct, hunger, protection by antitoxins.

(*b*) Non-automatic preservation actions, e.g. food-taking, guarding against accidents, injuries, etc.

II.—Compensatory preservation actions. All actions in the direction of civilization ; sexual desire.

III.—Supercompensatory preservation actions. Those actions concerned not only in maintaining but in furthering life, e.g. the wish for immortality :

(*a*) Reputation ; (*b*) fame ; (*c*) rearing of children.

The hypochondriacs, neurasthenics, conversion hysterics, show in their recollections a high percentage of illness, accidents, deaths, fear. We may presume they are the people who experienced in their childhood a fear of life much greater than that experienced by others; and we deduce, therefore, from their recollections that they are the BI type. As recollections seemingly show similar results in apparently healthy persons, the question arises whether recollections could be used in prophylaxis and thus add another weapon to modern psychotherapy.

We now see again BI as the foundation and the arrows as the countless experiences which we meet with in life. These all leave their traces, which may then be seen in their relationship to the "you" in BII and the relationship to one's own goal in BIII. In BII we have the relationship IIa : IIb : : IIc : IId, i.e. "you" is to "competition action" as "incapacity feeling" is to "comparative achievement." In BIII, IIIa : IIIb : : IIIc : IIId, i.e. "aim" is to "aiming action" as "feeling of inadequacy" is to "aiming achievement." Balances II and III overlap at many points; but it is important to differentiate between them because the relation of one's aim to one's associates is different, has a different effect on one's personality and must be treated differently.

Balance I is the foundation of every human being; and it is of importance how one maintains this balance. It is decisive for the forming of his general attitude. Purpose and direction is the general attitude expressed in Balance II, or the relationship of IIa : IIb : : IIc : IId, and in Balance III, or the relationship IIIa : IIIb : : IIIc : IIId.

Treatment.

After having obtained a general picture of the patient's general attitude during the first few interviews, and having read the history, I proceed as follows: At first I see the patient five times weekly for 30 to 45 minutes. In many cases I allow the childhood's recollections to be told to me verbally, as well as in writing, and in some cases they are first given verbally. Then I allow the patient to relate to me all important or unimportant experiences and happenings of his life. Frequently I only demand certain experiences, e.g. sexual life, successes, etc. During the treatment the patient tries to write down his dreams and brings them with him for investigation. (If patients do not remember their dreams they are advised to relax as soon as they awake; and with closed eyes to try to recount the dream to themselves and then write it down, paper and pencil being handy at the bedside.) These dreams are then generally analysed.

Symbolism seems to rest on an unsound scientific basis. This and free association give analysis far too much scope for its own imagination and for subjective evaluation. For this reason I do not employ it. I use the patient's own attempt at interpretation, the mistakes he makes in the repeated narrative, the atmosphere and impression of the dream and the "directional" association.

For example :

" Do you know a man in reality who resembles the one in the dream ? " Answer : " No." " What did he look like ? " Answer : " Fair, with moustache ; tall, with glasses." " Do you know a man with a fair moustache, tall and with glasses ? " Answer : " Oh yes, Stanley, but he does not wear glasses."

I am not able by this method to interpret all dreams ; but for the comparatively short time the treatment lasts it is more than adequate.

Now I have reached the stage where I can make my plan of campaign, i.e. if the patient is more a BI type, then I concentrate my attention on the investigation and analysis of the earliest anxiety experiences ; and lay more stress on the bodily development, such as garden work and certain forms of recreation therapy. (I must ask you to accept the word " type " with reservation, because there are either none or hundreds of types, on account of the diversity and multiplicity of human characteristics and conduct ; but I cannot make myself properly understood by avoiding the use of it.)

If the patient belongs to the BII type, i.e. changeableness, irritability, flight of ideas, feelings of incapacity, ideas of persecution, restlessness, agitation, moral deficiency, i.e. anti-social type, then I direct my attention to psychic traumata in childhood which have rendered the patient embittered.

With the BIII type, i.e. shy, reserved, day-dreaming, often depressed, with ideas of reference, retardation, lack of initiative, difficulty in thinking, i.e. unreal type, I begin with an explanation and analysis of masturbation in order to diminish the divergence between goal and reality.

These are people for whom more often than not a total change of occupation is necessary. Their difficulties in concentrating or mixing with people on account of feelings of inadequacy are combated, apart from individual treatment, by following forms of collective and institutional treatment.

For more than six months now we have had a patients' Social Club at the hospital for the following reasons :

1. That the patients inside hospitals should have, as it were, a certain amount of " outside life."

2. That patients should become socially active and responsible.

3. That a practical solution should be found for the difficult question of loneliness.

4. That the relationship between both sexes should be made less strained.

5. That further intellectual entertainment should be provided.

6. That the physician gets a further opportunity of studying the patients in their social relationship.

The Club is completely autonomous, as only patients are members and have a vote. They choose their own chairman, secretary and committee, and have various sub-committees for a variety of activities (indoor and outdoor sports committees, entertainment committee, magazine committee, etc.). The Club

meets three times weekly, once for sport, once for entertainment, and once for intellectual work. It also publishes a bi-monthly magazine in which only articles by patients appear. The magazine committee of patients decides what is to be printed, and the editor corrects everything (although it may be said that the " powers that be " have an opportunity of seeing that the articles are in order).

By " community " treatment I mean bi-weekly discussions in the club which I direct. About 50 patients are present and about one-third of them take an active part. Various questions are asked which may stimulate them to discussion ; for instance, about such subjects as " Why do we laugh about the downfall of others ? " and so on. These discussions are useful chiefly for releasing the pent-up energy of many patients and to counteract especially the anti-social feeling of BII type. I must, however, point out that these discussions are not easy to direct, and it is quite possible, if allowed to go in the wrong direction, that harm may be done. Such pitfalls must be guarded against.

The " Circle " I call a weekly gathering of about ten of my patients for a more intimate exchange of views. I do not ask the patients anything about their personal problems. This is done in the collective treatment in America, but encourages the exhibitionist instincts of many patients and only skims the surface. These patients belong particularly to BIII type, who need to be drawn out of their reserve and who have to be trained to express themselves before people, and in this instance, before people who will not laugh at them. Patients write their answers to problems which are placed before them, and these are then discussed. Then I put questions to the whole group ; but I also ask certain persons of the group particular questions at times.

One particular problem which has occupied us for a long time is that of day-dreaming. In many cases, particularly those of the BI and BIII type, i.e. schizophrenias, depressions, hypochondriacs, neurasthenias, this circle has rendered great service in certain phases of the disease.

Thoughts.—I allow most of my patients to write down for 10 to 15 minutes what is going through their minds. That helps the relationship between them and me, and between them and the surroundings, and dispels misunderstandings. It furthermore trains the patient to a free expression and gives me a rapid picture of his mental state at the time.

The ideal that the institutional psychotherapist should direct the whole of the occupation therapy department cannot always be realized ; but it has been carried out in connection with patients who are undergoing psychotherapy. By personal contact, individual conversations or meetings with the chiefs or assistants of the occupational therapy I have always tried to give them an essential description of the personality and disease of the patient, and to determine the foundation on which their occupational therapy should be built. Contact is then maintained continually ; and it must be emphasized that the occupational therapists can render a great deal of assistance, but can also do a

great deal of harm. In my work they have been of inestimable value. I have made the observation that the interests of the therapists can be still further increased if the doctor, in a practical way, takes part in the solution of their problems and tries to stimulate them to a more scientific view-point and application of their problems.

The conception that occupational therapy is principally concerned with hobbies does not hold good for all cases. Of significance in this question is the relationship BIIIa : IIIb, for which reason I first of all obtain a picture of the earliest and the later ambitions, or of the difference between them and their realization.

In many cases the patient is satisfied to work at his own particular occupation in hospital; but there are some for whom it is important to create a new interest, and to get them on to a job which is more in line with their childhood's ambition. In this connection there are serious difficulties in hospitals because our departments are not so arranged that we can always provide the desired occupation. A not unimportant group are those patients who have failed in their occupation or vocation. They react too slowly and get left behind in the general competition of modern life, and therefore land in hospitals as schizophrenics, depressives or psychopaths. Many of these can be trained in a particular occupation even if not in the outside world yet still in a hospital community, and valuable results are produced. We cannot postpone indefinitely the question of providing special occupational facilities for these people, just as we have in certain tuberculosis communities. At present one can do the following: The patient receives training in a certain profession while in hospital. After some time he can be sent to another hospital if agreement has been reached between the two Medical Superintendents. There he can go on working in his newly-learnt trade. The patient receives at first board and lodging only. This arrangement should be satisfactory to both sides, as the patient can continue his training without having to worry about ways and means and the Superintendent need not face extra expense, but is able to find for his patient the necessary after-treatment. This can be applied to gym. assistants, to female occupation and utility departments, and to male artisans and clerks. In the nursing profession it can be done too. In such cases the sympathetic attitude of the superintendent or psychotherapist would make adaptation easier, but it does not seem advisable to inform any other member of the nursing staff of the past history of the new nurse.

In eight cases I have been able to train patients to a high degree of efficiency in certain occupations:

Patient I. Chronic schizophrenia, aged 24. Learnt shorthand and typewriting in hospital and now teaches other patients.

Patient II. Obsessional neurosis, aged 29. Has learnt shorthand, typewriting and book-keeping.

Patient III. Psychopath, aged 18. Learnt book-keeping and is now discharged and getting a job.

Patient IV. Schizophrenia. Has been able to learn the elements of printing and has been discharged.

Patient V. Obsessional neurosis. Has learnt physical training.

Patient VI. Anxiety neurosis. Was taught carpentry, was discharged and now works in America.

Patient VII. Depression. Has worked as a nurse in another hospital for four months.

Patient VIII. Works as a nurse in our hospital and is satisfactory.

Link system.—When a patient is to learn an occupation, trade or craft, many lose patience and perseverance when they have only gone half way. It is of the utmost importance to intervene at this moment; and the best remedy I find is to make the pupil a teacher so that whilst he is still learning from patient (*a*) he can himself instruct patient (*c*).

We must now ask the question: What is the essential of psychotherapy, and what do we mean by personal treatment? In our answer to this question we must attempt to define what we mean by mentally ill or mentally sound. I am inclined to say that normal mental health is the state in which a person can utilize to the utmost his talents for the benefit of society and himself, and at the same time maintain an equilibrium of the three balances. According to this, one may object that no one is really in normal mental health, but for practical purposes whoever approaches this equilibrium must be regarded as a normally adapted person.

Theoretically, we all have an inclination to neurosis and if this tendency does not become overt it seems to me that it is a proof of how strong preservation actions, and especially primitive ones, are. The treatment will therefore consist in the first instance of re-establishing "maximum efficiency with maximum equilibrium."

How is it possible?

All schools of psychotherapy agree that the earliest childhood is the most important factor—whether emphasis is put on childhood trauma or the apperception scheme is of secondary importance. The question is what can we call the processes used in psycho-analysis and other systems of psychotherapy which make the patient change his attitude to life and illness? Psycho-analysis tries (1) to make the patient conscious of childhood experiences; this is an act of increasing self-knowledge; (2) to transfer feelings; this is an act of emotion.

Self-knowledge seldom causes any change; self-knowledge and transference sometimes do. Psycho-analytic treatment is sometimes taken as far as the reaching of the level of cognition, and this is only achieved through the sacrifice of much time. This long process makes the patient so inactive that the state of cognition is not always followed by deeds.

I try (1) not to make the patient conscious of childhood experiences, but to gain for myself a knowledge of his general attitude; (2) to develop an aim-transference, an aim-experience, and cognition.

The step from self-knowledge and transference to deeds and realization is much bigger than that from these four points to deeds and realization.

I have already explained "general attitude." The aim-transference is different from transference because I feel it is not enough to let the patient build me into his system of transference. I attempt to behave in such a way that I satisfy his personal needs of transference after I have found out intuitively what his needs are, e.g. sometimes a child brought up without a father will not be affected by the very kind psychotherapist, but the experience of the more strict but not bad father might be highly successful.

The aim-experience is easier to realize in an institution. It is comparatively easy to get a girl adapted who is shy and has feelings of inferiority regarding her appearance and power of attraction if one lets her experience success, e.g. on the dance floor. The same applies to patients with feelings of inferiority regarding their intellectual abilities, etc.

The method of the pure logical cognition is used for the more intelligent people, but it is possible to adapt it to a certain extent for any type. It is possible to let patients not think through but experience the most difficult problems in a simple form.

With this we arrive at the nucleus of the whole problem. The long-lasting analysis is a rigid scheme which saves the principle and ignores reality.

The beginner, or inexperienced surgeon, will, in a critical moment, go through all investigations before deciding to operate. The experienced surgeon will, at a glance, know of the decision to take in order to save a patient's life. The first man will have acted correctly, according to the law of science, and while doing so will, unfortunately, allow the patient to die.

It is a mistaken ambition to want to appear scientific at the expense of our patient's health. We may attempt to use scientific methods for the investigation of psychological diseases. The practical application cannot yet follow preconceived plans or our present-day methods of science. It is an art; and art does not follow the laws of differentiation but those of conceiving things as a whole. This makes a detailed description of therapy very difficult. I regret this fact without being able to change it at present; but it does not seem to me to be Utopian to hope that in a few years one should be able to reproduce psychotherapy by recording it on a sound film, and in this way solve one problem of scientific research, namely, that of being able to give an objective demonstration.

CASE 195.—P. D—, aged 47, married; insurance business. Anxiety neurosis with hypochondriacal symptoms. First seen April 5, 1937.

10.iv.37: He is undoubtedly suffering from arteriosclerosis with marked hypochondriacal symptoms and feelings of inferiority. In November, 1935, he started with headaches and insomnia. Company's inspector sent for him and advised him to accept an agency from the health point of view. He did so but was worse off financially to the extent of £150 per annum, and has since very much regretted his step. He has made an effort to get back, but company would not consent.

14.v.37: Does not seem to make any progress. C/o worry, sleeplessness, poor appetite, cannot carry on with his work.

In January, 1938, a report from Tavistock Clinic states: "There seems to be no possibility of a change in his work. His wife and child are thoroughly exhausted by his gloom and depression. If it were possible for him to have a break and be in other surroundings for a while it might be beneficial."

28.vii.39: No improvement.

2.ix.39: Special psychotherapy commenced.

14.x.39: He was always very sensitive, but since being asked to resign has become more sensitive, excitable and nervous; hence he gave a bad impression when he went to the firm to ask to be reinstated. I explained that he must behave in such a manner that his employers will think him fit to hold a responsible position. Finding that an official of the firm disagrees with the man who persuaded patient to resign, I suggested that he write to this official for support.

i.40: His change of attitude has helped him to regain his position. Symptoms disappeared; feels completely changed and well.

26.iv.40: Quite recovered, no headache, very happy, symptoms disappeared. Came out first on list in his work last month; has already an increase of £13 per annum in his salary.

We have here a case of hypochondriasis with a background of arterio-sclerosis. He was treated for four years without improvement.

He is a high-grade BI type; this is expressed in his recollections, 50 per cent. injustice. This case illustrated to me again that fixed methods and rules hinder the psychotherapist in his work.

The question arises whether arterio-sclerotic organs (if the arterio-sclerosis is not highly developed) can be considered in their effect as an organ inferiority. If they can, this would explain the sudden disappearance of all the symptoms the moment the exogenic factor of the neurosis was removed.

CASE 106.—Aged 25, married. Agitated melancholia. Admitted 27.iv.38. Patient was unable to give a complete and connected account of herself. She has persecutory delusions—"My husband is going to take a case against me; they wanted me out of the way"—and self-accusatory ideas.

The summary after examination stated: "The incongruity and persecutory content of her delusions make it necessary to be guarded in giving a prognosis."

When psychotherapy was commenced on 8.v.39 patient was in the seventeenth month of certified hospitalization and was very resentful and hostile. It was found she belonged to the BII type, with developed masculine protest.

She had been a nice-looking child and later was popular, successful and very active. She wanted to be a boy. With regard to marriage, she had turned down two men and her husband. Later she agreed to consider her husband because he was "so persistent," but she put off her marriage from year to year until she could find no further valid excuse for doing so. When she got married her husband wanted to undress her. "This was too much," patient states. She was frigid, and after two months of married life she went away to her parents and attempted to hang herself on the morning of her husband's arrival at her parents' home.

After treating patient, with a great effort the husband agreed to further my plan by telling patient that he would agree to her returning to the job she had before marriage, and that if she still wished for a separation after a short time she should have it. He also promised to show no affection towards her, in fact, not even to visit her.

The plan worked out as anticipated; patient came to see me weekly. She lost her hostile and agitated manner and became sensible and balanced. Life cured her quickly of the illusion that every man would be attracted by her. Although I asked her not to see her husband and to promise me that there would be no intimate life, she spent a week-end with him without telling me. She ceased attending clinic and went home after a few more weeks. She appears to have changed her attitude

to her husband and to married life, as the following letter illustrates. She had been invited to the Social Club and replied on 14.iv.40: "Thanks for your kind invitation which I am sorry I cannot accept owing to the fact that I am expecting a baby within the next few weeks."

It seems to me that the vicious circle—attempted suicide, consequently responsibility for the authorities and observation, consequently patient becomes more resentful and hostile, consequently still greater responsibilty and caution on the part of the medical staff—causes some patients to remain a long time, occasionally for life, in hospital.

CASE 217.—D. E—, aged 23; teacher. First seen 29.xii.39. Patient shows dissociation, retardation, thought blockage and certain paranoid trends, namely, a feeling of being watched and ideas of interpretation. She cannot concentrate, lacks interest and giggles. States mother and young man are dead (has no young man), has delusions that her books have been rearranged, which signifies some secret code, that people can look through her brain and that she recognizes patients' voices to be those of her former friends.

Physician's summary reads: "I think this is an early stage of schizophrenia and might respond well to insulin treatment."

Patient reached top standard in school and became a fully-qualified teacher. However, her recollections show 49 per cent. intellectual inferiority feeling. It was found that her position in school was only reached by extraordinary efforts; she has always been slow of comprehension. Her headmistress states she is her best teacher, but it is always difficult to make her grasp anything new. Patient thought her children read and spelt well to spite her as they knew she could not master this subject. Her intelligence test proved superior intelligence with non-verbal, but difficulty with verbal material.

Patient's mother, who was disappointed in marriage, has centred all her love in her daughter. Father is very strict, and patient's desire for a kind father substitute prevents faculty of criticism when in contact with men. She is a BIII type, shy, has no social connections and lives an unreal life in day-dreams.

Five main points had to be treated: (1) Intellectual inferiority feeling; (2) masturbation; (3) sex problem; (4) social contact; (5) day-dreaming. The different forms of collective and institutional treatment were used intensively.

Her improvement was not steady until the end of February; she had difficulty in concentration, lacked initiative and had fits of crying. From then until the end of March improvement was so great that she was discharged and started teaching again on April 1. She is now perfectly well, with no symptoms or complaints. She is jolly and happy, active at school, and helping in the Social Circle at East Ham.

CASE 135.—A. P—, aged 22. 2.ii.37: She is suffering from schizophrenia. There is thought obstruction, affective blunting, and hallucination of smell and hearing are experienced. She gives expression to visceral delusions, stating she has no chest, food does her no good and she is wasting away. She hears laughing and jeering references to herself and is convinced that an evil odour is given off from her system. She is resistive, uncertain in conduct, and at times impulsive.

Psychotherapy commenced 22.xii.38. She had worked as a sewing-machinist, but her childhood ambition had been to become a shorthand-typist. I gave her the means for learning by herself; her schizophrenic symptoms were so far developed, she was so out of touch with reality and her environment, that I considered it more as an experiment. She learnt to type and completed the whole course of shorthand, and has been teaching other patients for some months. With success her symptoms disappeared. She is slower in movement than other people—her mother is of the same type—and quiet, nevertheless she is thoroughly active in the ward, at the Social Club, takes part in dances and discussions. During 14 months she had one relapse of two days, following a cold with high temperature. At this time delusions returned; she thought doctor and nurse were spies. Later she confessed she was worrying about a pupil with whom she was having no success.

- One cannot really say what is primary and what is secondary, but the connection between success in life and the disappearance of even real schizophrenic symptoms is so obvious that it is worth while considering them.

CASE 132.—H. T—, aged 18; shop assistant. 21.i.39: Schizophreniform psychosis. His expression is wan and weary; he has a general air of listlessness. In the ward he is slow-moving, quiet and unobtrusive and requires much urging. At meals he is uninterested in his food and has to be pressed to take sufficient. There is moderate retardation.

He complains of feelings of exhaustion and lack of energy and interest. Eight months ago he had a cycle accident, colliding with a lorry and breaking his arm.

Some months later, during the film, "Night Must Fall," suddenly a terrible fear gripped him; he wanted to dash out of the cinema, and felt he would go mad.

He began to feel a compulsion to search for and pick up small pieces of glass and pins from the floor, and feared if he did not do so others would be injured. This obsession became progressively worse until it prevented him continuing his work. The compulsive phase passed gradually into one of depression.

14.ii.39: He has started to show some catatonic phenomena—stereotyped movements, e.g. bending down and touching his knees, also periods of spasm-like rigidity; he bent his head over the back of his chair, screwed up his eyes and pursed his lips into a pig's mouth, whilst he gripped the arm of the chair with his hands and extended his legs out parallel with the floor.

15.iii.39: Psychotherapy commenced. The therapist encountered great difficulties in his inactivity and dullness. It was found that his feelings of guilt over frequent masturbation from 13 to 17 years of age were so strong that he was looking for God's punishment.

An analysis of his masturbatory complex improved his state a little temporarily. Much greater improvement was obtained when the psychotherapy was combined with active treatment. He was made leader of physical training in the ward and put in charge of the garden group of patients.

He was discharged on 13.viii.39, recovered. He is now clear of symptoms, works diligently, mixes well with both sexes, is active and happy.

Summarizing, we can say: This patient showed retardation, difficulty in thinking, thought blockage and stupor. In certain phases symptoms of obsession and depression. Whatever the diagnosis given, it would have been of no help for his treatment; only a knowledge of his type, his life and conflicts could make it possible for us to help him.

CASE 112.—D. H—, aged 21; solicitor's clerk. First seen May 23, 1938. Depressed, self-conscious, self-absorbed, marked feelings of inferiority and inadequacy; could not concentrate; headache when reading and fears of insanity and suicide. She was very restless and fidgety, thought people were looking at her and knew exactly how she felt; had difficulty in thinking and was retarded.

Her illness commenced in August, 1937; first symptoms were that she worried about her work and thought something awful was going to happen at home. After a time obsessional symptoms became prominent, she had to keep going over the day's work in her head, had to go to the bathroom to see if the taps were turned off and continually look to see if there was dust about. The most prominent symptom was a religious one; she felt she must "gather the people into the fold." This became so exaggerated, disturbing both home and church life, that her minister sent her to the Clinic.

She was treated psycho-analytically from May 23, 1938, to January, 1939. I was then asked by the analyst to take over the case. She was tense, fidgety, spoke abruptly and was difficult to follow.

She strove to keep the conversation on religion, but recognizing this as a subconscious effort to keep me away from the real trouble, I refused to be led.

Her childhood ambition had been to become a teacher, an outstanding teacher,

but in spite of good testimonials she states it was not fulfilled because " I was not clever enough."

Asked to retell a story she liked, she told of a girl who sacrificed herself by not marrying the man she loved because she was ill and did not want to be a burden to him.

Summarizing, we can say briefly :

(1) I did not follow her up the *cul-de-sac* of her symptoms, but neglected them.

(2) I found her feelings of intellectual inadequacy super-compensated in a very high spiritual, almost unreal aim, and therefore a condemnation of all sensual desires.

(3) I treated the religious intolerance indirectly through discussions on the development of human culture.

(4) I made an effort not to change but to utilize her general attitude.

(5) With this utilization and incidental changing of her general attitude her obsessional and other symptoms completely disappeared.

(6) At the same time her life problems were solved. The patient is now perfectly well, at work, happy, and engaged to be married.

Statistics.

In about a year I have treated 70 patients; 60 are discharged, 5 will be discharged within a month, 1 in a few months' time, and 4 remain with a bad, or at least uncertain prognosis. Of the 70 patients, see Table I :

32, i.e. 46 per cent., have recovered ; 19, i.e. 27 per cent., have greatly improved ; 10, i.e. 14 per cent., have improved ; 3, i.e. 4 per cent., have slightly improved ; 6, i.e. 9 per cent., have not improved.

On analysing the cases, we find 3 under slightly improved are all cases who interrupted their treatment (1 neurasthenia, No. 175, 1 obsession neurosis, No. 156, and 1 schizophrenia, No. 140).

In the 6 cases not improved, 2 refused to continue their treatment at a point at which they had considerably improved, 1 child—an out-patient—had to be sent to an institution because we could not take him as an in-patient at the hospital, and 3 schizophrenics—2 chronic and 1 acute—were taken off psychotherapy in the hope that insulin would provide a swifter cure. None were cured.

The patients were examined from the point of view of solving their most important life problems such as occupation, social contact and sex relations, as I consider these to be often a more definite sign of improvement in their mental health—especially from the standpoint of prognosis—than the disappearance of symptoms. The result (see Table II) showed that 36, i.e. 51 per cent., solved their problems to a greater extent than at any other time of their life ; 14, i.e. 20 per cent., reached the level attained before illness (restored) ; 11, i.e. 16 per cent., solved their problems better than while they were ill (improved) ; 3, i.e. 4 per cent., a little better than while they were ill (slightly improved) ; 6, i.e. 9 per cent., no better than while they were ill (not improved).

We learn from this that patients (see Table I, col. 2) under " greatly improved " have really recovered ; those under " recovered " (Table I, col. 1)

are, with regard to their life problems, in a better state than at any other period of their life.

All the cases, apart from six with whom I could not get in touch, have been seen and re-examined at the time of writing. Not one of the 60 discharged patients has had to be readmitted to any hospital. Two cases, Nos. 113. neurasthenia, and No. 170, depression, need further out-patient treatment. All those discharged are in the same or an improved condition as at the date of discharge. The 70 patients were made up of 40 in- and 30 out-patients.

From the financial point of view the employment of a psychotherapist would be practicable if work were carried on under this system. Lengthy analytical treatment, lasting about two years, means a maximum of four patients a year, which, for a public mental hospital, is out of the question as an economic proposition. But if, instead of four patients, 70 could be treated in a year, then the appointment of a psychotherapist in every public mental hospital would be justified.

In the bigger hospitals it would be advisable to employ a team consisting of a psychotherapist, one or two young doctors, and one or two students. I am

TABLE I.—*Recovery Rate Distributed According to Diagnosis.*

	Recovered.	Greatly improved.	Improved.	Slightly improved.	Not improved.
1. Depression	4	3	2	..	..
2. Hysteria	1	..	..	..	..
3. Conversion hysteria	..	..	1	..	..
4. Anxiety neurosis	6	3	2	..	..
5. Compensation neurosis	..	1	..	..	..
6. Enuresis	1	1	1	..	..
7. Neurasthenia	1	1	2	1	..
8. Hypochondriasis	1	1	..	..	..
9. Obsession	1	4	1	1	..
10. Manic depressive	1	..	..	..	..
11. Agitated melancholia	2	..	..	..	..
12. Melancholia	2	..	1	..	2
13. Involutional melancholia	1	..	..	..	..
14. Schizophrenia	5	2	..	1	3
15. Puerperal psychosis	1	..	..	..	..
16. Sex perversion	2	..	..	..	..
17. Frigidity	1	..	..	..	..
18. Moral deficiency	1	2	..	..	1
19. Chronic alcoholism	..	1	..	..	..
20. Inferiority complex	1	..	..	..	..
	32=46%	19=27%	10=14%	3=4%	6=9%

TABLE II.—*Showing the Solving of Life Problems According to Diagnosis.*

	Better.	Restored.	Improved.	Slightly improved.	Not improved.
1. Depression	5	2	2	..	..
2. Hysteria	1	..	..	..	..
3. Conversion hysteria	..	..	..	1	..
4. Anxiety neurosis	6	4	1	..	..
5. Compensation neurosis	..	1	..	..	..
6. Enuresis	1	1	..	1	..
7. Neurasthenia	1	1	2	..	1
8. Hypochondriasis	1	..	1	..	..
9. Obsession	5	..	2	..	..
10. Manic depressive	1	..	..	..	..
11. Agitated melancholia	1	..	1	..	..
12. Melancholia	1	2	..	1	1
13. Involutional melancholia	1	..	..	..	..
14. Schizophrenia	6	1	1	..	3
15. Puerperal psychosis	..	1	..	..	..
16. Sex perversion	2	..	..	..	..
17. Frigidity	1	..	..	..	..
18. Moral deficiency	2	..	1	..	1
19. Chronic alcoholism	..	1	..	..	..
20. Inferiority complex	1	..	..	..	..
	36=51%	14=20%	11=16%	3=4%	6=9%

sure the doctors and students would accept the minimum conditions if they could get experience and their own analysis at the same time. Even if it were necessary to provide a good salary for the psychotherapist, this would be justified by the large number of patients who could be treated under this team system.

DIAGNOSIS.

You will be surprised that I have spoken about the therapy without mentioning diagnosis. It was not unintentional; I am really at a loss, for diagnosis as it stands to-day is practically no help to me in my treatment. It does not help if I know the case as anxiety, depression, or even schizophrenia; especially at the commencement of treatment diagnosis tells little about prognosis; so far we have no biochemical or anatomical support for it.

A rigid forming of diagnosis can be harmful because (*a*) the value of the first few sessions—often the best for influencing the patient—can be lost in discovering the diagnosis; (*b*) the physician becomes satisfied with the diagnosis; (*c*) he emphasizes instead of minimizes the symptoms, and that sometimes in the mind of the patient increases them; (*d*) the patient is

marked down by the diagnosis, then through direct and indirect mutual influences of the hospital and the patient, he is harmed. The present method of finding the diagnosis is wrong from the standpoint of psychotherapy; it hails from the organic psychiatric period.

Psychic processes are aiming processes and therefore can only be seen teleologically and not situationally. If I make the diagnosis depression, it tells me nothing unless I can see the path from the past to the future.

It would appear difficult, but I think necessary, that the step should be taken from the horizontal situational diagnosis to the vertical aiming diagnosis.

Limits, Mistakes and Difficulties.

Limits.—The defining of limits can be the key to success, but if they are made to enclose too small an area they may be harmful. Until recently it was thought that the psychoses were outside the province of psychotherapeutic influence. This is no longer true. Even organic lesions have been drawn into this sphere, since it has been accepted that psychological factors are of decisive, if not primary importance in the production of organic or even anatomical lesions, e.g. gastric ulcer. It may seem as if the limit had been reached when the patient can no longer be approached psychologically; but even then it may be possible to apply other forms of treatment, i.e. the indirect method, occupational therapy, the method of the third person. Treatment is impossible if the patient is stubborn and refuses to co-operate. If measures such as a change of psychotherapist are unsuccessful, we are unable to do anything for such cases.

Mistakes.—Psychotherapy is a very highly specialized and difficult work and requires a long training, clear thinking, a good general education and common sense. Patients are often extremely sensitive and therefore the smallest mistakes will have a serious effect. Unfortunately they cannot always be avoided; but at least it can be hoped that we all learn through out mistakes.

Inhibiting factors.—There can be no doubt that the regulations issued by the Board of Control represent a turning-point in the history of mental welfare in this country. They are certainly of great value for the majority of hospitals although in some modern hospitals one would wish for certain changes. It does not appear necessary to have special institutions for the treatment of neurotics. It would seem desirable to retain the whole scheme of mental welfare for each administrative unit. This makes it easier to combat the prejudices of the general public against mental hospitals; and makes it easier to deal with patients whose condition is temporarily deteriorating. But it would be desirable if some of the restrictions could be waived in the case of nerve units. It is important that patients should have as much responsibility as possible, as this is an important factor in treatment. At present it is not possible to make a

patient responsible for discipline in a social club, for example, as male and female patients are not allowed to be together without supervision. For the same reason it is not practicable to allow patients to teach others of the opposite sex.

In the older hospitals, where a physician does not treat patients very intensively, it is certainly right to make the superintendent, as the most experienced member of the staff, responsible for the patient's life. However, in more modern institutions, in which the physicians treat the patients more intensively, it seems harmful for the patient and unfair to the superintendent to place all responsibility on the latter.

In the problem of change of occupation it would be of greater value if there were the possibility of promoting patients to be apprentices and assistants, in order to be able to place them later as full-time workers.

It would also be advantageous if means could be found whereby patients could be paid according to the work done by them, as is done in some private hospitals.

Conclusion.

In my paper I have intentionally not mentioned any existing psychotherapeutic system. I recognize my debt to my teachers. Although I am a grateful pupil of Adler, I appreciate the genius of Freud.

I tried to use the things they have *in common* as far as they have proved helpful in my work; and I wanted to avoid the controversy between the schools that emphasizes their differences. Freud, too, saw the necessity for a wider outlook when he said (1): "The task will then arise for us to adapt our technique to the new conditions. I have no doubt that the validity of our psychological assumptions will impress the uneducated too; but we shall need to find the simplest and most natural expression for our theoretical doctrines. . . . It is very probable too that the application of our therapy to numbers will compel us to alloy the pure gold of analysis plentifully with the copper of indirect suggestion; and even hypnotic influence might find a place in it again as it has in the treatment of war neuroses." This attitude would appear to be the most useful, as no one has been able to give a satisfactory scientific foundation of psychotherapy. It would be difficult to do so, as a scientific foundation of psychotherapy as a natural science would have to be based on experiment, and for experiment we must have repetition under exactly the same conditions, and this is impossible when dealing with human nature. It seems to me we must content ourselves with the words of a famous American psychiatrist (2): "Psychotherapy is the art of applying a science which does not yet exist."

From the practical scientific point of view I am not satisfied with my work as, unfortunately, I cannot say how many of my patients would have improved without my help. I am as dissatisfied as I am when I read that with insulin

one can have results varying from 26 per cent. (3) to 88 per cent. (4). On the other hand, one reads papers that show normal remission rates with occupational therapy or with prolonged narcosis up to 54·6 per cent. (5), whilst Langfeldt (6) states that 67 per cent. of atypical schizophrenics improve without treatment. If I bring these examples it is only to show how uncertain our methods of psychiatry are to-day, for we have to reckon with so many uncertain factors. It is a good thing that we sometimes forget that we cannot prove the direct efficiency of our treatment, and that many cases recover not because of, but in spite of, our help. As Bleuler sarcastically points out (7): "Pneumonia takes twenty-one days with the aid of a good physician, three weeks without his aid; and with the aid of a bad physician much longer."

Is psychiatry really in such a bad plight? I think not. It is true we cannot offer a scientific foundation, and we prefer not to rely upon an apparent one. Up to now, unfortunately, the only measure we have is that of result. But one who is habitually in close contact with patients and who observes so often the sudden disappearance of symptoms after the removal of causes, and the completely different relationship of the patients to their life problems, will surely find in this sufficient justification for his work. He will recognize the significance of modern psychotherapy and the possibilities of success. This justification is what compelled me to read this paper to you to-day.

May I express finally my, and perhaps our, wish that our scientific and practical work in psychotherapy may be so much intensified that these words of Dr. Crookshank (8) will become untrue: "Organic disease is what we say we cure and we don't; functional disease is what the quacks cure and we wish we could."

Summary.

(1) 70 patients suffering from neuroses and psychoses were treated psychotherapeutically in a public mental hospital during a year.

(2) 87 per cent. recovered or improved; 4 per cent. slightly improved; 9 per cent. did not improve.

(3) Some cases were treated which were unsuitable for orthodox analysis.

(4) The method is a short but deep and intensive psychotherapy which tries to use certain things common to Freud and Adler with individual, collective and institutional forms of treatment.

(5) The theory of the three balances is explained and special attention is given to a new method of reading earliest childhood recollections.

(6) It is tried in:

(A) Individual treatment, to make contact through an—

(1) Aim transference, to get a picture through the knowledge of—

(2) General attitude, and to change the patient through the process of—

(3) Experience and cognition.

This is supported by—

(B) Institutional treatment :

(1) Individual occupational therapy.
(2) Change of occupation.
(3) " Exchange " system.
(4) Individual recreational therapy.

(C) Collective treatment :

(1) Social club.
(2) " Community " treatment.
(3) " Circle."
(4) Magazine.
(5) " Invitation " system.

(7) The after treatment in the out-patient department is supported by—

(1) Social circle.
(2) " Collective " treatment.
(3) " Invitation " system.
(4) " Exchange " system.

(8) The result of the treatment of 70 patients has been so encouraging that the employment of a full-time psychotherapist on these lines in all public mental hospitals can be advocated.

I take pleasure in expressing my gratitude to Dr. R. Ström-Olsen, Physician-Superintendent, for his instigation, for his helpful advice, for translating and correcting, and for providing the facilities and permission to publish the results. I also want to express my thanks to Dr. S. L. Last, Dr. F. P. Haldane and Dr. B. M. A. Henderson for constructive criticism, and to Miss K. Thompson for her great help.

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Discussion.

The PRESIDENT, after expressing appreciation of Dr. Bierer's most interesting paper, said there were one or two points on which she would like a little information. How did Dr. Bierer choose his cases, or did he choose them himself? She was also delighted to hear that diagnosis was no help; she thought it was a terrible pitfall in their work. Instead of taking each particular case on its merits they were apt to try to put it in some particular group which at once tended to cramp their attitude with regard to it.

Under what arrangement did he suggest that payment should be made for work done? Was it not possible that one might get that feeling of "I want to help" quite regardless of payment? In her little hospital of 60 beds no one was paid, but everybody was expected to help in any way they could—to help wash up, polish, or in the garden. She felt it would spoil the psychotherapeutic effect if payment was given, and if there was any form of satisfactory transference patients nearly always said they would love to help the staff.

Another thing which she had been delighted to hear was that fixed methods and rules hindered the work of psychotherapy. It required no red tape of any kind; one ought to be able to give the environment which was most suitable to the particular patient quite regardless of anything else. At her hospital patients were allowed to sleep there and go out to their work, or alternatively to come to the hospital during the day and return home to sleep. Some patients came in just for meals, for the social contact. They also tried to run a magazine, but this was a variable quantity for the good reason that their people did not stay long enough. It was quite true that the less red tape, the less fixed methods and rules were utilized, the more successful the psychotherapy would be.

Dr. BIERER, in reply to the President, said that Dr. Ström-Olsen would be more competent to answer the question regarding the choice of patients. He thought most of them came from the out-patient clinic, and were sent to him either by Dr. Ström-Olsen or his deputy.

He had wanted to watch the difference in treatment between psychotherapy and insulin for schizophrenia, but there were not enough patients for this to be carried out.

He was rather impressed at St. Andrew's Hospital at Northampton with the system of payments. The patients were given a piece of ground and seeds and the hospital bought all the vegetables for the normal price. One of the patients earned £80 during the year. He was aware that this might be difficult to arrange at a public mental hospital, but he thought it feasible from the economic point of view because the hospital did not lose money, and it would help the patients. The great difficulty was the question of what to do with the patients working in occupational therapy not in the garden.

Dr. STRÖM-OLSEN said that regarding the selection of cases he thought Dr. Bierer had enough influence with him to get the patients he wanted. Sometimes they were sent to him as a last resort, with remarkable results. He had nearly all the psychotherapy patients.

Dr. CLIFFORD SCOTT said that although he had been out of mental hospitals for a year he had been interested in this problem for a long time, and was more than interested to hear Dr. Bierer speak so enthusiastically of his results. Environment was very valuable, and a man working in a hospital had a great advantage over one working in private—something which he had noticed in changing over from hospital to private work.

The plea which Dr. Bierer made for co-operation between hospitals was important. He remembered talking to people about the difference in size of mental hospitals in this country and those in America. When he first started he was in a

hospital with 8,000 beds; it could be imagined what a town it must be and what an advantage it held in arranging matters. There were so many patients that one could build up the facilities of a town of 15,000. That demonstrated why co-operation was essential, especially with the London County Council, where there were hospitals within walking distance of each other.

In listening to Dr. Bierer the speaker was trying to come to a conclusion as to whether part of his work was scientific and not artistic, and also what his scientific work was linked to. It was linked up with his personality, study and writing, and he thought Dr. Bierer must be using a great deal of intuition in coming quickly to a judgment of the central problem. The person who had a great deal of experience could do it more quickly, but as a psycho-analyst he found that his judgments were altered after perhaps two years of analysis and that was why one made mistakes.

Dr. Bierer mentioned a scheme of classification and he wondered whether it was generally useful. It seemed to be quite new and unique and for understanding one would like a little further elaboration.

Many speakers talked of psychiatry as a science; others did not think of it as science. Psychiatry must be somewhere between astronomy and chemistry and he should hate to think he was not to be called a scientist. Every case was an experiment; they could not compare similar cases, although some were similar. Nature gave them indications to watch just as Nature gave the astronomer his experiments.

Dr. Scott was very pleased that Dr. Bierer had mentioned that diagnosis was to be avoided at the beginning; he did not think it should be given up altogether, but should be made at the end. They should go ahead and deal with the problems whilst the patient was under their care. They did not need diagnosis, but after they had finished with the patient the diagnosis could be made.

Dr. J. H. MacDonald thanked Dr. Bierer for his attitude towards psychotherapy, which had defined the psychotherapist for him. There was a very prevalent tendency whenever the words "psychotherapy" or "psychotherapist" were mentioned to conclude that they were synonymous with psycho-analysis. His experience led him to believe, and he was more confirmed than ever after listening to Dr. Bierer, that they had all been doing their best for years to be psychotherapists and had used active psychotherapy with helpful results. They had realized that in making use of their occupations and amusements they were trying to get the patient interested in something outside his own troubles, and if they succeeded they were able to approach him more closely.

Dr. Bierer had demonstrated something which he was constantly preaching to his assistants—"Get near your patient, get to understand him, and find out what his troubles are, and let him understand that you are trying to understand and willing to help him." It needed no psycho-analysis in the strictest sense of the term to do that; it needed sound judgment, experience and a dreadful lot of common sense, and that was one of the reasons why, when a junior assistant had failed, the senior would often succeed. He said to his assistants from time to time, "There is a case you ought to help; you must spend half an hour or three-quarters with him every day; get to understand him," but he found sometimes they did not do it and he did it himself, with the result that the patient felt at once that he was talking to someone older than himself, who had had experience of the world and its difficulties, and one could often get the patient to understand and be more co-operative. The whole thing came down to enabling the patient to re-adjust himself to circumstances as they were and not as he would like them to be. They could alter the environment, but the environment to which the patient was returned was one over which the doctor had no control, and every psychiatrist was a psychotherapist in the sense that he enabled his patient to see his difficulties, to understand them and to readjust himself to the actual circumstances of life.

At the same time he felt that one had to sit back and think carefully when they compared certain results from this method, which it was agreed was not strictly

scientific, and when they compared the scientific approach with the results of strict medical science. One might not believe all one read about insulin, cardiazol shock and even prolonged narcosis; one must believe that a considerable number of these patients had improved whether it was entirely due to the effect of the drugs or any other change which took place in the system. They should draw a definite distinction between what was organic and what was not.

When the marvellous change which had come over the outlook of the G.P.I. and the extraordinary results from chemical modes of treatment were remembered, the whole future of psychiatry was widened and was much more pleasant and hopeful than before. They must not label themselves pure—should he say ?—pharmacologists or even pure psychologists, for the majority would still remain psychiatrists, doing their best to understand the " wherefores " and " whys " of mental disorders and applying common sense, judgment and experience to them.

He had often been told by those interested in the question of neuroses that there were not enough psychotherapists at work, but he thought a man who had spent many years as a psychiatrist was a psychotherapist—if he was not, then there were none !

Dr. DONALD BLAIR said it seemed to him that the matter had to be dealt with from a practical point of view. It was important to settle the question of psychotherapy in mental hospital practice, and the question was how much they were psychotherapists and how much specialists were needed, the training of whom took a long time. The problem of being a psychotherapist without being an analyst was a matter of the greatest importance, because one of the things that psychiatry was suffering from was the number of specialists within a specialty. What opportunities had medical officers for treating patients ? Speaking as a medical officer in the L.C.C. there was not much ; they had as many as up to 500 patients under their care; how could they give time to individuals ? Were they supposed to ? Every patient must be considered from the organic point of view and from the psychotherapeutic point of view. Psycho-analysis was a very long proceeding ; Dr. Scott had mentioned a case where at the end of two years he found the original diagnosis was wrong. It would be impossible to treat people for that length of time.

The question of cardiazol and insulin treatment was of great importance because it had been emphasized that in these treatments (which were not now supposed to be as good as they once were) the result depended on a certain amount of psychotherapy.

The average officer should get more opportunity for the actual giving of treatment, he had to do research, to take examinations, and spend time each day writing notes. They had to get down to the practical politics of how much they could do; with organization a great deal more could be done, and the introduction of an expert would be of great advantage to many hospitals.

Dr. T. P. REES asked whether it was necessary for a psychotherapist in a mental hospital to have a medical qualification. If psychotherapy was as beneficial as it was said to be then they were certainly neglecting their patients, but it seemed to be impracticable from a financial point of view to carry out extensive psychotherapy in mental hospitals by qualified medical practitioners. The cost would be prohibitive. There were technicians working in the laboratories; was it not possible to have people of the same rank as laboratory assistants in mental hospitals ? They could have five or six lay psychotherapists working under the direction of a psychiatrist who was also a psychotherapist.

Dr. HALDANE asked how these psychotherapists would be trained.

Dr. S. A. MACKEITH strongly supported Dr. Bierer's suggestion that mental hospitals should have a psychotherapist or people trained in psychotherapy on their staff. In a hospital where he recently worked an assistant doctor stayed at the hospital for longer than a year and was an analyst. Not only was he able to throw

light on individual cases, but also in a way which might not have been expected his analyst approach to cases was a good general stimulus to all. That was an important point, and arising out of it he deprecated the tendency in the discussion to accentuate a differentiation between the psychotherapist and psychiatrist which was tending to become completely out of date. They were trying to incorporate in one progressive all-round sort of psychiatry the better and most useful parts of the point of view originally called the psychotherapist's point of view and the more old-fashioned psychiatrist's point of view.

It would be a pity if they allowed themselves to stray away from that progressive point of view which had developed. As an example he wished to mention a very recent paper in the *International Journal of Psycho-Analysis* in which continuous narcosis was discussed from the analytical point of view. Such an article was an extraordinary kind of co-operation between these two wings of the psychiatric army. Another reference in the same direction was Dr. Bierer's own conception of a mild arteriopathic case of organic inferiority. This might not be the whole picture, but it was a most suggestive and helpful way of regarding it.

He asked Dr. Bierer if he could give some indication of the kind of psychotic patients he found it most easy to help.

Dr. BIERER, in reply, said Dr. Scott had tried to analyse his system, but he had no special system and had no ambition to invent one. He had tried not to mention other methods nor to compare them with his own because many years ago, in Vienna, he went through the controversies between the Freud and Adler schools and he was trying to avoid this. The point was whether they could help the patient. If they tried to classify, everybody tried to show their classification was right; he only wished to help.

About the problem of science; he would not like not to be called a scientist, but he would dislike being called a scientist if he was not one. He was so far a scientist in that he used scientific methods for the investigation of psychological problems. In his practical work such methods were inapplicable because practice followed the rules of art. It was his wish to work by scientific means, and he objected to some Americans who differentiated between the deep intensive scientific therapy of psycho-analysts and all other methods, which they called suggestion. Psycho-analysis was not scientific, because Freud tried to give the foundation of psycho-analysis as natural science but he did not succeed. It was wrong to call psycho-analysis the scientific study of psychotherapy, but he must emphasize that in connection with their investigation they were scientists and all their work was scientific.

Dr. Bierer thanked Dr. MacDonald for his remarks because he believed long practice turned practitioners into psychotherapists without any analysis, and on his visits to mental hospitals in England he had found the older doctors had much greater success with their patients. When he spoke about a long experience he was not thinking of two or five years' analysis. If a hospital employed a psycho-therapist he should be a doctor because he should have authority. If he was not a doctor his authority with his patients suffered. He might have under him a non-medical psychotherapist, but he would have to be well qualified. In a hospital where there was a psychotherapist as well as young doctors and students who were interested in psychotherapy it would be possible to form a team of the doctor, a younger doctor, and one or two students. This would not be very expensive and would be a good foundation for hospital work.

He thanked Dr. MacKeith for his remarks on the connection between psycho-therapy and other treatments. He had not done a lot, but in some cases it was useful to combine prolonged narcosis with psychotherapy and perhaps insulin.

With regard to successes, he had had eleven schizophrenics; he did not know whether they really were such patients although they had the symptoms. The shy Balance III type had shown very good results, but it was difficult with chronic schizophrenia. He had not had any impressive results with them where they were of

long standing, and he had not had enough experience with manic-depressives so that he could not express himself about these cases.

Dr. W. GORDON MASEFIELD was very glad to have the opportunity of voicing the thanks of the Association for the very stimulating paper. It had done them all good to have their attention drawn to the individualist approach to their problems. He was surprised that everybody was so afraid of being called a scientist. His own definition of science was " orderly and organized knowledge," and he hoped there was no one present who did not believe that he was in possession of such knowledge. He believed he had some; especially with regard to actual human behaviour.

He thought Dr. Bierer was very brave to take up psychotherapy when his knowledge of the language was not very expert, and he congratulated him on his astonishing achievements. He was also brave when he asked his patients to write down what they were thinking of while they were in front of him. He did not think he should ask his own patients to do so! They all wished for more elastic regulations in their hospitals, and that the time might come when red tape contained more elasticity in its composition.

On behalf of those present he thanked Dr. Bierer very sincerely for such an instructive paper.

COMMENTARY ON A CASE OF ACUTE SYSTEMATIZED HALLUCINOSIS.

(RECORDED BY THE PATIENT AS "THE REPORT OF A NIGHTMARE").

By M. J. NOLAN, L.R.C.P.I., L.R.C.S.I.

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THIS case is a perfect example of that rare form of mental disorder, acute systematized hallucinosis (sensory insanity) described by Bianchi, as characterized by "hallucinations of several senses, repeated in a uniform manner, determining a range of false thoughts rapidly systematized, acute and curable."

With the doubtful exception of taste, every sense was hallucinated; all the sensory disturbances were distressing, and all contributed to the clinical manifestation of the paranoid delusional content which had been *situ* complex physical and psychological factors.

The overt onset was so acute that it could be timed to the hour, the obvious onset in all such cases being the explosion of a magazine to which a secret train has been laid previously by a correlated chain of group-factors.

The chief group factors, long in solution in the pool of his mental personality, by pathological affinity rapidly crystallized in the shape of acute hallucinosis. These group-factors are indicated on the subjoined schema. They constitute a "Big Six" which overruled normal mentality, setting up a revolutionary triarchy—"Religio-Sexual-Political"—the misused power of which found expression in a reign of terror.

The overthrow of reason was brought about with the suddenness of a *coup d'état*.

It lasted but six days, at the end of which thermidorian influences of renewed physical energy and the re-establishment of normal psychic association effected a complete restoration. The narration of this upheaval has been described very aptly by the patient as the "Report of a Nightmare." The document is the best evidence of how unscathed he has emerged from a very dread ordeal. It is, moreover, a very human document, laying bare moral weakness and mental suffering.

It was written on the first day of his escape from the dominance of his untrammelled senses.

Report of a Nightmare.

1. "At about 11.30 p.m. on Saturday, 17th inst., after having lain in bed all day I was reading a book obtained from the Free Library. I had lighted a candle by the side of my bed, and medicine given to me by Dr. W—, M.O. to R.U. Constabulary was on the chair beside the candle. I suddenly became aware of music which seemed to come from the air, and from rear of our house. The music consisted of modern songs which were beautifully sung. I would say there were eight voices singing in harmony. The songs sung were 'I want to hear my dear old Granny's song at Twilight,' 'Swanny,' 'Danny Boy,' 'Tears of an Irish Mother,'—I lay listening awhile to this singing."

Commentary.—Bianchi holds that "the almost constant factor is the hallucinatory explosion of the disease." In this case it is determined by physical exhaustion and mental fatigue resulting in inability to concentrate on reading, expectant attention, auditory hyperaesthesia. The first auditory hallucination is musical—a vocal octet. Familiar airs of pathetic sentiment give vent to sublimated emotion. He concentrates on the songs for a time as "music facilitates attention in place of inhibiting, etc." His musical taste has developed in him a sense of rhythm noticeable all through the "nightmare," which is marked by a rhythmical progression comparable to that of Tchaikovski's "Fifth Symphony"—a motto theme of sombre character expressing itself in all the movements; the persecutory theme returning rondo-like throughout, elaborate in contrasts and rhythm.

2. "Then I took it into my head that they were doing this for my benefit, or that they had come to take me away, and I became frightened, very much so. I remembered a story I had once read a long time ago, in which it stated that the Devil and his followers could always be defeated by the presence of the Bible or the Testament, and, as I took this singing party to be some of the Devil's followers, I arose from my bed, and obtained a New Testament from the kitchen, taking it to bed with me. I began to read some of the verses aloud, and to say 'The Lord's Prayer,' and prayed to the Lord for courage and strength to fight against these my enemies. As I was praying the 'voices' seemed to move further away from the house."

Suspicion of motive, a feeling essential to the efficient performance of his official duties in relation to the *bona fides* of others, is the *point d'appui* of doubt which now arises in his mind. This doubt involves an effort of attention, "conscious reflection, judgment, and reasoning," but owing to the inhibition of the lower automatic processes his conclusion is erroneous. His religious affect calls up a memory picture—a spiritual combat—and his ego ideal suggests that he will be the victor. Attention weakens, the auditory hallucinations become fainter as the "voices" move away, their origin being purely psychic.

3. "I laid my head on the pillow with the intention of going to sleep, when a 'form' came beside me, dressed in a long white robe, he had a pale face and a white beard. He whispered to me to 'hold fast to the New Testament' and 'not to let it go, and I should be all right.' I knew it was in answer, and composed myself to sleep trusting in him."

First visual hallucination—a normal conventional figure of the Christ—a monochrome (white) form, symbolic of purity. This hypnagogic hallucination is associated with faint ("whispering") hallucinations of religious appeal. The ego-ideal again suggests a feeling of exaltation. These hallucinations—the visual bright Christ form, and the encouraging admonition in gentle tones—are of the "hedoniphronic" class, and are examples of a kind infrequently experienced during the "nightmare."

4. "I hardly dozed five minutes when I opened my eyes to behold a different man or 'form' bending right over me. This form had large wings (black in netting form) which entirely enveloped me and the bed, and shut out all light. He had his face quite close to mine and kept asking me for 'the Book,' which I may state I was holding tight in my hands. His breath was foul and smelling of tobacco. To all

his requests for the Book (in whispers) I answered ' No ' and then started singing hymns, and he hummed the tunes along with me.

(" My mother and father heard me singing these hymns but did not take any notice of them, thinking I could not sleep and was occupying myself in that wise.)

" All the time this man with wings, while asking me for the Book, kept slowly folding me in the bed-clothes and eventually I found myself under an aerodrome sort of structure with black flaps, which when moved I could see the stars in the sky, and the air seemed cold."

The post-somnial hypnagogic hallucinations now experienced are of the " nociphronic " or distress-bearing type, and are in marked contrast to the last described. They furnish an example of " associations of contrast " which Bianchi states " are much neglected by psychologists, and which are among the most active and the most frequent in the process of thought." The large black-winged figure is in very close proximity (spatial hallucination), so close the foulness of its breath is perceived.

Olfactory hallucinations, it is generally stated, are most frequently found associated with " insanity of onanistic foundation." In the writer's experience but few cases of insanity are due solely to such a cause. Olfactory hallucinations are found in cases having any marked sexual trend other than masturbation very frequently. In this case the patient was very erotic, freely indulging in normal promiscuous intercourse. The " whispered " requests are in this instance faint because of the many simultaneous sensory disturbances—visual, auditory, olfactory, haptic and spatial. When the patient sings the hymns, these " whispers " are transferred to " the humming " accompanied by the Devil—a synchronous psycho-auditory hallucination. " The gradual enfolding " is explained by a general cutaneous hyperaesthesia, the " aerodrome structure " by a memory picture, " the stars " by the class of phosphenes " fixed in shape and position," and the " coldness of the air " to a haptic hallucination.

5. " There were now three or four men, all dressed in dark clothes, and they began a system of torture to get possession of the Book. The torture consisted of hot iron bands being pressed against my sides, a kind of hot fluid being poured under my back, and electric wires being bound round my stomach. This torture I stood, and I may add it was not too severe. I was taken then to what I took was the wilderness owned by the Devil, and further torture of a like manner was administered to me with the addition of the faces of animals being pressed close to my face to frighten me ; also the drawing of swords across my throat, but I answered ' No ' to all requests for the Book, and had made up my mind to suffer death first. This latter place I was in was crowded with soldiers and horses, and in the air there were forms flying around like angels, some of them all black and some all white, and a curious feature in the sky was the shooting stars.

" When the torture failed to get them possession of the Book, one of the officers standing by said that I must be made of marble, and that it was a pity I was not bigger in height, as he would keep me there."

Further " nociphronic " hallucinations in the shape of the " dark forms " of his persecutors now arise from his delusional affect. The special torture to his side, back and stomach are due to paraesthesia or hyperaesthesia of special origin. Passivity, a psycho-motor hallucination of removal, is experienced. The zooscopic hallucinations, with associated hallucinations of touch and weight, are drawn from memory pictures with suitable haptic disturbances. Hallucinations of men and horses of normal shape, engaged in " nociphronic " combats in the air, are war memories of infantry, cavalry and air force. The " shooting stars," " a curious feature," are explained by phosphenes of the class of " moving lines of light not fixed." The basic exalted ego-ideal is gratified by the suggestion that he was worthy of enlistment in the superhuman ranks, were it not for his small stature, and this unveils the inferiority complex.

6. " I was then taken to a small house and put into a bed in charge of three large-sized dogs, very fierce-looking, and through the partly-opened door looking into a sort of kitchen I could see a woman sitting, but she never spoke to me.

"I sat upon the bed the better to make a fight for it when the dogs should attack, and started reading the Testament. All of a sudden I saw my mother enter the kitchen from the direction of stairs to bedroom; I was all surprise to think that she had been taken prisoner too. I shouted to her, 'Mother, don't come into this room or you will be eaten,' and told her to tell Father the same. She eventually made me realize I was in my own house. I was sitting upon the bed trembling, my inside shirt and drawers were wringing with sweat, and I told my mother so. She gave me a hot cup of tea and a change of clothing, and I lay down to have a fresh sleep and rest, but it was no use, I couldn't. The 'voices' and 'persons' I had heard and seen in my dream would not let me go."

Here he enters on an illusionary phase—"the small house" his home; the "three dogs" his fellow constables; "a woman" his mother.

Recognition of his mother returns quickly, but orientation as to place is retarded, and needs her reassurance that he is really at home. All domestic happenings are impressed on his memory. During the day the "voices and persons heard in the dream return again"—this diurnal continuance of the dream hallucinations is a marked feature of the "Nightmare"; the continuity is associated with time sense, and the condition is purely psychic. It is a very important element, as it confirms the patient's belief in the reality of the hallucinatory content.

This continuity also accounts for the clear recollection on convalescence of all the sensory disturbances and contrasts with the usual post-recovery condition from the type of acute hallucinosis described as "oneiric," after which there exists no more definite memory than that of "one long dream."

7. "I was not long settled when the spirit form of a girl came and asked me if I was lonely this morning. I said 'No.' She then told me I was to attend a meeting to-night (Sunday) on the roof of the Y.M.C.A. in H—— Street. I said I would. I rose at 11 a.m. and washed, shaved and dressed, had my dinner and went out to see Dr. W— for medicine for my father. I got the medicine and told him I had this dream or nightmare. I went out on the road with my chum after that for a long walk, but could not get my night's experience out of my mind. When I returned and had tea, I told my parents I was going to sleep in barracks and that I could not sleep in my room at home again."

The "spirit form" of a girl suggesting companionship (sexual content) is a psychic hallucination of the type "voices without sound" and "spiritual voices." The proposed meeting-place is due to a religious affect. Conduct during the day is apparently rational, though the dream experiences are still uppermost in his mind. In the afternoon the "voices" accompany him everywhere singing, and reminding him of the rendezvous.

There is clear orientation of places, persons and time. Towards night the phobia of the demon attack returns, and precautions are taken to arrest it by changing his sleeping apartment from his home to the Barracks.

8. "As soon as I left the house to go down town, to see my chum, prior to visiting my lady friend, the 'voices' started singing in the air and accompanied me all the way, telling me not to forget to turn up at 8 o'clock. Therefore I was again terrified. When my chum 'I. C.' came along I told him and he said it was nonsense.

"We then went to the barracks, to the canteen, and had a bottle of stout. I then told him I should have to go, and asked him to come along with me, which he did.

"I tried to get to the roof of the Y.M.C.A. but could not manage it, so I went and saw the girl and told her I could not go out with her, as I was wanted elsewhere.

"So I went to barracks, got into my room and shut the window and door to ensure safety from the 'spirits,' but still they spoke, warning me to attend the meeting or take the consequence. So I determined to chance it, and have another try to get into the place mentioned, and send my chum up to warn my Mother to lock all windows and doors as they were threatened also."

The "voices," now warning and threatening, nevertheless continue and compel him (excito-motor) to make another effort to get to the Y.M.C.A.

building; the psycho-sensorial hallucinations which influence him are of sexual appeal. [*N.B.*—The events he now records do not fully describe the chief incidents of the day. There is no failure of memory, but there is deliberate suppression, as he was fully conscious of their very serious nature, and being himself a policeman, he feared the charges made in his committal warrant would possibly result in prolonged detention here.]

Failing to force his way on to the roof of the Y.M.C.A. building he becomes violently excited, rushing wildly about, threatening to shoot anyone who attempted to take his Bible from him.

9. "I arrived at the Y.M.C.A. but could not gain entry to the roof and was giving it up in despair, when my father came along, took me by the arm, and wanted me home. I told him I wasn't going home, that I wasn't going to bring them into the trouble I was in, so as soon as I came to C— Street R.U.C. Barracks I knocked and asked them for protection for the night. Dr. W— came out and asked me to write out a report of all the foregoing, which I did. During my writing a voice was whispering and told me what to put down on the paper. I was then taken in a Ford car to my own bunk in the Military Barracks. I was undressed and put to bed, and a sergeant and two men put to guard me, because I knew I was to be killed.

"I was afraid to sleep and was vigilant all the time, listening to the threatening voices. I was troubled with them all day until dinner-time, and then a regiment of flies (men in spirit form) came to the Barracks and asked me to come with them and I should get a good position under the command of the Colonel. Lieut. M—, my platoon officer, came in then and told me to get up for a little fresh air.

"I got up, dressed and got into the Ford car, and eventually arrived here (the mental hospital), after being led to believe that I was going to hear the band of the regiment mentioned playing."

In response to auditory hallucinations he constantly answers imaginary telephone calls, and sends off "S.O.S." appeals. At the Barracks he makes a written report in the form of charges against his persecutors.

He acts under the dictation of a "whispering" voice. This auditory hallucination of psychic origin synchronous with ideation may be regarded as a form of *l'écho de la pensée*—the whispering seems to come from the outside, close to his ear, and it exercises a strong excito-motor power. [At this time the sergeant and guard were placed on him to prevent his shooting people.] His auditory attention is vigilant. "Voices" are heard threatening unceasingly, until the "regiment of flies" come along to replace the threats by cajoling promises. These latter he disregards, but consents to act on the suggestion of his platoon officer who appeals to his musical taste. It is noteworthy that the sensory and psychic disturbances, hallucinatory and illusionary, are to a certain extent stable, and determine secondary judgment. The objective and subjective harmony of the waking experiences reinforce and widen the systematization of the ideation.

10. "On entry to this place (the mental hospital), which I thought was an hotel, I had my particulars taken and was put to bed—a very strange proceeding, seeing that I was intending to go back to Barracks that night.

"I had a bath, and then tea. I then was looking at a picture above the fireplace and the figures in it began to take action and kiss and hug each other, they being boy and girl. I looked at the other pictures in turn and found that they were all full of life, and were human beings, who assumed the shape in the pictures for convenience sake, so as to be near me (but of these later).

"I was pursued by the people who were after me in N—; and I was living in terror of their taking me away and putting me to torture as they had done before.

"The voices of these people were shouting at me constantly, and warning me as to what would happen if I failed to go with them when the time came; in short I was to be killed that night. I had made up my mind to stick to the attitude I had taken at a previous experience, not to give in, but to trust in God to help me defy these evil spirits.

"At the same time I was afraid of them, and constantly wondering if I should ever see home again. That night two of these 'spirits' stood outside the door leading from the ward into the dining room—(I thought it was the street door).

"They asked me to come out to face death like a man, and if I did not they would fetch me. I refused and they began the torture. I lay in bed watching two dogs, which came at once to them at a call; a long silken rope was attached to the collar of one of the dogs. It was instructed to run down the ward in which I was, to go right round the far side of my bed and bark up near the next side.

"The dog did this (all animals are human beings in that form assumed for the occasion) and then they both pulled, but the rope was not strong enough. They tried again the same method, and succeeded in getting the rope round the back of my neck, and then started pulling. I put forth all my strength and the rope again broke. Then they swore and said 'Curse you, M—, we'll get you before morning.'

"They began to send electric wires along the ceiling, and to drop them on me, and as they burnt the flesh I put my head under the clothes. The two then transferred themselves to the left-hand window of the ward, and working outside began to send these fine wires from the window along beams on the ceiling.

"I think it was done with batteries, and when the beam was full they would drop them one by one so as to fall on my face. Well, I hit on a great idea to outwork them, getting the bolster from under my head, one hand at each end of it, I held it above my head, and try hard as they could, they (the spirits) had to admit themselves defeated, and even praised me for having been so clever. I never enjoyed anything better, among all my dangers, as that bit of fighting, and my arms were getting tired holding the bolster, when they finished."

Note acute perception of new surroundings in mental hospital. From his bed in the middle of the ward, and facing the fireplace, he can see three walls. On same line with the fireplace a door with large glass panels opens into a dining room. On the walls within his view there are seven coloured pictures. Facing him over the mantelpiece (1) Lovers in Watteau costume; to the right side of it (2) "Making the best of it"—a snowed-up coaching party at a country inn—ladies, gentlemen, soldiers and dogs; to the left side (3) "Impudent hussies" seeking to attract a pious Puritan. On the wall to the right (4) a girl in dark dress holding a letter. On the wall to the left (5) England, Ireland and Scotland, emblematical female figures; (6) a queen in regal attire; and (7) a peaceful landscape.

These details are necessary to illustrate how very strongly as external stimuli they play a role in the character of the ideation. They supply a definite groundwork for the hallucination which, as Ziehen points out, lends so largely to the formation of ideas. Coupled with this accelerating medium there exists the condition of hyperprosexia, a condition of an attitude of readiness, of expectant or anticipated attention which, according to Bianchi, shortens reaction time by practically a third ($\frac{250}{1000}$ to $\frac{80}{1000}$). The combination thus established gives rise to a *simultaneous* hallucinatory or illusionary condition which in Kraft-Ebing's opinion is the "most infrequent of hallucinatory phenomena." All the figures in the pictures, even the dogs, take action; they are all full of life; they are all enemies in disguise. They shout, warn, threaten, they inspire fear. They plan, and attempt to carry out his strangulation. Samson-like he bursts his bonds, compelling his canine persecutors to swear in their rage, and so he releases his exaggerated ego-ideal which underlies the persecutory delusional content. In this spirited contest the dogs in picture No. 2 supply the sensory stimuli; the memory picture from Proverbs, "He is fast bound by the ropes of his sins," furnishes a part expression of the religio-sexual complex. [The case-book note at this date reads: "Immediately on getting into bed he fixed his eyes on the picture of a lady and devoted all his time talking to her. He has a different name for her each time he is asked who she is—she is "Miss A," a girl of his own standing with whom he kept company, but did not wish to marry; she is "Miss B," a girl not of his persuasion with whom he also kept company, and desired to marry, but could

not, owing to the opposition of his parents. Neither knew of the existence of the other until recently, and when they became aware of the facts a triangular quarrel followed.'

The general setting of the hallucinations shows mental clearness—the position of the window and of the ceiling beam are accurately described.

The " electric wires " dropped to burn holes in his face are distressing evidence of cutaneous hyperaesthesia. Later these haptic hallucinations occur in other regions of his body. Now they excite an active defence response, and the " great idea " which is really a very poor one gives rise to an elation which gratifies the ego-ideal, by extracting praise from " admittedly defeated spirits."

11. " After they had gone the whole army of spirits came in the shape of little bits of whitish coloured hairs, every one about an inch long, and they were singing all songs in unison, soldiers' songs especially, with an occasional remark such as ' Sergeant M—, come on, we are waiting.' They made me plenty of good promises, saying they wanted me to come as an instructor to the battalion. They were soldiers. The leader then spoke to me and asked me to get up and go home, and I told him that I couldn't come then, that I was sick, and said that if they would wait until the next night I would go. He said ' that was good,' so they went away singing ' He's a Jolly Good Fellow,' and telling me that they would come back at ten o'clock the following night."

The " Spirit Army " appears as a nociphronic microptic hallucination, dark coloured and hostile, in marked contrast to the more usual gay coloured and friendly Lilliputian type. It is an army of men who have assumed the form of " hairs." These " hairs " may be the elementary evolutionary stage of the " flying insects " which Stoddart mentions as a feature of the disease, and which appear later. " The moving faces and devils " described by the same author in this connection we have already seen.

Synchronous with this visual hallucination is a highly organised auditory hallucination — of " singing in unison." Not only are the words heard, but the coincidence in pitch of the singers' voices is specially noted—it is evidently not a first attempt at " community singing." The degree of perfection attained may be attributed to the fact that the patient's brain not only set the periodicity and proportion of the airs, but also created the performers, and they could only interpret the music as he conceived it, and with such capacity as he could give them.

The " good promises " of promotion and the exit of the Army singing his praise again gratify his ambitious ego-ideal.

12. " When they had gone another army came, a different Battalion. They were in the shape of small cockroaches, but they came to take me away to their headquarters to shoot me for the murder of their Colonel. I spoke to a girl they had with them, and she asked me to come, and I said, ' Why should I come with her to have my life taken ? " She said, ' John, I love you and would do anything to save you, but you killed my Father (the Colonel of the Regiment), and I cannot keep the rest of the men from avenging him, even if I tried, so you'd far better come with me, and die as a soldier should."

" I thought then I should stave off the last moment, and hit on the idea of putting these people off also until the next night. I repeated the story I had told the previous crowd, and told them I would go the next night at 9.30 p.m. (half an hour in advance of the time stated for the previous crowd). They then left, the girl asking me for a kiss before she left, which I granted.'

Now the crude hallucination of " whitish hairs " is evolved into an army of " *small* cockroaches," the microptic feature being preserved, as the insects are not of full size. Then sally out a horde of nocturnal voracious assailants —association idea. The girl is brought as a decoy (sexual affect)—she is now the girl " B " and is with the cockroaches—" The Irregulars." It is possible that " B's " father had rank in the Irregular Forces, and that he had been in

conflict with the patient at the time of " the troubles."] The instinct of self-preservation proves stronger than that of sex.

He now shows the same considered judgment in resorting to the same subterfuge to get rid of the " cockroach army " as he had adopted with regard to the " Hairs," carefully timing their return so as not to coincide with the latter. Observers have noted that the time sense is lost in such a mental state as the patient suffered from, but in his case it is exceptionally well preserved : it is indeed practically hyperaesthetic as his other sense.

13. " I must then have gone to sleep, because I had no more visitors calling me until daylight. After I woke a voice started to talk to me, which I eventually found came from a girl in a picture on the right-hand side wall, and she said I was to come outside for a few moments, or if not she would kill me where I lay.

" She insisted on my coming to her in spite of my denials, and I got out of bed, but was put back again by the attendant. She still persisted, and I tried to convince her that I could not go, so she got angry and gave me five minutes.

" At the end of that time she asked me to come again, but I said ' No.' She then blew out her cheeks and her eyes opened wide, and from the back of the picture came thousands of flies, which all came circling in the air in my direction until a couple lighted on my face. She then seemed to call them back, to give me another chance to obey her bidding. I got out of bed again, but was put back, and then I excitedly asked the attendant to let me outside for a few minutes on a matter of life and death, as it meant an awful death not to do as she said.

" I pretended to the attendant that I wanted to catch a wireless call from Headquarters, and that I must get near the open air. At last the attendant led me out, kept me a second, and led me back again. When I was out the voices came from the further part of the room, but I was not permitted to go, so that my journey was of no avail.

" She started from the picture and said she would kill me, and then gave me the reason. She said her daughter had been in company with me, and that now she had a baby and it was mine, and she would take all the money I ever earned to keep it.

" She also said she had been to N— and told my mother all about it, and told me I was disowned and need never go home again, so that filled me with consternation because I did not know any girl of the name ' Lois,' and I denied it to her.

" Her own name was by marriage Mrs. R. D—. Eventually she seemed to lose the subject, and wandered into telling me about her from W— direction, and about the happy times she spent round there, and mentioned the names of people I knew.

" She was still talking to me constantly until Dr. Nolan and Dr. Deane came round, and all the time these gentlemen were talking to me she continued to call, asking me was she not more important than they ? When the doctors left she began talking and told me all about Robinson Crusoe, the whole story illustrated behind her in the glass, but to complicate matters my two girls came (in spirit form) and they wept and would hardly speak at all, saying that I would be killed and that they could not help me, and that they were very sorry.

" Then they got jealous because of my talking to the lady of the picture. I said she was only a friend. My own girl stayed and would not go home, and I gave her all sorts of ' blessings ' for going and joining the ' Devil's gang of evil spirits.'

" She said it was because I went away and left her, but I turned her down and said I was fighting against the Devil and therefore would fight against her."

The auditory hallucination now is at first hypnagogic, but after an interval passes from that into the fully awakened stage, and it is located as coming from picture No. 4, " A girl in a dark dress holding a letter." She is now Miss " A " soliciting him to go outside (sexual affect) ; his denials excite the wrath of a woman scorned ; she sends an " army of flies " to destroy him—the third of the microptic armies—" Hairs," " Cockroaches," and " Flies."

[*Note.*—At this time he was in a state of motor restlessness, constantly trying to get out of bed. He would not explain the nature of his obvious annoyance, nor the cause of his fear, though he appealed to the nurse to let

him out " on a matter of life and death." He also thought out the ruse of a wireless call from H.Q.]

It is to be noticed that as he gets further from the picture of the girl her voice becomes more remote, the removal of the illusionary visual stimulus reduces the intensity of the psychic auditory hallucination, spatial perception in this, as in other matters, being preserved. In this instance again the time sense is strikingly accurate. In this respect all through the " Nightmare " and associated with orientation, as well as systematization of the ideas, it is in marked contrast to the more common acute unsystematized hallucinosis, showing an incoherent sensory flight of ideas—transmutation as in ordinary dreams is of course playing its important part. The identity of the figure in the picture changes: she leaves the frame (illusionary) and reveals herself to be the mother of a girl he is accused of having seduced—an idea of reference.

At first she threatens, later seeks to ingratiate herself by references to mutual friends, and reminiscences of early happy days—memory pictures. At this stage he notices *she* loses grip of her subject, wandering from it into gossip. This is due to his inability to concentrate, and to a psychic flight of ideas not definitely connected with external stimuli. His power of constructive thought is weak and trails off into boyish memories of Robinson Crusoe, whose whole story he sees in the background of the picture; sees as in a glass darkly.

These scenes efface the central figure of the girl—she goes out of mind as out of sight. [At this time he was noted as " fairly settled," but it was difficult to gain and retain his attention as he was evidently preoccupied.]

The association of ideas brings into prominence his two girls, rivals for his affection, but in anxious agreement for his well-being. Their jealousy of the Picture Lady gratifies the sexual content of his hallucinations.

The exaggerated ego-ideal is pronounced in this as in many other events of the " Nightmare." An involution of the transmutation now follows, the two girls now resolving themselves into one—his own girl " B." She remains in opposition to his wishes. He upbraids her for joining his enemies, and declares his determination to fight against them, and consequently against her.

14. " That night about 9.30 o'clock the army of cockroaches came again, singing their war songs and jubilant over the expectation of dragging me with them. I got the command to get up, but refused and prayed to God to give me strength to fight and resist them. They laughed and said it was no use praying, that they would kill me.

" After I refused several times they then began to flock all over the bed, under the clothes and around my body, and the feeling was the most terrible I ever remember.

" All the time they marched over my body, until they were in thousands inside my drawers and shirt, and marching on my throat, until I was desperate. I got out of bed; they laughed; I ran to the bathroom door to get into a bath and drown them, but the door was shut; I ran to the fireplace to get the jug there, but I was put back to bed by the attendant. I asked to see the doctor, saying I was being eaten alive, but he said I could not see the doctor until morning."

The " cockroach army " returns punctually, " according to plan," again singing and jubilant, confident of victory. This is a fresh phase of the religio-sexual conflict. His prayer defence is derided. The army infests his bed, the bed-clothes and his person—a war memory of vermin in the trenches.

He experiences the " most terrible " feeling. [*Note.*—At this time he was very excited, making a dash for the bathroom to drown the invaders. He also snatched at a milk jug, to pour its contents over them, as he was in terror of being eaten alive.]

He experiences the feeling of the army of cockroaches marching over his body, practically the same " feeling of beetles crawling over them " from which patients suffer in this disease, as described by Stoddart, cockroaches being called black-beetles, though they are neither " black " nor " beetles."

" laughing cockroaches " are certainly more uncommon than " Laughing

hyenas " or " laughing jackasses." But they are really men-soldiers in spirit form, and their mirth is of the sardonic type. Their laughter is no true auditory genial convulsive laughter; it is usually a psychic concept of the cynical attitude of the torturers. [It is to be noted that the patient is never deceived by the disguises assumed by his persecutors—in whatever shape they appear they are made to speak and act as men and women.]

15. " In despair I lay, thinking of the awful death I was going to die when suddenly the other party, the ' Hairs,' lined up for me (the 10 o'clock party). Then they came, and when they saw me they called for fight, and a desperate battle ensued all round my body. Cries of ' pain ' and ' agony ' and ' murder ' I could hear, with groans of the dying and shouts of the triumphant. Then the Lady of the Picture took a hand in my defence, saying, ' Take off your shirt and shake it.' I did so and shook it well, and hit it with my hand. Then you should have heard the yells of the soldiers. They called me a bastard, a cowardly cur, a whore, and all the names they could think of.

" The ' jubilant army ' moved away, broken in body and spirit, but said they would come back for me the next night, and for God to help me. They even called me a Sinn Feiner for murdering defenceless British soldiers."

The army of " hairs " returns at the appointed hour—a desperate battle follows with the " Cockroach " army, the patient's body being the seat of war. The auditory hallucinations are generalized, and are in accord with the varying emotion of defeat or victory aroused by war memories. The Lady of the Picture comes in as his ally, bringing up the strong sexual content. The " hair " soldiers indulge in abuse and obscene language—ideas of reference.

There is a dream-like transference of identity of the combatants. The " cockroach " army which entered the fray so jubilant now retires defeated.

They accuse him of the murder of some of their number, and of British soldiers. [Case-book entry at this date : " Talkative, coherent, bright, intelligent, restless. A woman's voice speaks in his left ear."]

16. " Next day I was lying talking to the Lady of the Picture, when the sound of music came wafted to me from outside, as of a great regiment marching towards the building with the band in front. Then I told the Lady of the Picture who witnessed the fray last night that I was ruined and done for now, because they had come in their force (human) to kill me. When the band ceased playing outside, the Commanding Officer said to some attendant outside, ' We have come for Sergt. M— and are going to shoot him for the murder of eighty British soldiers last night.' I was in terror and told the attendant inside the room about it, and that he was to tell them that it was against all rules and regulations of any army to take a man off a sick-bed and shoot him. So he said he would not let them in, and went away.

" I then heard the voices outside saying, ' Send the murderer out. Come on M—, don't be afraid.' Others mad with anger said they would break in the windows and drag me out.

" I next heard the officer shout, ' Firing party, 'shun !,' ' Load magazines ' and ' Stand at ease ' until I should be brought out. But the doctor would not let them take me, so they said they would wait. Then they posted sentries round the building to prevent my escape."

He is " talking " (conversing) to the " Lady of the Picture "—auditory hallucination drawn by war service—military music and the march of armed men. The visual hallucination is now in accordance with the auditory, as the enemies have thrown off all disguise *pro tem.* and come in " human form " to kill him. Terror transforms the sounds of " wafted music," soft and gentle, to the stern voice of the Commandant ordering the death sentence to be carried out. The patient in vain quotes " Rules and Regulations," which, if they ever existed, were in those troubled times more honoured in the breach than in the observance. During this triangular " war " of divided civil, and crown forces, combatants of all three parties were not infrequently taken from bed to execution. The graphic scene of the " voices " commanding the Firing Party was drawn from the personal experience of the patient. [At this time he

is noted in the Case-book as very excited. He is composed only by constant reassurances that he is in hospital, under the care of doctors who will protect him. It is very difficult to gain his attention owing to the hallucinations, which he does not reveal fully at the time.]

17. "The Lady of the Picture then came to my aid, and proceeded to tell me of a plan to escape. She told me to get three or four flies, and after squeezing out all the substance of the body to eat them one by one, and then to lie back in bed, take deep breaths, drawing my body in at the same time and to continue until I found myself getting thinner. She said that was the method employed by human beings who had to take spirit form.

"I could not get any flies, so she sent her army of flies across and told me to catch a number of them. I caught two, and failed to get any more, so I ate as she told me and followed the directions, but the number of flies was not sufficient, so I did not get any thinner.

"She then told me there was another way, and that was to push one of my front teeth until it lay out at an angle of 45° from the rest, and then to wish to be an animal, a bird, or whatever I liked. So I tried her plan working on my teeth until I was tired, even to making one bleed, then I gave it up and told her it was no good. I couldn't do it. I then said I would face the guns instead of attempting my escape. She was all concerned, and said I was foolish.

"After that a few of the soldiers had got in through the window in the shape of small lizards, and these gathered together under the next bed, until their number should be strong enough to kill me. During this time I sat up in bed with a pillow in my hand waiting for the attack, but it did not come until hours afterwards. Then they got underneath my bed and started to bore through the mattress, and when their sharp noses eventually bored through, I felt them, but constantly shifted my position.

"It was getting dark outside, and the scene took an active turn, for looking through the door I could see soldiers on guard, and a few of them would say, 'Shoot him while the officer's away.' I would lie watching them lifting their rifles to their shoulders to fire, but every time they fired, there only sounded a small click, and they said the cartridges were damp.

"Next on the scenes came our 'Specials' from N— and a fight started between the soldiers and the Specials; it lasted an hour with shouting and cries and groans, until the soldiers got the best of it. There the soldiers took up guard again and the Specials were at the side window, telling me to die like a soldier, standing upon my feet, when they come to shoot me.

"Then it was that another picture took a hand in the proceedings; this was on the left-hand side and she was a Queen. When I went to answer her, she asked me what kind of a soldier I was to lie in bed and talk to her, and that I was to stand to attention; and every time I was getting into bed she spoke, so I was constantly getting in and out until the attendant took the picture away altogether.

"I was lying in bed and I was in direct line with the door, so Major B— sent word to me to get out of bed and stand to attention, as they were now going to shoot me, so I looked through the door and saw them advancing. They (the soldiers) halted, had their arms inspected, so I got out of bed and stood to attention, but I was put back to bed again; it happened they had some other soldier to shoot before me, so they led him away to be shot, the band playing the 'Dead March,' and that ended the memory of that night."

The Lady of the Picture ("his own girl") now devises alternative methods by means of which he can take on "spirit form." By reducing himself in size he is able to evade the army of his enemies who are at this time in "human form." The first method is that he should eat three or four of the "flies," those soldiers in spirit form who, it will be remembered, are at her command. As he is unable to catch them she provides the victims.

When masticating them he is to draw in deep breaths and to retract his abdomen, a cannibalistic difficulty, though the desiccated "flies" were enemy corpses in tabloid form. As a Free Library reader he may possibly have

read in Lady Wilde's *Ancient Legends of Ireland* the old charm "How to go Invisible," in which a black bean placed in the mouth is essential, the associated idea being a dead fly. Or the entry of the idea into the patient's consciousness may have had origin in a very early memory.

The writer heard an old woman exclaim when she saw a little girl snatching flies from a window-frame and eating them like a cat, "Don't! don't do that, child. If you do you'll shrivel up."

The anthropophagic plan fails, owing to insufficiency of victims. The Lady suggests the alternative plan—forcing out one of his front teeth to an angle of 45°. He tries hard to do this but fails. [The point of clinical interest is that at this time he was observed to snatch at imaginary objects in the air. He would not, or could not, say why he acted in this manner. He was, however, very obviously trying to snatch at flying objects after the fashion described by Stoddart—"sometimes they (patients suffering from this disease) catch imaginary insects between their fingers." Neither could he account for the origin of the idea that his effort prompted to force out one of his front teeth. It, too, may be an early memory arising out of the unconscious. The same old woman quoted above was a veritable mine of folk-lore, and whenever a child lost a deciduous tooth she always promised the little one "a gold tooth or anything else wished for," if he or she did not put the tongue over the site of the lost tooth—needless to say a perfectly safe promise! [Or he may have read in Joyce's *Old Celtic Romances* of the "Fairy Queen of the Quicken Trees," wherein Finn, who had obtained the gift of divination, when he wished to look into futurity, put his thumb under the tooth of knowledge, a painful process, so painful that when he did so "he sank back in his seat and groaned aloud."

Some expert psycho-analyst may supply other interpretations. Charles Lamb in *Witches and other Night Fears* says, "There is no law to judge the lawless, or canons by which dreams may be criticized," and he tells us at length how in Stackhouse's *History of the Bible* he found the source which inspired many of his own nocturnal terrors.

J. M— now sees a detachment of the soldiers in human form change into "*small* lizards" in order more easily to effect an entrance into the room through the windows in the manner described. The micropsia still prevails in the memory picture of lizards he had seen in France. [At this time, owing, no doubt, to haptic hallucinations of spinal origin, he was very restless and difficult to keep in bed. Afterwards he could give no clue to the idea associated with this transformation, which, as is usual in dreams, was accepted without question or wonder at the moment. Possibly the bifurcated tongues of the lizards suggested serpents, and they again his devil enemies.]

In this phase of the systematized hallucinations the sexual content is predominant—there is no further reference to the religious (the Bible) conflict. The Dead March played for one other than himself is a satisfactory end to the struggle for self-preservation.

18. "Next day I was visited again by two girls and the Lady of the Picture, and they said they were coming into bed with me. I said they could do whatever they liked, but they would not get anything off me. They came, and I could feel their warm bodies lying beside me and their breathing, and they were suffering with a sensual desire to have connection with me. To get rid of them I did as they wanted, and I could not satisfy them, as they wanted connection all the time. I then desired them, and where I felt their bodies (spirit form) squeezed them as hard as I could, and made them squeal out in pain. I had hit on the proper catch to squeeze them about the waist and then the back would be broken, so that they got afraid of me, and were afraid to do as they had done.

"The ladies of both pictures then said they were coming in and I told them I would break their backs, that they wouldn't have me for such a fool. So the Queen came first, and I waited until she got right in, and I squeezed her in the right place.

"I got real angry and though she shouted 'You are killing me' I intensified the pressure, and told her that was what I meant to do, and I did, because

afterwards the other lady who befriended me so often before told me I had killed her and that she was lying at the bottom of the bed, and I heard her moaning."

Now again the pictures supply the sensory stimuli during the day—" The Impudent Hussies " and " The Lady of the Picture " all seek sexual intercourse with him. The psycho-sensory hallucinations are auditory and haptic, and the wantons, though in spirit form, convey very crude corporal impressions.

A reluctant compliance with demands for coitus expresses " the indignities to the sexual organs " associated with genital hallucinations. The inability to satisfy a wholesale demand on his sexual powers is resented by indulgence in a wicked and cruel sadistic equivalent. This initiates in squeezing the victims to squealing point, then goes on to fractures of the spine during intercourse. "At the foundation of sadism there is a physiological though weakly constituted association of lust and cruelty," says Kraft-Ebing, "and under pathological conditions this association may be interpreted beyond measure, namely, when the lustful colouring of cruel ideas has reached the intensity of a powerful affect—lust-murder." In this case the ideation of lust-murder was simultaneous with, not subsequent to, coitus. A Queen is his first victim; his sadism is appeased only by the dying moans.

19. " I was eventually told I could get out of bed, sit at the fire, just as I was. Getting up, a voice said, ' John, push like hell,' and when I found it was my friend the Lady of the Picture, I did as she asked. Then I got up. I sat at the fire and she came and sat beside me and talked to me. She was constantly asking me down for meals at her house, and she said she lived in C— Street, D—. I said I could not go until I got better, and she said certainly I could. I had with her one day and one night, and anything I got to eat she tried to turn me away from it saying, ' I am surprised at you, John, suffering such food, and not even a knife and fork.'

" She said, ' Come down with me and you'll see how nicely I will look after you; and you can eat your food like a gentleman, and be away from all these other ignorant fools.' But I refused every time until she then said she would kill me, that I had ruined her and should suffer for it. But that night she came again and got the fate of the Queen. I crushed the life out of her and was glad."

His mind now reverts to the Lady of the Picture, to whom he is bound by ties of gratitude. She solicits him and he readily complies with vigour.

She then endeavours to entice him away, but fails in her object. She continues to cling to his company, trying now by threats to coerce him, but is satisfied he is obdurate. Not to be denied she comes at night to share his bed. She suffers the penalty. He " crushes the life out of her, and is glad "!

Here is a very fearsome example of association of contrast already referred to—in this instance " the well-known hate-love ambivalence of the love life."

In this final scene " the sadistic component of the sexual instinct attains independence."

20. " Nothing exceptional else happened, except voices and noises in the daytime. I had to speak to those spirits, still looking for my blood in all corners of the room, more especially from the book-case, where a few of them would gather and shout at me, and sing now and again. Sometimes they would light on me in the shape of ' little hairs ' and work themselves right down to my private parts. Then I would squeeze again and they would go down to my boot, and then could not get out, and constantly kept shouting ' Let me out,' until finally I moved, unloosed my boot and let them out.

" I did this pretty regularly. The attendant said that I should take no notice of the voices, so I began to put them off, and think of things which did happen, and to dimly understand such things were impossible. They drifted slowly away since then. " I. M."

" Referring to my previous report in which I stated that the voices had decreased daily, getting less and less each time, I may now state that these voices and noises have decreased now, but at night when in bed before falling asleep if I *use my mind and imagine I hear the voices, and think of the time they troubled me so much, then I*

seem to hear the voices again, but barely audible and unintelligible. When I switch my mind off to some other subject the voices cease, so that I always manage to turn away my mind to every-day topics, and thus am not bothered with the noises.

" My health all round at the present time is good, and I am feeling strong and fit.

" I. M."

The emotional crescendo, as is usual in dreams and nightmares, is followed by an awakening—the systematized experience is shattered and is followed by a devolution of the hallucinations—the voices and noises, diurnal and nocturnal, are no longer clearly differentiated. The persecution by the " spirits " which have reverted to " hair " form is gradually warded off by a mechanical downward squeezing process. His power of attention is under more control, he can listen to advice and act on it, and he can appreciate an effort to explain to him the origin of the hallucinations, and the genesis of his delusions. About this time it was noticed that he was troubled by intermittent hallucinations in his left ear. He described them as due to a woman's voice. It was suggested to him that this arose possibly from cerumen, and that it would probably cease when his ear had been syringed. After this was done the voice seemed to become more remote, and he accepted the suggestion that it was imaginary.

His residual hallucinations were mainly of hypnagogic type and (as noted in the postscript to his Report written before his discharge) had to be " rung up " so to speak. During his convalescence the patient was usually worried by the fear that he had contracted syphilis, though he was positive that he " had never had it to his knowledge." Wassermann's sero-diagnostic test gave a positive reaction, and of course he got specific treatment, though not informed of the fact. He suffered much loss of blood from haemorrhoids, and this increased his anaemia. He quickly responded to treatment, ate and slept well, and occupied himself usefully at clerical work when not out of doors. His conduct became normal in every respect, and his temperament bright, cheery and optimistic.

After his discharge he obtained suitable employment, and continued well.

Special Points of Interest.

1. *The nature of the case.*—" The history of hallucinations," says Kraft-Ebing, " contains part of the history of all peoples, and of all religious opinions."

The statement may be said to be equally true of the history of the hallucinations of any one individual of any one period. They contain a part, and that a very large part of the degree of civilization, and of the religious opinions of that person at the particular time of their manifestation.

" I. M— " shows himself to us in the mirror of introspection, and his painful emotional state (the hyperalgia of Eminghaus) reflects not only the man, but the very stirring times in which he lives. His mental disturbance is essentially a disease of the sensory sphere ; his personality determining the facies of the disorder as seen by the physicians. The case comes very distinctly under the systematized form of hallucinosis as classed by Ballet. The facies is a distortion of religio-politico-sexual features, and would be most accurately described as " the acute systematized hallucinations of I. M—" inasmuch as his habits, vices and occupation set up the change of emotional disturbances which constitute his mental make-up, and which are inseparable from his ego.

At bottom his insanity is essentially the same as that we find described

under many variants : the exhaustive psychosis of Kraepelin, the hallucinatory mania of Mendel, the hallucinatory confusion, paranoia dissociativa of Ziehen, the acute hallucinatory insomnia of Westphal, the delirium of inanition of Broquet, and the sensory insanity of Bianchi, the one essential common to all being, as the latter authority stresses, that the delirium (delusionary state) is produced by hallucinations.

2. *The personality of the patient.*—His egoistic passions, "love," or more correctly "lust," "religion," in the sense of adherence to a sect with an entire lack of the morality which religion inculcates, "politics" of the inherited type, and tending to fanaticism engendered by his upbringing, his occupation, and the stress of an acutely hostile environment. That the first-named two emotions are interchangeable is well established and in the period of the patient's attack—it was during the Great War—moral levity, "the usual product of the constant imminence of danger and death," was much to the fore. The psycho-pathological basis of the "nightmare" may be attributed to the exhaustion of illicit excesses, and the strain of repression of normal affections. The repressed wish of young manhood is more potent in precipitating mental breakdown than those infantile suppressions now so eagerly sought for in explanation of the psychoses. The strong but vain desire to marry a girl of religion different to his, and one whose social associations were antagonistic to his loyal service to the Crown, furnishes in this case a very tangible cause of all the trouble. But though it is unnecessary to seek a Freudian standpoint of origin, the nightmare was one long anxiety and punishment dream such as Freud holds "puts in the plan of the interdicted wish fulfilment, the punishment appropriate to it, and is thus the wish fulfilment in the sense of guilt reaching to the contemned impulse." Through all there is a subjective and an objective harmony—"The various images are held together by an emotional thread," both during day and night.

3. *The patient's environment.*—(*a*) At home, in a frontier town where opposing party currents foamed and raged, and where he was in constant danger of a violent death, he still kept company with a girl from each camp and kept each one in ignorance of his liaison with the other. In the Barracks his special occupation kept him on tenterhooks hanging on to a telephone—sending and receiving official messages. In this active scene of party strife he had abundant material for immediate sensory stimuli, and the resultant secondary hallucinations gave full play to the creative fancy, selecting and bringing together the sequent images, weaving into their warp and woof the fully-developed dream of a typically crescendo character.

(*b*) In the mental hospital : It was a coincidence of some importance that the subjects of the pictures in the ward readily lent themselves to the motif of his phantasy—to the various contents of his emotion, love, religion, and loyalty, as of the seven pictures within his view six were brought into action.

The seventh, a dull-toned landscape, found no place directly or indirectly

in the film of his "nightmare," having no affinity for the hallucinatory project of his conative conflicts.

4. *The systematization of the hallucinosis.*—The subjective emotion which constituted the basic unity of the "nightmare" was fear, the manifestations taking form in the attacks of "enemies" civil (including "irregulars") and military (powers of evil, "soldiers") all subject to transformations.

Taking the transmutation in sequence we have:

(1) The devil in *propria persona*.

(2) A regiment of "flies"—men in "spirit" form opposed to the R.U.C.

(3) "Enemies" masquerading in the characters of the subjects of the pictures—men, women and dogs.

(4) The army of "hairs."

(5) The army of "small cockroaches."

(6) Return of the "army of flies."

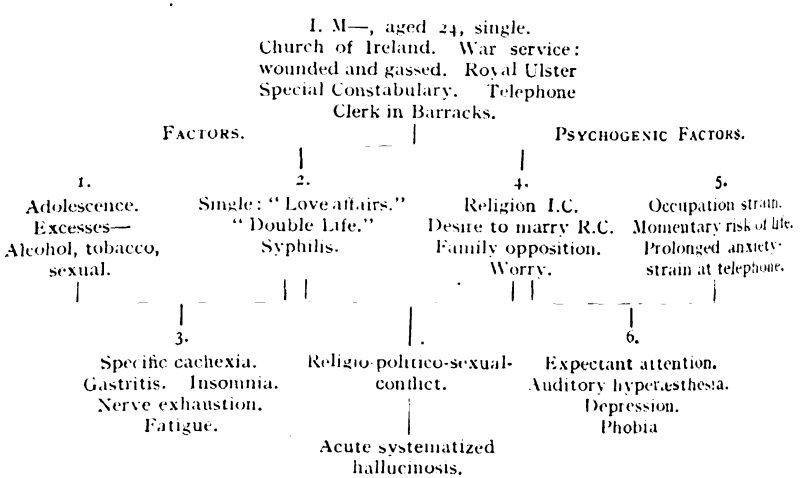
(7) Return of the "army of cockroaches."

(8) Soldiers in "human form," some forming a special detachment of small lizards.

(9) Return of "hairs" and "cockroaches" for final attack on him and engagement between themselves.

In conclusion it will be noted that during the six days and nights of this attack of acute hallucinosis no feeling of acute confusion was experienced by the patient—every incident, however strange, was accepted without question, and fitted with the plan of campaign, which was carefully systematized, and recalled with paranoic memory and adoption.

Schema of Aetiological Group-factors in the Case of I. M—. Acute Systematized Hallucinosis.



SOME POINTS IN THE TECHNIQUE OF INSULIN THERAPY OF THE PSYCHOSES.

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MANY papers have already been published on the technique of insulin therapy for the psychoses (Müller, 1936; Sakel, 1937 and 1938; Frostig, 1937; Küppers, 1937; Braunmühl, 1938, and others). Nevertheless, some of the details of the method still offer problems to the careful therapist who wishes to avoid impairing his therapeutic effects by excessive caution, but is unwilling to incur unpredictable risks. While investigating this therapy during 1938 at the Maudsley Hospital, we endeavoured to evolve a technique which was both effective and safe, and which could be individualized to each patient without thereby losing its precision. In the following paper we offer suggestions concerning some of the technical details that have appeared to us important in achieving these ends. As far as possible we have omitted points on which previous papers have given adequately clear and consistent instructions.

A. GENERAL MANAGEMENT.

1. *Charts.*

A complete and detailed series of charts was found advisable to avoid dangers arising from careless supervision of the treatment; its many other advantages were obvious. We have found the following charts to be the minimum desirable:

(a) *The temperature chart.*—On this should be entered the following details:

(i) Temperature, pulse rate, and respiration rate daily at 6 a.m. and 9 p.m.

(ii) The diet taken during the day entered as "full," "half," "excess," etc., and any tube feeding also noted.

(iii) Daily insulin dose, duration of coma, and duration of waking. An asterisk is inserted to indicate any complications arising on any particular day.

(iv) The weight recorded weekly or bi-weekly.

(v) A space also available at the side of the chart for entering the average coma dose of insulin and the maximum safe period of coma for the particular patient, after these have been ascertained.

(b) *The daily treatment chart.*—Many forms of this have been devised. It should include a space for half-hourly records of the pulse and respiration rate, and also room for recording the administration of drugs or glucose, the onset of coma, and the time taken from interruption to wakening.

(c) *A treatment board.*—On this is placed the essential time data of the coma of each patient, such as the times of onset of sopor and coma, the time of projected and actual interruption, and the time of awakening. It is displayed prominently in the treatment room and is filled in by the nurses or doctors during treatment. We find this lessens the probability of overlooking a patient's interruption time when other emergencies arise, and it is also useful when filling up the more detailed records kept at the end of each morning's treatment.

(d) *An insulin dosage book.*—Doses for the next morning's treatment are entered in this at the conclusion of the day's treatment, and it is left in charge of the ward sister who gives the morning insulin doses. This also provides a ready reference book for rapid collection of data on dosages used.

2. *Diet.*

To obtain satisfactory and consistent insulin effects a regular and correctly balanced diet seems to be most important. Measured normal meals are given to all our patients; and to achieve this, the taking of the diet is closely supervised. Any excess of the standard diet is avoided if possible, especially an excess of carbohydrate, since too much carbohydrate enhances the probability of "after-shocks" by increasing the insulin-sensitivity. When the patient is having a constant diet, a regular daily routine, and the same length of coma each morning, it has been rare in our experience to find sudden or severe changes in the response to the morning insulin, or the occurrence of "after-shock." Tube feeding is resorted to without delay when defects occur. Deviations either way from the standard are recorded on the temperature chart. When all food is refused, a standardized tube feed is given at lunch-time and at 5 p.m. It has been our experience that these precautions minimize variations in response to the morning insulin dose and greatly reduce the liability to "after-shock." It is frequently overlooked that the morning dose of insulin is still being absorbed for a further 18 hours after it has been injected

B. Criteria of Coma.

It is generally agreed that the duration of unconsciousness is the best index of the severity of a period of hypoglycaemia. Yet one writer suggests the desirability of daily comas of two to two and a half hours' duration, while

another considers that in order to keep within the limits of safety only three-quarters of an hour should be given. The real difficulty seems to us to lie in defining when coma has begun, because it always begins gradually, and the signs of the initial stages differ among individual patients. In these facts lies the probable reason for the widely divergent views on the ideal length of coma. However, provided that the same criteria are applied consistently from day to day, patients' treatment can usually be graduated satisfactorily, but no real comparison of technique and results will be possible unless similar criteria are used in various clinics. We have adopted the criteria of coma advocated by Küppers (1937) which seem to us to have advantages over all others. He overcomes the difficulty of the gradual onset by differentiating two stages in the loss of consciousness:

(*a*) Sopor or pre-coma.

(*b*) True coma.

Because of individual variations it is found that reflexes, motor phenomena and most other physical signs cannot be used as criteria of the onset of either of these stages, and reliance has to be placed on tests for the presence or absence of "conscious" or purposive reactions.

By sopor is meant the loss of adequate orientation or speech. The onset of sopor is usually indicated by the loss of a normal response to speech. Although the patient is often apparently in coma, further testing will generally elicit some confused but purposive responses. Confused slurring speech may even be possible, but adequate orientation is always lost. There may often be difficulty in deciding when a patient reaches the stage of sopor; since this difficulty only arises during the lighter degrees of sopor, it is not of much practical importance. It is, however, important to recognize when definite sopor deepens into true coma. The onset of coma is distinguished by the loss of all purposive conscious-like responses even on careful testing. The common methods of testing for the presence of coma include raising and dropping the patient's arm, trying to make the opened eyes follow a moving object, and, finally, if doubt remains, giving a painful stimulus. There should be no responses from visual, sound, or touch stimuli; painful stimuli may still produce movements not directed towards the stimulus. The eyes may remain open and some non-purposive movements persist, although coma is present, but testing will always demonstrate the absence of any purposive responses. It has been found that many patients, while still aware of the test stimuli, and not in coma, lose all initiative to respond. With experience these patients may be distinguished from those in coma, and if necessary testing with painful stimuli will generally reveal the difference. Dr. Guttmann kindly tested a number of patients, in sopor and coma, by electrical stimulation of the vestibular organ. He found that the onset of coma according to these criteria corresponded to the stage when the vestibular response became a tonic deviation of the eyes instead of a nystagmus. This confirmed the fact that these

criteria corresponded to a definite depth of unconsciousness, and also suggested a further confirmatory test for the presence of coma that has proved useful with doubtful cases. If the patient's eyes are held open and the head turned sharply to one side, the eyes will slowly deviate back to the mid-line when coma is present. If the patient is not yet in coma they may fix on an object, remain deviated, or exhibit nystagmus. Using the above criteria Küppers feels that the average safe maximum duration of hypoglycaemia is sopor lasting for one and a half hours or coma for three-quarters of an hour, which agrees with our experience.

Because of individual differences in the earlier nervous phenomena of hypoglycaemia, the onset of sopor does not always indicate a hypoglycaemia of equal severity, nor is it so precisely definable as is coma according to Küppers' criteria. For this reason, we feel the regulation of hypoglycaemia in this treatment is probably best done by concentrating on the duration of the coma rather than the sopor. We have occasionally found however that if the patient remains merely at the stage of sopor for a long period, the hypoglycaemia can still become irreversible. Therefore it is useful to note also the time of onset of sopor, and interrupt after an hour and a half as a precautionary measure. The onset of Küppers' sopor appears to us to correspond with the onset of coma as described by Sakel, Müller and many others; while Frostig widens the concept still further and includes even the occurrence of myoclonic twitchings as a sign of the onset of coma.

c. Induction and Duration of Coma.

In the management of Stage II the length of the coma is much more important than the actual dose of insulin required to bring it about. Coma should be brought about gradually, allowing a slightly longer period of unconsciousness each day until a maximum safe duration has been reached. We feel it is more satisfactory to discover the safety limit for each individual patient than to rely on a generally advocated safe length of coma. After this has been determined for each patient, all comas should be kept just within these limits. That the maximum safe duration of coma has been reached is indicated in two ways—either by the development of some sign of excessive depth, or more usually by the fact that the time taken to awake after the nasal feed exceeds twenty minutes. With marked improvement in physique, longer comas may become possible and the safe limit raised. This will become apparent by significant changes in the depth of coma or the waking time. Attention to these points will tend to prevent the occurrence of irreversible coma. It is important to remember that any abnormally severe coma is apt to cause an increased susceptibility to the next day's insulin. And even if this was not of sufficient severity to warrant a day's rest, a shorter coma should be given the following day. As a general rule maximal comas within the safe limit should be administered each day, although it may yet be discovered that certain cases benefit

more from submaximal comas. The time of onset of coma should also be standardized to occur during the third hour. This should be done by adjusting the insulin dose at the same time as the safe duration of coma is being worked out, since the safety limits for a coma beginning in the third hour will not apply to a coma beginning in the fifth hour. When raising the dose of insulin to 300 U. has not achieved a satisfactory coma it is probably unwise to raise it further, and some other method of facilitating coma onset, such as the "zig-zag" method (Braunmühl, 1938), should be tried.

D. Signs of Excessive Depth.

The appearance of signs of excessive depth calls for premature interruption at any stage of coma. It has been found a useful practice to examine each patient just before routine interruption for any of these signs, and alter the next day's coma if anything suspicious is found.

1. *Circulatory.*

The peripheral circulation and the blood pressure have proved the most useful indicators of circulatory embarrassment, and a repeated examination of the finger-tips during coma is generally advisable. When in doubt the systolic blood pressure should also be repeatedly taken, and if it fall below 100 mm. the coma should usually be interrupted. Blood-pressure readings are also a great help in guarding against cardiovascular shock. A falling blood pressure and rising pulse rate should always be a danger signal, especially if combined with signs of failure of the peripheral circulation. Unless interruption is done in time with such cases, it is often difficult to get into a vein without cutting down and the tube feed will probably be vomited or poorly absorbed.

Problems often arise in connection with pulse irregularities. If these first appear during the later stages of coma or are associated with a pulse rate of below 60 (suggesting the possibility of heart block), nasal interruption should be performed within five to ten minutes. Earlier pulse irregularities, however, often subside with the full development of coma, but when they are frequent and persist for over half an hour, caution is needed. As a general rule, provided the blood pressure remains above 100, the pulse volume is good and the pulse rate ranges between 70 and 100 per minute, those patients may be left for three-quarters of an hour to an hour before interruption. Many of our cases who had these extra systoles in the initial stages of treatment lost them as treatment progressed.

2. *Neurological.*

Although the motor phenomena are of little help in determining the onset of coma, they are useful indications of its depth. Angyal (1937) has described their development in stages, although considerable individual variations occur.

In the earlier phases various types of movement may appear; these are clinically important only because of the exhaustion that may result if they are excessive. They may be minimized, if desired, by premedication with luminal gr. 1½, but if extensive they should not be allowed to continue for over one and a half hours. In the deeper stages of coma, waves of increased extensor tonus occur which are well seen in the arms as combined extension and pronation; the presence of these indicates that the patient is reaching the safe limit of therapeutic coma. Frequently we have found that they are exaggerated or precipitated by an associated respiratory embarrassment or impending circulatory failure. Freeing the air-passages, often best accomplished by inserting a Hewlett's airway, may relieve these and allow coma to be continued. If there are no signs of circulatory insufficiency and these waves are only spasmodic, interruption of the coma may still be delayed for a further fifteen minutes. If, however, there is any suggestion of poor circulation, or these waves become persistent for longer than one minute, a nasal feed should be given immediately.

Generalized tremor when the patient is not cold is another important sign of excessive depth, and calls for early interruption. Sometimes the patient will awaken spontaneously after the beginning of coma, generally after a period of severe spasmodic movements. Braunmühl (1938) recommends the interruption of the coma in such patients. If this is not done, and the patients are allowed to relapse into coma again, the total length of coma allowed should never be more than half that usually given to such patients, or they may go into an irreversible state.

The condition of the reflexes is of little help. Widely dilated or pin-point pupils and an absence of light reflex when present generally indicate excessive depth of coma, but these are by no means reliable criteria. More important is the observation of any change from the usual neurological pattern seen during previous comas, since this suggests the possibility of excessive depth. If unconsciousness seems deeper or different from that usual for the particular case the circulation should be examined for signs of inefficiency, and this combination of signs is always the indication for immediate interruption.

E. Interruption.

600 c.c. of 33 per cent. sugared tea is probably the best routine nasal interruption feed; but if vomiting occurs frequently, smaller amounts may be necessary. After an epileptic fit, it is useful to put in the tube feed a mixture containing aspirin, phenacetin and caffeine. When the gastric juice is only weakly acid, a teaspoonful of salt should be added in case chloride deficiency is present through excessive sweating.

If the coma had been very deep before interruption, it is unwise to allow half an hour to elapse before giving intravenous glucose; an early intravenous injection may prevent irreversible coma. Whenever the administration of

intravenous glucose is indicated, at least 100 c.c. of 33 per cent. glucose should be given, since then a recurrence of hypoglycaemia is impossible for at least half an hour (Fraser and Stanley, 1939); and the needle should not then be withdrawn unless the patient is fully awake. (See under "Complications.")

We have found that the administration of 100 c.c. or more of 33 per cent. glucose intravenously is much facilitated by the apparatus illustrated in Fig. 1.

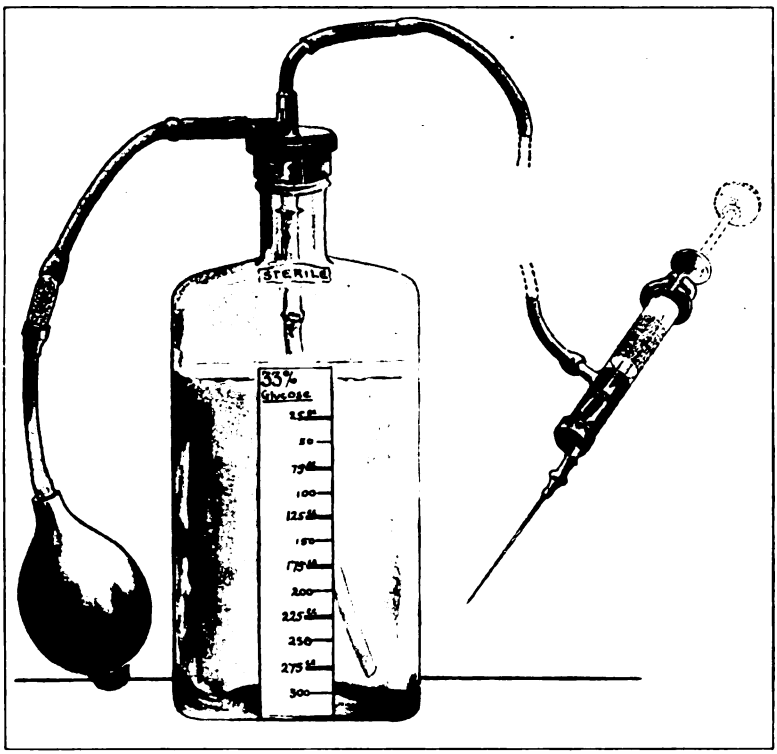

FIG. 1.—Apparatus for rapid administration of intravenous glucose for interruption of hypoglycaemic coma, used as described in the text.

The "wash bottle" principle is utilized, and the pressure in the bottle is raised before starting to use it. Gently withdrawing the plunger of the syringe readily tests whether the needle is in the vein, and if so the plunger is still further withdrawn past the side-valve connecting with the pressure bottle. The bottle then automatically comes into action and the 100 c.c. of intravenous glucose runs in at a speed depending on the pressure in the bottle. If saline is to be injected immediately afterwards, this can be done simply by the nurse unscrewing the bottle of glucose and replacing it by another bottle containing saline, without withdrawing the needle or any movement on the doctor's part.

The manipulations necessary with other methods are avoided, and the doctor can concentrate on preventing the needle slipping out of the vein when the patient is restless or shocked. The pumping procedure, the checking of the amount of fluid given and the change of solutions is the responsibility of the trained nurse. The apparatus is assembled before treatment is commenced in the morning and is always ready for immediate use.

F. Epileptic Fits.

A distinction should be made between *early* and *late* fits (G. Gross-May, 1938), but since all intermediate stages of transition occur between these two types precise delimitation of late fits is not easy. The early fit generally occurs 45 to 100 minutes after the administration of insulin and is preceded by but few neurological disturbances, among which coma is never included. Intravenous interruption of early fits is not necessary and a nasal feed should be used. The late fits on the other hand may be followed by delayed recovery or severe shock unless an immediate intravenous interruption is given. A typical late fit occurs after a period of coma, and probably indicates the occurrence of excessive cerebral glycopenia, and hence it is commonly associated with signs of vascular shock. Some have classified fits occurring after the fourth hour as late fits, while Braunmühl (1938) considers late fits those occurring after the second hour. In view of this wide disagreement it is probably best to delimit late fits by their individual relation to previous sopor or coma and the presence of associated signs of shock. Thus, those cases in which fits occur after either half an hour's sopor or any length of definite coma and which are succeeded by signs of vascular failure should, from the point of view of treatment, be classified as late fits. Furthermore, we have learned from experience that even with fits initially regarded as early, if the patient still shows a " post-epileptic confusion " or signs of vascular shock fifteen minutes after the nasal feed, intravenous injection should be given or more serious complications may ensue. Some regard early fits as being of therapeutic value ; this is rarely considered to be the case with late fits, which instead indicate the need for shortening the length of coma or reducing the dose of insulin.

G. Complications.

(a) *Vomiting after the Nasal Feed.*

Besides the usual causes of this complication it is sometimes an indication of slight shock or collapse and calls for a shortening of the patient's subsequent comas. If there has been much movement, pre-medication with luminal, gr. 1½, may eliminate the exhaustion produced thereby and so the vomiting. If the vomiting is excessive shock is almost certainly present, and a large amount of

glucose (250 c.c. of 33 per cent. solution) should be given intravenously. For a further hour nothing more should be given by mouth, and then it is better to give a small solid meal with ordinary tea rather than the usual somewhat sickly sugared tea.

(b) *"Irreversible" Coma.*

Delayed awakening after the nasal feed is best classified into two main heads—either simple prolonged hypoglycaemia or true irreversible coma.

The former is an unimportant complication and responds immediately to intravenous glucose. The latter type is distinguished by the persistence of unconsciousness after the administration of intravenous glucose ; and in severe cases there develops vascular shock and hypertonus with writhing movements resembling states of anoxia. The milder cases may merely show delayed local recovery—such as a monoplegia or asphasia—or slight confusion of short duration. The severe case may not recover consciousness for days, but if circulatory collapse is avoided death rarely occurs.

Little is known of the pathology of this condition, except that it depends on the abnormal persistence of some cellular changes that have developed during hypoglycaemia. An alkalosis is also present. There may be some "block" to the diffusion of sugar across the cell membranes, and anoxia caused by the vascular shock is undoubtedly a contributory factor. Treatment must therefore include measures to facilitate the entrance of glucose into the cells, to combat the alkalosis and anoxia, and to restore circulation to its maximum efficiency.

Our experience has convinced us of the value of giving a large amount of intravenous fluid to these cases, a value presumably due to the improvement produced in the circulation and dehydration. When the intravenous injection of 100 c.c. of 33 per cent. glucose reveals this complication, before the needle is withdrawn an additional 150 c.c. of 33 per cent. glucose should immediately be given, making 250 c.c. altogether, for reasons to be mentioned shortly ; and in addition through the same needle :

(1) 10–30 c.c. of 10 per cent. $CaCl_2$.
(2) 1,000 units of aneurin (vitamin B_1).
(3) Coramine 2–4 c.c. and caffeine if there is much shock or weak respiration.
(4) 500–1,000 c.c. of saline with 5 per cent. glucose.

A nasal tube should immediately be inserted, delivering 5 per cent. CO_2 in oxygen ; ½ c.c. adrenaline should be given intramuscularly if the pulse rate is under 100 ; and warmth, etc., applied as for shock and the end of the bed raised. The essential consideration is to avoid cardiovascular collapse, and the pulse must therefore be watched throughout and the large intravenous injection of saline given slowly. After the completion of this treatment the degree of shock should be subsiding and the rectal temperature will generally be rising,

but the patient may be extremely restless. An injection of morphine and hyoscine is often useful to allay this.

An hour after the first injection, a second injection of 250 c.c. of 33 per cent. glucose together with a further 500 c.c saline should be given if necessary. By this time the danger of acute collapse is usually past, and the treatment simply consists in the nursing of a restless shocked patient and the administration of adequate sugar to avoid hypoglycaemia. It has been shown (Fraser and Stanley, 1938) that in the absence of any intestinal absorption, 100 c.c. of 33 per cent. intravenous glucose can be relied on to prevent any recurrence and hypoglycæmia for half an hour and 250 c.c. for an hour, and that neither upsets the fluid balance significantly. When there is no significant shock 4-hourly nasal feeds can probably be relied on for this. Pulse rate, respiration rate and temperature are all noted at half to one-hourly intervals. On any signs of increasing shock further 5 per cent. glucose saline is given intravenously and respiratory stimulants added if necessary. The administration of the CO_2 and oxygen can be discontinued when the vascular shock has subsided.

Four-hourly nasal feeds of 600 c.c. of 33 per cent. sugared tea should be given until the patient is able to drink. Before each feed the gastric contents are withdrawn, and if a large proportion of the previous feed has not been absorbed, a further 500 c.c. of 5 per cent. intravenous glucose should again be given. These measures are adequate to prevent recurrence of hypoglycaemia, which might otherwise be overlooked.

After recovery of full consciousness treatment should not be resumed for at least another two or three days, though this severe complication does not necessarily imply that treatment should be abandoned. In fact, in several of our cases, who had irreversible comas, treatment was recommenced and carried to a successful conclusion. On resumption of treatment, half the coma dose of insulin should be given for the initial dose and the comas kept short.

Other and better methods will probably be evolved to treat this alarming symptom, but at present we find that adequate intravenous glucose saline and the general treatment for shock outlined above are the most satisfactory measures. Lumbar puncture is recommended by many authors, but we have so far not been convinced of its efficacy, and there are even theoretical reasons for thinking it might be disadvantageous. Adrenal cortex hormone may prove to be a useful addition to the above outline of treatment for this complication, but this possibility has not yet been adequately studied.

H. The Assessment of Results.

This technical detail is perhaps the most difficult of all. Careful observation and repeated checking of the actual findings is more than ever necessary in this treatment, which has aroused so much uncritical enthusiasm and so much

theoretical criticism among psychiatrists. The routine procedure at the Maudsley Hospital has been as follows: Each case is examined clinically for a week to a fortnight before commencing treatment. Careful histories and a detailed assessment of the mental state are completed before treatment is commenced. The case is then shown at a hospital conference which includes the major part of the medical staff. The diagnosis at this conference must be unanimous or the case is disqualified for inclusion in the selected group. The doctor who referred the case to the insulin ward is asked periodically to make an examination and give an opinion on the changes that have taken place.

During treatment the charts referred to above are carefully kept and the clinical data of the patient's progress recorded, especially any significant alterations in the mental state occurring after individual comas or fits. At the end of the treatment special attention is paid both to the extent and quality of remission made. Before discharge the cases are again shown where possible to a clinical conference of doctors. Each case is asked to write out a full-length account of his illness; and unless he gives a good description of the abnormal experiences, indicating complete insight into their nature, the patient is not classified as full remission. Intelligence tests are given to try and assess any possible intellectual impairment that may have resulted from the treatment. Relatives are closely questioned as to the presence or absence of signs of deterioration in its finer degrees and the value of their opinions carefully assessed. On discharge each patient is asked to attend a follow-up department every two months when possible. A study of the life situation to which they have to return and a comparison to that before the illness is also attempted. In this way we hope eventually to arrive at some conclusion, but for the present all that can be said is that the results seem encouraging enough to warrant further investigation.

Summary.

Some of the technical details of insulin therapy are discussed:

(1) Recommendations are made concerning charts and the supervision of the diet.

(2) The criteria of coma are discussed and those recommended by Küppers are advocated; these are based on a recognition of two stages, sopor and true coma. An additional simple test of true coma dependent on vestibular function is described.

(3) Some points about the induction and duration of coma are discussed, and a method of individualizing this to each patient recommended.

(4) Some of the indications of excessive depth are described.

(5) The importance of differentiating early and late epileptic fits is emphasized and both the criteria of differentiation and treatment for each discussed.

(6) Nasal and intravenous interruption are briefly referred to.

(7) Details for the treatment of irreversible coma are outlined.

(8) Brief reference is made to methods used for selecting cases for treatment and for their subsequent clinical supervision with a view to assessment of the results of treatment.

Our thanks are due to the late Prof. Edward Mapother for his advice and the opportunity to treat cases under his care at the Maudsley Hospital.

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SEVERE TOXIC EFFECTS OF SODIUM DIPHENYL HYDANTOINATE IN MENTALLY DEFECTIVE EPILEPTICS.

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Selection and Dosage.

The anti-convulsant value of sodium diphenyl hydantoinate (S.D.H.), marketed in America as Dilantin and in England as Epanutin, as found by Putnam and Merritt and introduced by them in the treatment of epilepsy has been amply confirmed by all subsequent reports, as it is by this one. Its clinical application, however, will, it is thought, be modified by reason of its toxic nature becoming more generally known.

Recently a trial series of 20 among 200 male mentally defective epileptics in this hospital was submitted to this form of therapy. Those selected were among the more severe cases of epilepsy, being approximately equal groups of idiot, imbecile and feebleminded patients respectively.

The new drug in replacing previous medication was prescribed with all the precautions recommended by those familiar with its use. It is perhaps due to this care that so few of the cases showed any of the early toxic manifestations hitherto described. These will not be discussed in detail, but it will be recalled that in most of the reports on S.D.H. the drug was discontinued at various intervals from the beginning of treatment and for various reasons. It is presumed, for it is not explicit, that the majority of interruptions in treatment occurred early. Toxic symptoms of a grave nature occurring six weeks or more after the drug was first given, if hitherto reported, have not been uncompromisingly attributed to its action.

The considerable diminution in the total number of fits must be defined as due to the efficacy of S.D.H. over and above the anti-convulsant value of the drugs which, over a period of years, had been found most effectual in each patient. Dosage became a matter for individual assay. It will be seen that, whereas the average dose was 0·3 gm. per day, in no case was the maximum of 0·6 gm. ever reached. This bears upon the question of cumulative effect which had previously been found unlikely. No evidence of pre-existing renal disease was present in any of the toxic or fatal cases in the present series. The

likelihood of specific idiosyncrasy, on the one hand, or high eliminative threshold on the other remains open. However, the statistics here given imply a marked intolerance to S.D.H. among those in whom organic changes in the central nervous system is found. In a few cases recourse was had to luminal in addition to the S.D.H. Its synergistic action in this connection has been well reported, and when used it was found helpful both in the control of seizures and of the unduly excited behaviour that sometimes occurred.

Comparable Reports.

The literature contains three comparable reports: (1) Weaver, Harrell and Arnold treated 14 cases at the Virginia State Colony for Epileptics and Feeble-minded Patients. In general the drug was found to be suitable, though sufficient is not said of the six cases, or 43 per cent., whose treatment was interrupted. (2) A. J. M. Butler treated 43 institutional patients. His opinion is that the mentally higher grade patients respond best to the new drug. From the table of statistics given below this fact is very clear, its determination being one of the objects of study. (3) R. Coope, reporting upon 19 non-defective epileptics at the Maghull Colony, Liverpool, is also favourable to S.D.H. therapy, though he concludes his article with an account of two deaths. From his treatment of these fatal cases one gathers that he does not attribute these unfortunate results unreservedly to S.D.H. This is easily understandable when one sees how gradual is the process of mounting toxicity. However, his accurate description of symptoms in the terminal picture closely corresponds to the cases of S.D.H. poisoning here described.

Typical Late Toxicity.

Six weeks or more after S.D.H is first introduced and quite irrespective of its ability to control the fits, the toxic symptoms make an insidious appearance. The patient is put to bed because of increasing mental dullness. Confusion gradually replaces the dull apathy and small groups of fits spoil the recently good epileptic record. Lapses from consciousness are preceded by absolute insomnia. Constipation is intractable and retention or oliguria is the rule. An intermittent temperature of 100°–102° F. appears late. In one case it rose to 106° F. 48 hours before death, while in the other cases the terminal temperature was subnormal. Widespread furunculosis occurred in one case, oedema of the face in two cases, an urticarial wheal along the muco-cutaneous margin of the lips in one case and gingival hyperplasia with bleeding in one. Death was due to bronchopneumonia in one case and to *status epilepticus* in three. Blood-pressure during seizures in one case was 120/90 mm. of mercury in the intervals between fits and a swinging pulse

Clinical Table.

Name.	Case No.	Age.	Dosage in gms.	Months on S.D.H.	Fits per month in the year before S.D.H. therapy.	After S.D.H. therapy.	General type of epilepsy.	Late toxic effects.	Behaviour changes.	Deaths.
							Feebleminded.			
C. H—	1	36	0·3	4	2·5	1	Essential	None	None	..
G. H—	2	32	0·3	4½	2	2	,,	,,	,,	..
F. M—	3	33	0·3	4½	Many *petit mals*	Much improved	,, *petit mal*	,,	Much general improvement	..
O. D—	4	17	0·2	3	22	7	Jacksonian	Tending to *status*; drug withdrawn	Much more difficult	..
R. H—	5	33	0·3	4½	7·5	4	Essential	Early headache, constant yawning	Generally more alert	..
E. E—	6	36	0·3	4½	17	8	,,	None	,, ,,	..
S. R—	7	41	0·3	3	4	6	,,	Gross late toxaemia drug withdrawn	None	Ten days after withdrawal.
							Imbecile.			
E. P—	8	21	0·3	3½	9	3	Idiopathic	Ditto	Much more difficult	..
A. B—	9	32	0·3	1½	7	8	,,	None	Uncontrollable; drug withdrawn	..
C. S—	10	41	0·3	½	3·3	14	Jacksonian	Stuporose and *status epilepticus*; drug withdrawn	Dull generally	..
C. L—	11	27	0·3	4½	22	15	Idiopathic	None	Generally more alert	..
G. W—	12	43	0·2	4½	2·8	..	,,	,,	Much more difficult	..
M. R—	13	23	0·3	3½	9	..	Jacksonian	Gross late toxaemia; drug withdrawn	None	Sixteen days after withdrawal.
F. J—	14	22	0·2	½	8·5	17·4	Idiopathic	*Status epilepticus*; drug withdrawn	,,	..
							Idiot.			
J. E—	15	34	0·3	4	17	0·0	Idiopathic	Confusion, urinary retention; drug withdrawn	Uncontrollable; drug withdrawn	..
H. L—	16	27	0·3	2½	15	1·5	Jacksonian	*Status epilepticus*; with recovery	Generally more alert	..
F. F—	17	27	0·3	2	6·8	4·5	,,	None	None	..
J. C—	18	25	0·2	1½	6·8	14	Idiopathic	Gross early ataxia; drug withdrawn	Generally more difficult	..
G. S—	19	29	0·4	1½	5·5	5·5	Jacksonian	Gross late toxaemia; drug withdrawn	Dull generally	Six weeks after withdrawal.
E. A—	20	33	0·3	2	17	10	,,	Ditto	None	Nine weeks after withdrawal.

pressure with 180/120 approximately as the reading during a fit. The pupils were dilated, equal and reacted sluggishly. The deep reflexes were sluggish and the plantars flexor.

Biochemistry.

After the second death the significance of the biochemistry in what was assuming the proportions of a definite toxic entity became more apparent.

Case 20.—The third fatality showed acetone in the urine, which was in other respects normal.

Case 13.—The fourth fatality was more thoroughly investigated.

Urine was scanty, concentrated and reddish orange in colour; it contained albumin, hyaline casts, haematoporphyrin verified spectroscopically.

Blood count: R.B.C., 5,080,000; polymorphonuclears cells, 80 per cent.; W.B.C., 18,600; lymphocytes, 7 per cent.; haemoglobin, 112 per cent.; basophiles, 1 per cent.; colour index, 1·1; urea, 50 mgm. per cent.

C.S.F.: Urea, 35 mgm. per cent.; no cells present; pressure, 90 mm. of fluid between fits.

Case 8.—Now beginning to recover after weeks of illness, during which his death seemed likely.

Urine: Specific gravity 1020, slightly acid, amorphous urate deposit. Normal in other routine examinations. Haematoporphyrin verified spectroscopically. Urea, 3·47 mgm. per cent.

Blood count: R.B.C., 5,610,000; polymorphonuclear cells, 48 per cent.; W.B.C., 8,000; lymphocytes, 44 per cent.; haemoglobin, 110 per cent.; eosinophiles, 0·5 per cent.; colour index, 1·0; mononuclear cells, 7·0 per cent.; basophiles, 0·5 per cent. Van den Bergh negative. Urea, 5 mgm. per cent. Total serum nitrogen, 1·036 gm. per cent., and total protein, 6·475 gm. CO_2 combining power, 49 vols. per cent. Titratable alkalinity, 0·022 molar.

C.S.F.: Pressure normal; no cells present. Chlorides, 740 mgm. per cent. Sugar, 70 mgm. per cent.

The haematoporphyrinuria apparently does not make its appearance until toxic features have been clinically manifest for some time. As a guide to mounting toxicity its significance will perhaps be evaluated by future experience. The most unusual feature, however, is the blood urea. The figures were given credence only after they had been confirmed by the results obtained on the same blood in another laboratory. Controls were run on all determinations. The readings which indicate the process of recovery are given in sequence from the most toxic day onwards. First day, 5 mgm. per cent.—repeated, 5 mgm. per cent.; second day, 5 mgm. per cent.; ninth day, 7·8 mgm. per cent.; twelfth day, 12 mgm. per cent.; fourteenth day, 12·5 mgm. per cent.; fifteenth day, 15 mgm. per cent.; twenty-first day, 18 mgm. per cent.; twenty-second day, 19 mgm. per cent.

Post-mortem Findings.

Inadequacy of investigation in the earlier deaths due to a reluctance in blaming S.D.H. for the unfortunate outcome make the statistics disappointingly meagre.

The brain was oedematous. There were no haemorrhages in cortex or base.

The liver and kidneys showed cloudy swelling and, in addition, there was acute congestion of the lungs and liver in one case with dilation and congestion of the right heart.

Case 20 was a congenital hemiplegic, with typical right-sided Jacksonian convulsions. He was found to have a uniform atrophy of the left cerebral and right cerebellar hemispheres respectively.

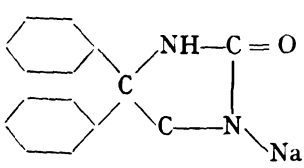
Micro-sections of the brain in three cases are in course of preparation.

Treatment.

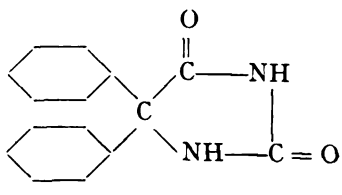
Once the coma becomes established, attempts at resuscitation except as seen in Case 8 were hopeless. Oxygen had the effect of increasing the fits, whereas CO_2 did seem to give some relief. Stomach wash-outs were of value, but the usual practice of leaving a bicarbonate solution in the stomach had no good effect. Intramuscular sodium amytal in one case and paraldehyde, luminal and potassium bromide given in others to control the status appeared to have far less effect than when similarly used in cases of *status epilepticus* not on S.D.H. The beneficial effect of withdrawing the drug seen in the case of the early toxic symptoms made no difference to late toxicity. Moreover, while attempting to interrupt the treatment in the remaining cases after the third death one of the patients developed the usual toxic picture and died in 16 days with bronchopneumonia. Most benefit appeared to result from adrenaline mⱡiv *b.d.* of a 1 : 1,000 solution, given because of some of the anaphylactic features, and from daily bowel wash-outs.

S.D.H. and Nirvanol.

In his criticism of the pessimistic attitude of Schlesinger to the advent of sodium diphenyl hydantoinate therapy, Lennox rightly differentiates it chemically as an entirely separate product. It is well known that in spite of the structural similarity of two drugs even a methyl radical will greatly alter the toxicity.



S.D.H.



Nirvanol.

However, here the chemical similarity of derivation and formulae is supported by comparable therapeutic and toxic effects. According to Schlesinger, nirvanol, though used in Europe in the control of epilepsy and latterly of chorea, had a well-known toxic syndrome. Indeed, these toxic changes had to be well established before any therapeutic value could be expected. He mentioned a case of nirvanol poisoning reported by Keller, the description of which accurately fits that of the cases here presented. It is too early to say how much Case 8, who made a tardy recovery, is likely to benefit from his experience in regard to the future control of his epilepsy.

Conclusions.

(1) In the present series the mortality of four cases represents a rate of twenty per cent. This result served as an inducement to publication earlier than was convenient for the completion of biochemical and histological investigations, in the hope that untoward events might be avoided by careful selection before the application of S.D.H. therapy, also that due regard be given to the seriousness of late toxic symptoms.

(2) Amongst oligophrenics, idiot patients are most prone to toxic manifestations and feebleminded patients less susceptible, while imbecile patients occupy a middle position. In spite of relief from fits, it is doubtful if S.D.H. is safe therapy for those with Jacksonian epilepsy.

(3) Wherever it is considered advisable to withdraw S.D.H., a period of weeks should elapse in this process before the final 0·1 gm. per day is withheld. Luminal or potassium bromide in correspondingly increasing doses are good initial substitutes.

(4) The toxic state is chiefly of interest biochemically by the appearance of haematoporphyrin in some cases and in one case by a remarkable fall in blood urea. Neither mechanism has been adequately explored yet.

Summary.

Sodium diphenylhydantoinate exhibited in the treatment of 20 male epileptic oligophrenics resulted in many toxic manifestations clinically identifiable with a state closely resembling nirvanol poisoning. There were four deaths, or a mortality rate of 20 per cent.

Idiot and imbecile patients particularly showed intolerance to the new drug though the feebleminded patients were not immune. These symptoms were delayed six weeks or more after the onset of treatment. There was thought to be a relation between intolerance and pathological changes in the central nervous system.

Post-mortem findings have been inadequately studied, but clinical interest attaches chiefly to one case with a persistently low blood urea and to two cases

of haematoporphyrinuria. There had been no exposure to ultra-violet light. There was no clinical jaundice.

I should like to record my thanks to the Medical Superintendent, Dr. R. M. Stewart, for his advice and for permission to publish the cases.

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RECENT HYSTERICAL STATES AND THEIR TREATMENT.*

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RECENT hysteria is not a disease. Its manifestations represent the pathological exaggeration of a normal protective mechanism. By this mechanism otherwise well-adjusted individuals are enabled to gain time when a sudden reverse of fortune or an overwhelmingly difficult decision presents itself. Its purpose is to ease the blow and thus to prevent that paralysis of effective response which may result from the too sudden realization of the full implication of a situation.

There are three methods by which this flight from immediate realization may be effected: the *flight into activity*, the *flight into non-realization*, and the *flight into incapacity*.

Of these, the first offers but temporary aid, and is seen where the individual, in his distress or indecision, takes refuge in some irrelevant activity. Nero is perhaps the classical example of this, but it is seen in widely varying circumstances. The man faced with a business reverse paces the room, whistles or makes stereotyped drawings on the blotting-paper; the prisoner dresses meticulously on the morning of his execution. In the pathological field, it is seen in the aimless movements of panic-stricken crowds, in hysterical screaming attacks or the frantic gestures of persons distraught. An important variant of this process is the *flight into anger*, where the insecurity and fear engendered by the situation are thrust aside and forgotten in a wave of anger directed against its cause. Such escape reactions can only be of brief duration, and if with their aid it is still impossible to attain an adjustment allowing of normal behaviour, they must soon be replaced by another form of flight. In such moments of panic, as Kretschmer has pointed out, atavistic motor patterns may be released (hypobulic mechanisms), and there is reason to believe that in certain individuals there is a constitutional predisposition for such psychomotor storms to be released by stimuli below the normal threshold.

When misfortune is sudden, few can face its full import in an instant. A period of bewilderment or a feeling of unreality may be regarded as a normal response, whether the ictus be physical or psychological. This period of partial realization will normally give place sooner or later to a fuller grasp of the situation, and with it the development of signs of anxiety in proportion to the threat to the individual's psychic or somatic integration. When he is

* Awarded the Bronze Medal for 1940 of the Royal Medico-Psychological Association.

unable to endure this anxiety, whether on account of its intensity, or because of a constitutional inability to do so, the original *mechanism of non-realization* may be perpetuated and developed as an hysterical symptom. Such symptoms vary from complaints of marked depersonalization to twilight states, somnambulisms and stupors. The feature common to all such recent hysterical states is an incomplete realization and a total or selective amnesia for the essential cause of the upset. In terms of the unconscious, a complex with an unpleasant affect is in process of incomplete repression, and the effect of the repressing force on the individual's conscious life is such as to reduce his whole appreciation of his surroundings. Even this group of reactions cannot afford a permanent solution of the patient's difficulties. It is unusual for a twilight state or a stupor to remain unchanged, as such, for a long period. Either the patient's realization of his circumstances must be modified in degree, or a more permanent protection has to be substituted for this temporary retreat. It is common in stupors and twilight states, in which the patient has little or no contact with his environment, for the hiatus to be progressively restricted until it exists solely in relation to the disturbing process. Thus a twilight state may undergo transition into a total amnesia, which gradually becomes selective for the causative event as points of contact with the every-day environment are gradually recalled.

The pathological mechanisms of non-realization contain, however, a new element, in that the patient is by their aid able to withdraw from the situation by virtue of his incapacity to carry on a normal life. It is this *flight into incapacity* which, unless its purpose is purely a temporary retreat, forms the basis of chronic, as opposed to recent, hysteria. As the clouding of consciousness of the fugue or twilight state gives place to full orientation, the individual may find himself still shielded from full appreciation of his difficulties or from the necessity of doing anything about them by the appearance of a protecting symptom, the aetiology of which seems to him a mystery. Such symptoms are the aphonias, amnesias and Ganser states, which are seen almost exclusively in the transitional states of recent hysteria. While they stand as a reason-proof barrier between the patient and his troubles, they also have the effect of rendering him *hors de combat*, and introducing him to the freedom from anxiety available to the possessor of an invaliding symptom. Such patients have taken a further step in the direction of chronic hysteria.

Such a progression to *functional incapacity* through intermediate mechanisms of non-realization is not the most frequently occurring. It is more likely to be seen after the sudden stresses of war, where existence itself is acutely endangered, than with the more delicately balanced anxieties and indecisions of civilized life. Functional incapacity is seen either as a *mode of retreat* or as a *means of adjustment*. In the first case, as seen in recent hysteria, its purpose is to spare the individual the anxiety produced by physical danger or intrapsychic conflicts by allowing of an honourable retirement from the situation

without great loss of contact from every-day life. In the second case, seen in chronic hysteria, the purpose of functional incapacity is to achieve a more or less permanent mode of life in which the patient is allowed by his symptoms to adapt himself only to that part of his environment which he wishes to face. He makes this adjustment, however, only at the expense of an admitted inferiority to his fellow men. His outlook on life ceases to be that of a normal adult and he becomes increasingly dependent on his symptoms, as a child is on its parents, and his personality tends to revert to an immature and dependent pattern which has, at least superficially, many of the personality-attributes of the child.

There are few children who do not avoid unpleasant tasks by a pretended illness, whether it be a headache to avoid homework or a pain to avoid eating spinach, but the likelihood of such a mechanism being employed as a means of avoiding more serious difficulties in later life will depend not only on the presence or absence of innate tendencies to react to stress in this particular way, but on the extent to which such evasions have been allowed to flourish and become habitual in early life. The process of facilitation by which a conditioned response becomes ingrained in the experimental dog has its very close counterpart in the development of the advantage-of-illness motive.

The opportunity for escape through minor physical disability is of daily occurrence, and few have not at some time availed themselves of it to avoid an unpleasant duty or explain a failing. The difference between the every-day use of this mechanism and its pathological use is one merely of degree, and the transition from its deliberate to its habitual or " unconscious " use is as indefinite as the borderline between malingering and hysteria. Those who have learned to avoid most of their responsibilities in this way will retreat at once from anxiety by the same means, while others of sterner fibre will take refuge in somatic disability only after a severe struggle in which anxiety and mechanisms of non-realization alternate for a long period. In such cases exhaustion is often the factor which finally determines the flight into functional incapacity.

Relationship of Anxiety to Recent Hysteria.

Anxiety is not usually a pathological state. Its normal purpose is to prepare the individual to take action when an unusual decision or situation presents itself. When only one course of action is possible anxiety is minimal, and consists of a physiological preparedness which is noticeable to the subject in proportion to the importance of the situation to him. The subjective sensations of this state, which does not endure for long, make up the state of " wind-up " or apprehension normally felt before important events. When, however, the situation is one demanding a decision between alternative courses of action and this decision is not taken surely and at once, the resulting state of conflict may lead to a state of pathological anxiety having subjective features similar

to those of apprehension but enduring for a longer period. This pathological anxiety is most likely to make its appearance when the conflict involves the instincts of self-preservation, of reproduction, and of the "herd instinct." In the latter are included the complicated codes of honour and duty whose conflict with the primary instincts is so often productive of the neuroses of civilization.

When to apprehension is added a direct threat to life, the emotion of fear is experienced. When this has persisted for some time the state of lasting fear is indistinguishable symptomatologically from anxiety due to conflict. Acute fear and its extreme form, terror, are exaggerations of the normal reaction of apprehensive preparedness in response to an acute stress. Anxiety is thus necessarily an integral part of the development of an hysterical illness. It will manifest itself in the clinical picture until the patient has either solved his problem or has taken refuge in incapacity. Outward calm is only attained when the conflict has been abandoned, and the individual is prepared to remain aloof from it at the price of an infirmity which sets him apart from his fellows. That this stage has been reached is signalized by the appearance of an altogether pathological tranquillity of mind, the *belle indifférence* of Janet.

Anxiety, whatever its origin, is subjectively unpleasant. Apart from the tremor, palpitations, hyperventilation, epigastric distress and vasomotor phenomena, the feeling of tension may make rest impossible and rapidly bring on a state of exhaustion which, if relief is not found, becomes intolerable. The extent to which an individual will have to experience the somatic components of fear or anxiety will depend on the state of his nervous system, and especially on the sympathetic, which acts as the link between his psychical and somatic components. If, on account of his constitutional type or by reason of some acquired condition (e.g. hyperthyroidism), he is especially sensitized, the strain will be the greater. However phlegmatic the individual, the force of circumstances can always be such as to cause in him an anxiety which is beyond his endurance. Wide as are the variations in resistance before this breaking-point is reached, there can be few who cannot have need of some means of escape. In that the defence mechanisms employed are exaggerations of normal methods of reacting to difficulties, it might be said that anyone is a potential hysteric.

The modes of flight which have been outlined are by no means always completely successful in protecting the individual from anxiety. When intense anxiety is being avoided by means of hysterical symptoms it is common for somatic components of anxiety, such as tremor, flushing and tachycardia, to be evident even though the patient professes complete unconcern. This admixture of anxiety and hysteria is more especially evident where mechanisms of non-realization are prominent, i.e. in recent hysteria. Where functional incapacity develops rapidly, evidence of anxiety is rarely absent, though the patient may not recognize it as such. It would appear that a time factor is

frequently involved in the complete removal of the anxiety component from the symptomatology. The admixture is rarely a homogeneous one. The appearance of calm which accompanies an invalidizing symptom by day may give place to terrifying dreams or episodes of somnambulistic violence by night. In recent hysteria in process of transition, anxiety, anger, amnesia and pathological indifference may be inextricably mixed. This shifting pattern of symptoms is the most characteristic diagnostic feature of the condition at this stage. It is illustrated in the following case:

An R.A.S.C. corporal, aged 24, was referred from his unit for multiple symptoms, including severe headaches and vomiting, fainting attacks, bouts of irritability and attacks of pain in the right iliac fossa. His history, elicited in the course of treatment, was briefly as follows:

He was of low average intelligence (I.Q.85), and had been regarded as the nervous child of a family of four. He had had nightmares since childhood, often walked in his sleep and was known for his uncontrollable temper. On leaving school he obtained work as a cook, and at the age of 23 had saved money and could anticipate steady promotion. He played football and boxed, and had numerous friends. He lived with his parents, but had never got on well with them, his father being alcoholic and his mother over-religious. He had only one love affair, which began five years before his breakdown. A year before he had become engaged and had begun to furnish a flat with a view to marriage, but his parents disapproved strongly of the match as he was a Catholic and she a Protestant. He became ambivalent in his attitude to the marriage, wishing to break away from his people and yet doubting if his affection for the girl was sufficient to warrant it. On the day war broke out there was a family quarrel, and the patient smashed all the crockery in the house and joined the Army the same day.

In the R.A.S.C. he was rapidly promoted to corporal, although he did not like the life, but after his transfer overseas he began to have intense nightmares and to become irritable over his work. Following a trivial abrasion he reported sick with intense pain in his leg. This was followed by an attack of vomiting and refusal to eat. After this he developed a variety of symptoms, such as headaches, abdominal and praecordial pain, and was reported to have been in a half-dazed condition at times.

On admission to hospital he was in a dazed condition with an amnesia which varied in its scope from hour to hour. He was unable to remember anything about his parents, or that he was engaged. He refused absolutely to eat or drink, and when tube-fed vomited at once, so that it was necessary to resort to giving intravenous glucose. His pulse was frequently up to 120, and he had attacks of flushing and palpitation, often accompanied by bouts of weeping. He would give no satisfactory account of himself, and such information as he gave was often absurd, corresponding with a layman's idea of the talk of an insane person. At intervals he became angry and threatened or attempted to attack his attendants. At night he had terrifying dreams and would wake up sweating and trembling. At times he would walk in his sleep and fight with anyone who attempted to put him back in bed. He had no memory of these episodes afterwards.

By day his state of consciousness varied. From an apparent coma he would become over-alert, starting at the least sound, but would have no memory of how he came into hospital. At other times he would remember more but was evasive and would avoid answering questions by saying his head ached, or suddenly retching. Even in his semi-stuporose phases he was restless, and when he walked while awake he had a gross staggering hysterical gait. There were no abnormal physical signs in the nervous system, except that the cerebrospinal fluid pressure was a little raised.

During the next few weeks his symptoms continued to show almost hourly

variations. His amnesia became restricted and it was at times possible to begin to discuss his home affairs. These interviews would be interrupted by attacks of ill-rationalized irritability, for which he was afterwards profusely apologetic. He would ask for interviews with the doctor, as he had something important to tell, and when these were granted he would forget completely what to say, and have to cover his embarrassment by making a petty complaint or a request for leave. He was difficult and irritable with the other men, and was involved in a series of fights. He would eat ravenously for a short period and then refuse food until acetonuria appeared. After becoming more co-operative for a few days he developed acute abdominal pain and vomiting, and his pulse became more rapid. A normal appendix was removed.

After his convalescence he became co-operative again and was able to review his personal affairs. He admitted the need for a decision about his future. It also became apparent to him that the fact that he was in the Army prevented any return to his people. During his irritable phases he would take the part of any patient who had a grievance and say that he was being cruelly treated. When an epileptic was led away by male nurses in an attack of furor he said it was a scandal, and in every way imitated and took the part of this patient, so that they upset the discipline of the ward. Finally he himself had an hysterical fit while in church.

In this case, as the original non-realization symptoms of amnesia and coma became sufficiently restricted to allow the patient a partial insight into his difficulties, severe anxiety appeared, was then lost in fresh amnesia only to appear during somnambulisms. The patient's desire to draw the physician's attention to his case and his complete inability to remember why he was doing so seemed to him to be the cause of the anxiety and irritability which he found himself displaying. As time allowed of no solution of his problems, he took refuge in the invalidism afforded by hysterical fits. Before this final means of retreat became established he alternated rapidly between acute anxiety and flight into activity, anger, non-realization and functional incapacity.

There is no essential dissimilarity between the hysterical reactions of war and peace. The intensity and nature of the strains involved in the former, and the rapidity with which they may overcome the resistance of individuals who would reasonably be expected to be immune from neurosis in time of peace, accounts adequately for the differences in clinical form. By illustrating the effects of more or less standardized strains on a variety of human material, the neuroses of war have given an insight into the recent hysterical states which might not otherwise have been obtained.

Determination of Symptoms in Functional Incapacity.

When functional incapacity without superficial anxiety finally makes its appearance, a number of influences may be concerned in determining its actual form. Many symptoms are determined by some feature of the situation which precipitates them. Some serve a purpose at the time of their onset which becomes obsolete, but is perpetuated and serves as a convenient cause of incapacity.

A woman, aged 50, who had led a sheltered existence was faced with the necessity of earning her own living and invested her whole modest capital in a drapery

business. This was not a success, but after an initial period of sleeplessness and worry she became calm and slowly spent her capital and ran into debt. When faced with the selling up of her shop and home she appeared unworried and went about her business as usual. One evening she went back to her house and found that a new lock had been put on the door. She raised her arm to put the key in the lock and in a moment would have found that it did not fit. This would have meant a realization that her property had been sold and that she was ruined and homeless. Her hand shook and the shaking spread up her arm and developed into a generalized convulsion. After the fit she had no memory of the circumstances, and stated that she kept a drapery shop and was unaware of any difficulty except that she was a little short of money. After some days she developed an inkling of the true state of affairs, and had a second convulsion, followed by paralysis of the right arm. This responded to a discussion of her affairs, and she was sent to a convalescent home, where she was given much sympathy by the matron. On the day of leaving the home she had another convulsion, again followed by weakness in the arm. She finally recovered when a suitable home and employment were found for her.

In this case the weakness of the arm, the original purpose of which was to preserve the patient's unawareness of her difficulties, was perpetuated as a means of achieving incapacity when this was needed so that she could escape the obligation to adapt herself to her changed circumstances by going to work. This mechanism, by which a symptom which has originally appeared in response to a need for immediate retreat into non-realization or inaction is retained by the patient as a means of providing more lasting functional incapacity, is frequently seen. Thus a paraplegia, the primary purpose of which has been solely to provide temporary immobilization, is commonly retained as the presenting symptom in a chronic hysterical state. Often the original symptom becomes modified to adapt it to its new purpose, an hypersomnia developing into a ptosis, or an aphonia becoming a stammer.

Symptoms may be transmitted or acquired from another person. The patient may be preoccupied with the illness of some person of affective importance to him and may for this reason develop similar symptoms, or he may have in mind the successful evasion of a similar situation by someone with whom he has come into contact, and develop the same symptoms. This is occasionally seen, as in the soldier previously described, where an acutely anxious patient or one who is emerging from a state of non-realization acquires a symptom from a neighbouring patient.

A factor in the choice of symptomatology, which is seen more often in chronic rather than recent hysteria, is the presence in the patient of an organic predisposition to a certain form of disability. The epileptic in whom the pattern of the fit is established and who has had opportunity to realize the retreat afforded by it, frequently takes the hysterical fit as his incapacitating symptom. Since the pattern is already a well-practised one, it is at times impossible to distinguish in these patients between the endogenous and exogenous convulsions. Two of the writer's patients who showed hysterical convulsions of epileptiform type, but who had no previous history of fits, showed

subclinical seizure-waves when investigated with the electroencephalograph. This would indicate that the pattern chosen by the patient was determined by an organic predisposition, even when it had never become fully manifest as such. Another example of the same mechanism is seen in the not uncommon appearance of tetany or convulsions following hyperventilation in hysterical patients. These patients have the latent tendency to tetany which comes to light when the patient uses hyperventilation as an intermediate mechanism in precipitating it.

An art student who lived with her parents was, while at home, spoiled, dependent and emotionally infantile. At the art school, however, she took pains to give the impression that she was ultra-modern and without fear of adventures, sexual and otherwise. She there formed an acquaintanceship, in which she took great pride, with a young man of advanced views. Her behaviour at one of the noisy parties to which she went became demonstrative under the influence of alcohol and she gave the man the impression that she wished to have intercourse with him. When they were alone, however, she became acutely anxious, and the accompanying hyperventilation brought on an attack of tetany which allowed her to evade the immediate situation.

She did not at first wish to give up the young man because of this contretemps, and they remained friends. On a later occasion she again avoided intercourse in the same manner, and when later she wished to end the acquaintanceship she developed attacks of tetany when due to go out with him. He in turn became sorry for her and she did not wish to tell him to go away, and was unable to escape from him until her attacks became so frequent that she was admitted to hospital. While she was in hospital he tired of her and ceased to visit her, and the attacks gradually ceased. She was able to return to her studies in a different place where her previous life was unknown.

In the same way patients who are in the early stages of organic disorders of movement such as choreoathetosis or spasmodic torticollis will frequently show these symptom-patterns in hysterical illness.

A post-office clerk, aged 25, following a period of irritability, sleeplessness and depression, developed jerking movements of her head to the right. She had hoped to marry a man who came to see her at the post-office every day, but after a disagreement he had ceased to visit her. She hoped that he would renew their friendship by coming to see her again, and developed the habit of turning her head from the desk at which she sat, to see if he had come in. The turning of her head became at first habitual, and then involuntary.

On examination the pattern of the movement was that of a true spasmodic torticollis. After a discussion with the patient, she was hypnotized and the symptom disappeared. It has since returned, and its spread to other muscles leaves no doubt of its organic origin.

Sometimes the symptom symbolizes an attitude or an affect felt by the patient towards his difficulties.

A girl who was learning typewriting had been advised by her parents to break off relations with a man who had proposed to her. She dreaded the meeting at which she had to tell him that she would not see him again. After a trivial head injury she became stuporose, and then developed an immobilizing paralysis of one leg (the man had a septic foot at the time) and uncontrollable tapping movements of her fingers for which she could not account. When put to a typewriter, these movements repeatedly spelled out the words, " Yes, dear."

In the same way the affect attached to an incident which has been purposively forgotten may express itself symbolically in the symptoms. The most common example of this occurs where the incident gives rise to disgust expressed in spitting movements or in hysterical vomiting. It is also seen where anger is symbolized in a generally negativistic and truculent attitude.

In acute anxiety hysteria, which does not differ essentially from recent hysteria with functional incapacity, the symptoms appear as a perpetuation of the subjective elements of the anxiety state from which the patient is seeking to escape. It must be emphasized, as has been seen in some of the cases described, that the final symptom-complex may be the resultant of a large number of factors. When, in the course of therapeutic exploration, it is possible to trace the origin of its separate components, material is obtained which is of great value in the subsequent reconstruction of the patient's attitude to his circumstances.

Recent Hysterical States—Classification.

In planning treatment it is very important that the relative prominence of the three factors of *non-realization, anxiety and functional incapacity with pathological calm* be carefully assessed. When the first two are present, the patient is still in some contact with his difficulties, and is not prepared to accept a solution which will leave him inferior to his fellows. The appearance of pathological indifference indicates that this solution has been accepted. Such an adjustment has in common with the conditioned response the fact that the more frequently it is employed the more difficult it is to eradicate. It is therefore necessary to take the patient's previous history into account as well as the duration of his present illness. Non-realization, on the other hand, is of better prognostic import. When by removal of difficulties or by the passage of time the anxiety can be reduced to a point at which the patient can face his environment fully once more, he may always find himself able to adjust to it without the need for a protective incapacity.

For this reason a classification of recent hysterical states is here attempted from which the roles of the three elements can be evaluated for purposes of treatment.

I. *Immediate Reactions.*—Flight into activity or inactivity.

(*a*) Hyperkinetic :

Panic reactions in which relief from acute realization and anxiety is sought by intensive activity of an irrelevant kind. Realization is poor and anxiety thinly veiled. These states are transient and never permanent, and are followed by recovery or transition into other mechanisms. They include

screaming attacks, aimless wandering, violent undirected anger, repetitive movements, e.g. hand-wringing, hysterical fits.

These are exaggerations of corresponding non-pathological (i.e. socially permissible) protective mechanisms shown in moments of anxiety : Talkativeness, repetitive movements, i.e. drumming of fingers, feeling of resentment against cause of anxiety, tendency to overconcern with detail, tendency to excessive muscle tone with clenching movements, over-alertness.

(*b*) Hypokinetic :

Terror reactions in which relief is sought in denial of consciousness. Non-realization is practically complete ; anxiety may be evident : Fainting, stupor, pathological lethargy, complete loss of motor initiative, hysterical coma, hypersomnia, cataleptoid states (Mira, 1939).

These forms are exaggerations of non-pathological subjective states which prevent the individual from feeling fully in contact with the situation or fully able to act in regard to it : Feelings of mild depersonalization or derealization, feeling of lethargy and tendency to yawn, described in normals under war conditions (MacCurdy, 1918), feeling of lack of interest and motor initiative.

II. *Hysterical Transition States.*

States in which a relative freedom from anxiety is secured by means of symptoms which either prevent the patient from fully realizing his difficulties or relieve him from the obligation to act in regard to them. These mechanisms offer no permanent solution, as their continuance would be incompatible with community life for any length of time, even in the protected position of an invalid. They serve to tide over the period during which anxiety would be beyond the individual's endurance, either until it subsides or until a more permanent solution is found in the flight into incapacity.

The refuge afforded by these mechanisms is very temporary, and they rarely endure for more than a few months at the most, and may last but a few hours. It is characteristic of them that they tend to recover and relapse frequently and to alternate with other hysterical states. In these transition states there is much variation in the degree to which anxiety is successfully avoided. Cases may vary from severe anxiety states in which transient clouding of consciousness or physical disabilities appear, to cases in which gross pathological calm and well-established " conversion " symptoms appear. In order to understand any given case an evaluation must be made of the three variables of anxiety, non-realization and pathological indifference.

Cases tend to group themselves about two poles, which allows of a classification of this group which is of value from the point of view of prognosis.

(*a*) Mechanisms of non-realization, in which a relative freedom from anxiety is attained at the expense of full realization of the situation. Signs

of anxiety are often ill-concealed, and tremor, flushing and tachycardia may be seen, even though the patient professes complete unconcern. Psychically the anxiety may show itself in nightmares and somnambulisms: Twilight states, fugues, total amnesia, selective amnesia.

(*b*) Mechanisms of avoidance or immobilization, in which the symptoms relieve the patient of the necessity to decide or to act. Here functional incapacity is the principal means of adjustment, but the symptoms in this group are not ones often used as a permanent adjustment, i.e. they are rarely seen in chronic hysteria: Aphonia, astasia, pseudopsychosis.

(*c*) Symptom-groups which are intermediate between (*a*) and (*b*), and in which non-realization and functional incapacity both play a part. No transition state depends on one mechanism alone, but in groups (*a*) and (*b*) there is a preponderance of one or other, e.g. Ganser states, acute regression, amblyopia.

III. *Recent Hysteria with Functional Incapacity.*

In this state, which may develop primarily or may follow acute or transitional reactions, functional incapacity is used as a means of retreat. It is to be distinguished from chronic hysteria by the fact that the end attained by the symptoms is temporary retreat as opposed to permanent adjustment. There is less tendency in recent hysteria with functional incapacity to the personality changes which take place in the course of chronic hysteria. To some extent also the symptoms observed are different in the two groups. Aphonia, for instance, is not often seen in chronic hysteria, while dermatitis artefacta and contractures are rarely seen in recent hysterical states. In recent states the anxiety component is also much more readily detected and mobilized, in contrast to the satisfied indifference of the hysteric of long standing.

Acute functional incapacity is likely to occur where there is some special reason why the syndrome selected should protect the individual from the situation he dreads. In recent hysteria functional incapacity is usually resorted to as an escape from a situation rather than from the anxiety due to indecision or conflict. Since the symptoms are thus directly purposive, those which cause immobilization or an excuse for not dealing with the problem, i.e. paraplegias or aphonias, are the most common. Cases of this group are especially common in military practice, where they afford the soldier an honourable means of avoiding danger. As has been observed, the actual form of the symptoms may be determined by the needs of the situation itself, or by the existence of some organic predisposition in the patient to a particular disability.

While this group differs from chronic hysteria only in the manner and degree in which functional incapacity is accepted as a solution, it is of advantage to separate it from the point of view of prognosis and treatment.

Importance of Organic Factors.

In any case where the normal adaptation to a situation has failed, the breakdown is the result of the stresses bearing upon the patient being able to overcome his powers of resistance. Organic disease, though not often the principal factor in determining mechanisms of retreat, may frequently serve as an additional strain which makes the difference between adaptation and illness. Constitutional defects of organic origin are frequently the most important cause of the patient's vulnerability to hysterical mechanisms. The fact that the grosser varieties of hysteria, at least, are far commoner in persons of poor intellectual endowment makes this form of organic deficiency of especial importance. Apart from inborn weaknesses, however, temporary debilitating conditions may cause an individual to retreat from a situation which he would face with ease when in good health. Of these, exhaustion, whether due to fatigue or to prolonged anxiety and lack of sleep, is by far the most important. In patients already strained by anxiety due to prolonged indecision or conflict a minor infection such as influenza or tonsillitis is frequently the precipitating factor of an hysterical illness.

There is good reason for supposing that certain diseases of the central nervous system predispose the individual to make use of hysterical mechanisms. The frequency of hysterical disabilities as complications of chronic encephalitis lethargica and of disseminated sclerosis has long been known. Chorea, general paralysis, and the late effects of some head injuries not infrequently commence with the release of hysterical mechanisms which may attract the physician's whole attention, so that the organic background for a time goes unnoticed. The case of epilepsy is a special one. During the periods of irregular cortical activity which may precede or replace the fit, amnesias, fugues and disorders of behaviour may appear which so resemble those of hysteria as frequently to be indistinguishable. It is clear that such symptoms are produced by a combination of factors, and that in epilepsy the organic component is the predominant one.

Not only can organic disease *per se* predispose to hysteria, but the sense of disability engendered by it acts as a psychogenic factor in weakening the patient's resistance. The functional psychoses frequently act in this way. Retreat from the sense of inadequacy, of guilt, or of the intolerableness of existence in depressive illnesses into a mechanism of non-realization accounts in part for the frequency of amnesias and states of clouded consciousness at the onset of depressive states.

A middle-aged labourer was found wandering by the police and unable to give any account of himself. There were a number of small cuts in his neck. During hypnosis his memory returned and he gave a history of a depressive illness some years before. He had recently become depressed and lost his employment, had no relatives from whom to seek help, and had contemplated suicide. He bought

a razor-blade with which to cut his throat and went to a pond, into which he hoped to be able to throw himself. He scratched his neck, stepped into the shallow water, and then wandered away and was found by the police. His illness thereafter took the normal course of a recurrent depression.

A cyclothymic element is always to be suspected when suicidal tendencies are shown during a fugue, or where a severe hysterical illness suddenly appears or clears up suddenly without apparent reason.

A girl, aged 19, who had a good record of work and was known as an active, cheerful person and was engaged to be married, became irritable and seclusive, wept a great deal, refused food, and finally developed an hysterical paraplegia. There were many unsatisfactory features in her home environment, but no real reason could be found for her sudden failure to adjust to circumstances which had previously caused no distress. There seemed no reason for her change of attitude to her fiancé, except that she said she did not feel worthy of him. She was co-operative except when attempts were made to make her eat, do occupational therapy, or to remove her symptoms, all of which were defeated by the appearance of invalidizing symptoms. The true diagnosis was not evident for several months, when the fact that she slept poorly, wept most in the mornings and became much more cheerful and co-operative under the influence of benzedrine suggested the presence of an endogenous depression. Fifteen months after the onset of the illness her symptoms abruptly cleared up and she took up her former activities again. Her hysterical symptoms had evidently been used to rationalize the effects of a depression which had made her wish to avoid marriage and retire into a state of inactivity.

As well as contributing to the onset of functional incapacity, organic disease has an important effect in determining its form. If the situation which the individual wishes to evade or about which he is in conflict does not demand a special symptom as a means of escape, he will be apt, in choosing the form of his incapacity, to fall back on organic patterns which already exist within him. In the same way the expression of suicidal ideas in the course of a transition state may not be determined solely by the desire for attention, but may represent the purposive revival of affects experienced in an attack of depression.

A special case in which organic disease may determine the form of functional disorder is seen in the post-concussion states in which amnesia due to the injury is perpetuated as hysterical amnesia, and the two conditions may be closely intermingled. A complete differentiation between some post-concussion states and hysterical transition states, for this reason, is frequently not possible, and MacCurdy (1918), in discussing diagnosis, observes how one may emerge imperceptibly from the other.

In any hysterical state there are always organic factors, if only those of constitutional predisposition or of exhaustion. In many conditions, such as anorexia nervosa or spasmodic torticollis, it is impossible to decide which is the predominant cause. It is fortunately unnecessary to decide this accurately for purposes of treatment, as both factors must always be taken fully into consideration.

Examination and Diagnosis.

Diagnosis of the general nature of a recent hysterical state does not usually present great obstacles. The difficulty arises not so much in differentiation from wholly organic conditions, as in the detection of important organic factors when these are present as a background to the hysterical state. A company promoter realized at a meeting that a speculation was about to be a serious failure and that this would inevitably lead to his prosecution. On walking into the street he completely lost his memory. On admission to an observation ward as "Mr. X," he had well-marked signs of general paralysis. There is no doubt that his was a case of recent hysteria, but such a diagnosis would have been glaringly incomplete. His recovery of memory under hypnosis following successful malarial therapy is an indication of the dual outlook necessary in such cases.

The organic background is rarely so obvious. In reviewing the histories of cases of chronic encephalitis lethargica, Huntington's chorea, and other degenerative states which reveal themselves slowly, the frequency with which functional conditions are diagnosed before the organic condition is manifest is very striking. For this reason it is never justifiable to label a case as "psychogenic" and treat it psychotherapeutically without allowing for the need of revising the diagnosis. One must beware especially when there is a very obvious psychological cause for the disturbance. Too often the broken engagement which appears to have precipitated the symptoms has been at the instance of the patient, whose attitude has changed as the result of the onset of a major psychosis.

For purposes of immediate treatment it is not always necessary to know fully the psychogenic determination of a functional illness. It is in fact unwise to pay too much attention to the more obvious motivation, as deeper causes are very likely to be revealed as the patient develops insight. It is, however, important to assess the relative importance of the factors of physical exhaustion, anxiety and non-realization. It is necessary to estimate the patient's powers of recuperation by reference to his previous personality and reactions to stress, and the degree to which he is willing to accept invalidism as a solution of his difficulties. Some estimate of general intelligence must also be made, and this is often very difficult in transitional states, where comparatively intelligent patients are unwilling to use their mental powers, and behave in the same manner as the feeble-minded, in whom the same conditions are more commonly found. In examining a case of hysteria a diagnosis is not enough. It is necessary to gain a preliminary impression of the individual's total personality in relation to his problems.

Treatment.

The eventual aim in treatment of psychoneurosis is to allow the patient to develop insight into the origin of his condition and to readjust himself in the light of that insight. If this object is attained, the presenting symptoms may lose their purpose and disappear.

While in recent hysteria this general principle must still hold, the introduction of a time factor necessitates modification of the procedure. In the group of acute reactions, very minor therapeutic assistance will often allow of recovery, and it is essential to make the most use of this favourable period and to prevent further retreat. In the same way, as fuller realization develops from a transitional state, it is most important that functional incapacity be prevented or reduced to a minimum, lest the habit of invalidism be established. It is this time factor which makes the removal of symptoms a matter of urgency, and allows at this stage of the legitimate use of the shorter therapeutic methods.

Panic Reactions.

These are not often seen by the physician, though similar states with a large demonstrative element are seen often enough in the course of chronic hysteria. It is perhaps as well that the physician is not at hand, as these states are often satisfactorily aborted by more robust methods than he would care to use. The hysterical screaming attack or fit is perhaps the only occasion in psychiatric practice where cold water and an exhortation to "pull yourself together" is ever legitimate, and if the attack is not part of a chronic hysteria it will sometimes bring about permanent recovery with full insight. In wartime it is well known that a tendency to panic is best controlled by a good example from seniors, and the certain knowledge that return to the base is quite out of the question.

In preventing panic reactions it is important that in difficult situations the individual should be in no doubt as to what to do, and, if possible, should have something to do. Uncertainty as to the immediate future and opportunity to dwell on unpleasant possibilities, if continued for long, are the principal factors in lowering resistance to hysteria. When non-pathological reactions, such as talkativeness, redundant activity, resentment and tension are increasing, they may be relieved if an opportunity is provided to make use of them in shouting, running and hatred, and it is perhaps for this reason that in war preliminary "jitters" is far from incompatible with courage.

When wandering and repetitive movements occur, it is important that those present should give no sign of being impressed, but at the same time their attitude should be a kindly and patient one. Where the reaction is the result of the patient's seeing an unpleasant sight or receiving unpleasant news, the condition will usually clear up rapidly if nothing is done, but where the

recovery means realization of, or return to, a situation beyond the patient's powers of endurance, it may be necessary to shield him temporarily from his difficulties.

Terror Reactions and Hysterical Transition States.

In their more severe form these states are seen in both military and civil practice, and invariably conceal severe fear or anxiety. They occur usually after severe physical exhaustion or after long periods of anxiety, and are especially found where the individual's future has a certain inevitability. In the writer's experience they have occurred in jilted brides, an absconding slate club secretary, unsuccessful speculators, a mother whose child had been suddenly killed, bridegrooms about to be taken unwillingly to the altar, and even children who could not face an unkindly teacher. In military practice they occur most frequently as a superstructure in men who have been blown up or buried by explosions.

Since such cases are brought for treatment when they have already evaded the situation they dread, the opportunity of returning them to the front line, the altar, or the schoolroom, even if it were advisable, has passed. The object of treatment is now to get the patient to come out of hiding, so to speak, by letting him know that the danger is past. It is first necessary, therefore, to remove him as far from the difficult situation as will assure him that there is no need to face it again. If the symptoms then do not disappear spontaneously, they must be removed by psychotherapeutic means. When this is done the whole situation must be discussed with the patient until he develops insight into the causes of his illness and can form for himself a plan of action for the future. Treatment can therefore be divided into three phases :

(1) Phase of rest and reassurance.
(2) Removal of symptoms.
(3) Therapeutic exploration and re-education.

Rest and Reassurance.

If it were possible to remove all cases of recent hysteria permanently from the situations which had precipitated their symptoms, there is no doubt that practically all would recover rapidly. It is obviously unwise, however, to make this the object of treatment, not only because it is unattainable, but because if the patient is to remain a useful member of the community, he must remain capable of facing without retreat the situations which the average citizen is expected to face. The object of temporarily protecting and reassuring the patient is not to give him permanent shelter, but merely to assure that he is in the best possible condition to face his anxieties when his symptoms are removed. It is essential that this period of recuperation should be accomplished as rapidly as possible, lest the patient be tempted to take permanent

shelter by means of functional incapacity. The longer the mechanism of retreat has been in operation, the more difficult it will be to replace by a normal attitude.

In transition states there is usually an element of exhaustion. This may be due to the strain of prolonged anxiety due to indecision or conflict, or, in time of war, to long periods of exposure to danger and fatigue. There is often, in addition, the effect of exposure and exhaustion due to wandering while in an amnesic state. For this reason rest in hospital, adequate nutrition and sleep must be provided before any attempt is made to remove symptoms. Patients after prolonged fugues are frequently exhausted and acidotic and may at first vomit food. They may also in their confused state, and as part of their wish to deny their whole existence, actively resist feeding. In these circumstances there should be no hesitation in tube-feeding or in giving intravenous glucose.

It is often wise at this stage, in cases in which anxiety is prominent, and shows itself in continued nightmares, somnambulisms and anxiety attacks, to encourage an increase of non-realization by the temporary use of drugs. Hyoscine is invaluable in such states, especially when combined with phenobarbitone, or with sodium amytal. It is important for these short periods of narcosis to avoid sedatives which are slowly excreted, as the patients must be clear and alert when psychological treatment commences. It is important to remember that many hysterical twilight and similar states are really acute anxiety states in which a certain amount of protective non-realization has occurred, and that their treatment will in every way be that of an anxiety state. Such cases will benefit often (Mira, 1939) from prolonged narcosis.

Removal of Symptoms.

The object of this stage of treatment is to demonstrate to the patient that his symptoms are unnecessary. When rest and an opportunity to view his difficulties in a more objective manner from an hospital bed without the need to decide or to act at once have improved his resistance, the patient may spontaneously develop a measure of insight. If he is reassured by an understanding physician that he will be protected from the accusation of cowardice or malingering, this insight may become complete and result in recovery. More frequently he develops some insight into his difficulties and shows a great improvement, but retains some part of his symptoms as a demonstration to himself and to the world that the whole affair has not been his fault. Such symptoms may remain for a long time but clear up readily if some forceful and impressive method of treatment is given, which will at once convince the patient of its efficacy and give him an excuse to get well. Such cases are usually very anxious for hypnotic treatment and respond more favourably to it than any others.

A woman, aged 28, who was making a fairly successful career decided after much hesitation to get married, and re-orientated her life accordingly. Her fiancé, however, ran away with another woman on the eve of the wedding, and the patient developed a complete loss of memory, astasia and aphonia. In the course of some months the aphonia was modified into a severe stammer and the astasia into an hysterical gait. After a year's invalidism she again became interested in her work, and was prevented only by her symptoms from obtaining good employment. At this point she was offered treatment by hypnosis, and permanent relief of symptoms occurred after a single session.

At the commencement, especially with the more intelligent patient, it is advisable to make an attempt to review with him the circumstances of his admission to hospital and to explore the possibility of his grasping the nature of the illness. Treatment by persuasion from the commencement is always preferable to suggestion, and where it seems likely to succeed the patient should be seen frequently and allowed to discuss his condition with the physician until he develops insight with as little interpretative interference as possible. If, on the other hand, the patient clings to his symptoms and allows them to prevent his full co-operation, care should be taken to prepare the way for later treatment by suggestion by giving the impression that cure is inevitable and can be accomplished more or less when the physician wishes.

The principal reason for the more frequent use of suggestion rather than persuasion in the transitional states is that the element of non-realization in the symptoms serves as a screen between patient and therapist, just as it does between the patient and his conflict. It is impossible to discuss the situation with a patient who has a complete amnesia or aphonia, and for this reason the symptoms must be removed first. Their removal will then assist in persuading the patient of their true nature.

While in treating objective functional incapacity the actual method of suggestion used is immaterial, provided that it demonstrates that the incapacity can be removed, in transition states the subjective nature of the symptoms and the presence of amnesia and non-realization often makes hypnosis the only applicable method. It has the special advantage that material discussed with the patient under hypnosis can form the basis of the re-educative treatment which follows the removal of symptoms. This is illustrated by the following case :

A man, aged 38, a labourer riding a bicycle, reported to a police station, having forgotten who he was and where he came from. He was dirty and exhausted and could not be identified. After two days in hospital he was referred for treatment. His vocabulary was full and he was normally orientated. On the first occasion, while pretending to co-operate, he would not fix his attention on the object used and no progress was made. On the second occasion, after similar difficulties, he suddenly became co-operative and almost at once became deeply hypnotized. On being asked where he was going on the bicycle, he said, " To work." He was then told that he was riding his bicycle to work and asked to give an account of his thoughts as he rode. After naming some of the turnings he passed on his way be began to become acutely anxious, evidently dreading going down a particular turning, and on coming to it he rode past it and straight on for 30 miles to a seaside

town, where he slept out. On the following day, after riding on aimlessly, he realized he had lost his memory. He then described how, when at work on the previous day, he had to dig at the bottom of a deep trench. On seeing some earth falling in from the top of the trench, he was reminded of a similar trench in which he had been buried by an explosion in the 1914–1918 war, and became acutely anxious. He had dreamed of the trench all night, and dreaded returning to work. In the previous incident, after being buried by the explosion, he had lost his memory for several days. While recounting these facts the patient spontaneously woke up and continued his story, until he suddenly realized what had happened.

In this case hypnosis removed a symptom which prevented discussion of the man's anxieties and allowed of a fuller investigation of the case. It will be noted that this patient was by no means co-operative with hypnosis. Many patients in intermediate state, while expressing willingness to co-operate, do not do so, and in fact avoid anything that will bring them in contact with their problems. When this occurs it may be taken to indicate either that the anxiety underlying the hysterical symptoms is too great to be faced, or that the patient is using his symptoms still further to invalidize himself. In the first case further rest and security are indicated before further attempts are made to remove symptoms, while in the latter suggestion must be continued.

While the anxiety component of a transition state is prominent, as is indicated by sudden increases in amnesia, violent nightmares, bouts of aggressiveness, or actual anxiety symptoms, there is little danger that the patient will take refuge in functional incapacity and he can safely be left. Many such cases gradually become clearer in time, and allow of a thorough discussion of their difficulties without the need to use suggestion at all. As is the case with true anxiety states, it is not here possible to abbreviate the treatment.

Therapeutic Exploration and Re-Education.

The treatment of a recent hysterical state does not end with the removal of the presenting symptoms. At the onset of treatment the patient is usually not prepared to accept the idea that his symptoms are not due to physical accident, and will protest against the suggestion that they may be psychogenically purposive. Their removal by suggestion may go far to convince him that they admit of a non-organic interpretation, but it is most important to utilize the opportune moment after their removal to assist the patient in gaining as full an insight as possible. If he is to return to a normal life and avoid further retreats, he must be guided in understanding for himself the mode of development of his illness.

Where the protective symptom has served its purpose and allowed of escape from the threatening situation, and this threat is an obvious one, as is seen in war neuroses, insight is often spontaneous after the symptoms have disappeared. Nevertheless, the physician has not completed his work until he has assured himself that insight has been attained. He must not be

content merely to remove the grosser mechanisms of non-realization, but must ensure that the patient sees his own position clearly and that he spares himself none of its realism. He must mobilize the patient's anxieties in retrospect and explore the thought trends which preceded his retreat. In this way the patient will learn to recognize in himself the tendency to retreat and will be able, while still under medical protection, to regard his difficulties from a safe vantage-point and decide his future actions in a more deliberate manner. If this is not done the process of retreat will be facilitated rather than guarded against, and may recur when he again faces a similar situation and again is unable to decide how to deal with it.

In guarding against recurrence the patient should either be prevented from having to face again the anxieties from which he has retreated, or he should return to his difficulties with a decided plan of action.

While he is being allowed to review aloud his problems in relation to his powers of response to them, the opportunity should be taken of estimating his potentialities and judging his probable attitude to the problems he is likely to have to face in the future. This aspect of the exploration will be considered under "Prognosis."

Treatment of Acute Functional Incapacity.

When an hysterical symptom has appeared it is often difficult at first to discover its true purpose. Whether the patient is a previously normal individual who has sought temporary refuge in disability under extreme strain, or whether the appearance of symptoms represents a stage in the development of chronic hysterical invalidism, the superficial clinical appearance may be much the same. Although the fuller aetiology will gradually become clearer as therapeutic exploration progresses, it is necessary to decide early certain general questions in order to determine the lines on which exploration will be carried out. It must be determined if possible whether the symptoms represent a temporary retreat or adjustment to stress, or are part of a gradual alteration in the patient's mode of adaptation.

Before proceeding to the removal of symptoms, it has to be decided whether it is justifiable in the patient's interests to disturb the existing state of affairs. It may be possible by means of suggestion to induce a patient to relinquish a symptom which is acting as a comparatively harmless means of adjustment to a difficult life. To do so may be to upset this adjustment and to precipitate unnecessarily a state of anxiety. Among those who suffer from chronic physical disabilities which make it impossible for them to compete on an equality with healthy people, it is common for functional superstructures to be developed which serve the purpose of pointing out to others a disability which otherwise might not be noticed and allowed for. When recovery from the physical state is unlikely, it is unwise to disturb such an adjustment. In the same way

individuals who are constitutionally inferior in intellect or personality may avoid full realization of their handicap by assuming symptoms which allow of an apparently normal adaptation without inconvenience to anyone. The man of sluggish mentality who covers his slowness in comprehension by pretending to be hard of hearing is employing such a mechanism, and often little advantage is to be gained by insisting on his admitting that he can hear normally.

In hysteria the disorder lies in maladaptation and not in the symptoms themselves. Unless, therefore, the underlying condition is given full consideration, the removal of one set of symptoms will only be followed by some other form of pathological adaptation.

In some cases of hysteria the maladaptation does not appear to arise as the result of environmental stress, but occurs as a primary and progressive lack of urge to continue as a normal individual (progressive or degenerative hysteria), and in such cases, as has been observed, symptoms develop after trivial stress or apparently from sheer ennui or desire for attention, the latter being a part of the characteristic personality change in the direction of a child-like dependence, which may be detected long before overt symptoms appear. In this type, if the process has not advanced beyond hope of readjustment to normality, the symptoms can only be removed as part of an attempt to get the patient to reorganize his whole life. Where there is no constitutional or organic inferiority which will render the end-result unworthy of the means, psychoanalysis may here be the only practicable mode of treatment. Often the most that can be done is to make use of the suggestibility shown by such patients to clear up superficial symptoms.

As has already been indicated in the case of mechanisms of non-realization, it is often advisable first to attack the symptoms of functional incapacity by means of suggestion, and the underlying maladjustment afterwards. This is especially so where the symptom itself (e.g. paraplegia) has outlived its usefulness and is now merely retarding the patient's return to normal pursuits. It is similarly necessary where the symptom (e.g. defect of speech) impedes the physician's access to the patient's mental content. Even where more thorough therapeutic methods are employed, suggestion may be needed for the final removal of symptoms, although their continued existence may seem quite unreasonable to the patient. In these cases the principal symptoms seem to be retained by the patient on account of a sort of spurious pride which prevents him from admitting demonstrably what he has already admitted in principle, i.e. the purely functional origin of his disability.

While the use of suggestion should be restricted in favour of persuasion in fully co-operative patients, it may be used more freely and often with greater success on those who are incapable of gaining full insight, even in the most favourable circumstances for treatment. Treatment by suggestion alone is often very successful in persons of low native intelligence. It is

especially effective in treating hysterical symptoms which appear as superstructures on chronic disease of the central nervous system. Where hysterical personality deterioration has reached a point where non-dependent existence is out of the question and insight unattainable, modification of the symptoms is often easily obtained by utilizing the suggestibility which is one of the outstanding features of the advanced hysterical character.

If it has been decided that removal of symptoms is to be carried out, it is unwise to resort to methods of suggestion until the patient has been given some incentive to respond to them. If recovery from a protective symptom will at once lead to the patient's return to the situation he is avoiding, he is unlikely to be very responsive. The patient may be urged into recovery either *a fronte* or *a tergo*. On the one hand the necessity for the symptom may be removed and its psychogenesis made obsolete. This is often done by affording the patient the refuge from the harassing situation afforded by admission to hospital or, in military cases, by removal from the line. On the other hand, the immediate advantages of being well and the disadvantages of remaining disabled must be brought home to the patient. It is here possible to take advantage of the tendency in the more infantile hysterics to alter their symptomatology for immediate ends, and in some cases partial recovery will occur merely to gain for the patient some minor privilege from which his symptoms debar him. No opportunity should be lost of letting the patient know what a nuisance his disability is to him. In intelligent patients who have developed some understanding of the causation of their illness in the course of the preliminary exploration, the incentive to recovery has to be created by developing an urge to attack their problems in the new light in which they appear after discussion. In such cases the symptoms will come to be regarded as an impediment to this urge, and the patient will eventually be only too glad of the excuse offered by suggestion to relinquish them.

When the use of suggestion is finally decided upon, the attitude of the physician towards his patient must undergo a radical change. He is no longer the patient's friend and confidant who is prepared patiently to encourage his understanding of himself; he must now become firm to the point of hardness and must convey to him with confidence that his cure is inevitable. He must be prepared to practise a deception on his patient in his interests, and must carry this out in spite of any pleas for a more kindly approach. The difference in attitude is so great that a physician who has revealed to the patient that he is as human as he is may be unable to take his new role in a convincing manner, and will have to send his patient to a therapist who specializes in suggestive treatment. If, however, he can carry out this part of the treatment himself and successfully, his rapport with the patient in the later work of reconstruction will be enormously enhanced.

With these principles in view, the patient who is to have his symptoms removed by suggestion should have his liberty restricted by isolation in bed

and should be allowed to associate, if possible, with patients who have lost their symptoms in a dramatic manner. He must be allowed to observe the privileges and social life in hospital enjoyed by those who have responded to treatment. The attitude of his attendants must be such as to convey to him in a casual manner that now that he has been selected for treatment by suggestion his recovery is inevitable as soon as the physician cares to carry it out. The latter should see his patient seldom and briefly; and his manner should be distant and impressive. Even the most intelligent patients can be made to feel that the powers of "the psychologist" or "the hypnotist" are a little more than human, and however unpleasant this attitude may be to the physician, the testimony of recovered patients bears out its success in inspiring confidence.

As soon as it is felt that suggestion is likely to succeed, an appointment is made and the patient is allowed to dwell on his treatment as the hour approaches. In the writer's experience the interested co-operation of a nursing staff who understand the principles of the method contributes enormously to its success.

In most cases it is advisable to use a method of suggestion which has rapid effects. Some classification of the methods within the writer's experience is here attempted. Some methods employ more than one of the principles described.

(1) Simple demonstration.
(2) Re-education.
(3) Conditioning out.
(4) Suggestion with vehicle.
(5) Dissociative suggestion.

(1 and 2) *Simple demonstration and re-education.*—This is the method of choice where the patient is unable to carry out some normal function, e.g. walking or sleeping. It consists first of demonstrating that the affected function is present and then of re-educating it until it approaches normality. For instance, if a patient who is unable to make sounds is asked to breathe deeply and a fairly strong faradic current is applied suddenly to the neck, a cry of surprise will usually result. This has the effect of demonstrating to the patient that his voice is still present, and he can usually be encouraged with further faradic applications to produce simple vowel sounds and gradually re-educated in normal speech. In the same way the patient who cannot use his legs may be put into a swimming bath where, in the urge to self-preservation, his paraplegia will be forgotten. His kicking movements can then be re-educated into walking at first in the water, and then on terra firma. Similarly the deaf patient can be made to look into a mirror while a pistol is let off behind him. His sudden start will demonstrate that he can hear, and he can then be made to hear sounds of gradually decreasing intensity. It is more pleasant to remove a symptom by re-education alone, and this is often possible when the patient has been partially convinced of its lack of physical reality

by a process of persuasion ; but the demonstration is frequently indispensable, and must not be evaded if necessary.

(3) *Conditioning out.*—The methods in this group include the more barbaric treatments of hysteria, and it is fortunate that they are becoming less popular, in this country at least. The principle of the treatment is to ensure that any manifestation of the hysteria is followed by an unpleasant stimulus, and that recovery is rewarded by relief from it. Thus paraplegias are driven to walk in order to escape the application of faradic brushes, and cases of hysterical vomiting are tube-fed after each occasion. The same principle is employed very unsuccessfully in the giving of unpleasant medicine to cases of chronic hysteria. The disadvantage of this type of treatment lies in the poor rapport which is obtained afterwards, the patient usually recovering temporarily and relapsing where he is out of reach of the physician. Nevertheless, the principle has some value when used in conjunction with other methods, and its use has already been referred to in the restriction of privileges of patients awaiting removal of symptoms. It is often useful, for instance, when an hysterical aphonia is proving difficult to re-educate after the first sounds have appeared, to apply fairly painful faradism to the throat at regular intervals. The patient will then not waste time, as to do so would prolong the application of the painful faradic stimulus. It is important, when removal of symptoms has been obtained by such coercive methods, to make the patient demonstrate his recovery in front of others, even if he asks for it to be kept a secret so that he does not look foolish. If this is not done he may relapse at once and deny any recollection of temporary recovery.

(4) *Suggestion with vehicle.*—This type of suggestion is indicated where the symptoms are subjective and their removal is not susceptible of objective demonstration. The principle consists of making the patient take a medicine, submit to a diet, make a pilgrimage or carry out some other procedure, and at the same time making him believe that it will result in cure. In its simplest form it consists of giving harmless drugs, together with strong suggestions as to their effects. It is often possible to use treatment in which the patient already has some belief, and whether the suggestion is applied in the name of Christian Science, Raja Yoga, autosuggestion, osteopathy, colonic lavage or will-power, the result may be excellent. The weakness of the whole method lies in the fact that when the symptoms have gone the patient still believes in their physical origin, and recovery cannot act as a demonstration of their true nature. The subsequent discussion may take the form of an effort by the patient to convert the physician to the successful medicinal cult.

(5) *Dissociative suggestion.*—The use of hypnosis has already been advocated in removing non-realization symptoms. As the most direct form of suggestion it is applicable to most types of incapacity provided that the patient is willing to co-operate or can be convinced that he cannot help doing so. It has the advantage that after the symptoms are gone the patient may be made to

relive affectively important incidents under hypnosis, and to discuss material which would be acutely embarrassing in a normal state of consciousness. It has the disadvantage that the patient may use the hypnotic state as a retreat, and may either become dependent on it or become prone spontaneously to other dissociated states, e.g. fugues. The technique will not be discussed here.

It has already been emphasized that no case of hysteria has been adequately treated if, in addition to removal of the presenting symptoms, the patient is not assisted to gain some insight into the mode of their causation. Unless purely symptomatic treatment is aimed at, the process of therapeutic exploration must be continued until this has been done. Very frequently, as the aetiology of the illness becomes clearer to the patient, the need of making some important decision as to future conduct becomes evident to him. Realization of the need to decide may cause the patient to retreat from the decision by a temporary relapse. Often he will try to place the onus of decision on the physician. If he is to become independent the patient must make his own decisions, and the appearance of a decided attitude to future problems is a sign that he is becoming fit to take a normal place in the community. It is only when the patient is to be regarded as constitutionally inferior and in need of permanent assistance that it is justifiable to give direct advice.

The difficulties encountered in urging a patient to decide for the future are illustrated, with other therapeutic points, in the following case:

A nurse, aged 30, of superior intelligence (I.Q. 140), good education and attractive appearance, had been listless and unhappy for four months. Following an attack of influenza she suddenly developed uncontrollable choreiform movements, worse on the right side of her body, together with a slurring dysarthria and a tendency to weep on slight provocation. At the same time an intermittent diarrhoea, which had appeared at the onset of her illness, now became much more severe.

She was an only child of rather severe Scottish parents, and apart from extreme fussiness over food, which at times had her family in despair, she was a model child, and was universally admired for her saintly behaviour and her prowess at school and especially at Sunday school. In adolescence, when her mother died, she became greatly attached to her father, kept house for him and restricted her contacts to relatives and to friends met at the church. While not without a romantic belief in love, she had a severe attitude in moral issues.

Her first acquaintance with sex matters was made during a friendship with a boy she met at church. While the sex-play which resulted aroused in her feelings of guilt, the possibility of other modes of life than that she was living was opened up to her, and she felt she would like to marry if it were not disloyal to her father. In the course of the affair the young man developed disseminated sclerosis and had gross intention tremor, a left hemiplegia and dysarthria. When eventually personality changes occurred in him she returned to her father and once more had no thought but to devote herself to him.

Five years before the onset of her illness she again fell in love, and was in doubt whether or not to accept the young man and leave her father. She decided to remain with her father, but a year later, after a painful illness, he died of carcinoma of the rectum. Throughout this illness, in which he had severe diarrhoea, she devoted herself to him, and at his death she was exhausted and depressed.

After an interval, however, her attitude changed, and she ceased to be religious,

went out to parties, and again became friends with the young man who had proposed to her. By this time he had developed severe rheumatic heart disease, and during their renewed acquaintance commenced auricular fibrillation and was given a hopeless prognosis. She again became depressed and anxious, but after an interval decided to get away from her old surroundings and take up nursing in London. She worked hard and her career was regarded as a promising one. While in London she developed a very profound friendship for another nurse and with her became converted to the Catholic faith. After some months, however, she met some friends, including a man, from her home town, and began to wish she could return. She became anxious, slept poorly and frequently suffered from diarrhoea. While in this state she was nursing a case of chorea in a young man resembling her first love. At this time she was obliged to go off duty on account of an attack of influenza, and on recovering she developed the symptoms described.

On admission to hospital she was dysarthric, tearful, sullen and unco-operative, and at first said she could not remember her relatives' address. On examination she had choreiform movements which were worse on the right, had a slurring dysarthria which became an anarthria when questions were asked about her illness, a gross intention tremor of the hands, and sudden urgency of defaecation. At first all attempts to discover the aetiology of her symptoms were defeated by her attitude. Direct questioning resulted in aphonia, and when driven into a corner she would have an urgent desire to defaecate.

She was isolated in a single room, and after a thorough physical examination was given a sedative and allowed to sleep. On the following day she became more co-operative and entered into a discussion about her symptoms, resenting hotly the suggestion that there was a functional element and showing in her rationalizations considerable intelligence and medical knowledge. After two weeks most of the facts already described had been elicited and checked by reference to relatives and friends. There was still, however, no insight, and she declared that her sole anxiety was as to whether she would be able to continue her nursing career. She said she had never worried over decisions and had never felt any strong interest in sex. In view of her good intelligence and the fact that she had apparently not retreated until she had experienced a great deal of anxiety, it was decided not to attempt to remove the symptoms by suggestion, as there was a good possibility of her gaining insight.

In the course of the next six weeks the symptoms were not discussed, and the patient gave an account of her life up to the time she entered nursing. She began to show an increasing amount of emotion in discussing her early love affairs. When the relation of her symptoms to those of individuals of emotional importance to her was pointed out, she at first insisted that the similarity was due solely to coincidence, even though by this time she realized that her symptoms were not due entirely to physical disease. Finally she was in the position of being able to formulate her own case and to realize the purpose of her symptoms. They did not, however, automatically disappear. No attempt was made to remove them, as she still had before her the most difficult decision of all, and she was quite unable to face the fact.

The next stage was reached when the patient asked the physician to decide whether she should return to her old life or continue nursing. This advice was refused, and she was told she must decide herself. This resulted in a renewal of anxiety dreams and reduced co-operation for several days. At the end of this time she said she must decide, as she could stand it no longer, and announced her intention of returning to work as soon as she was well. Her whole case was then reviewed with her, and she expressed surprise that her symptoms remained. She was told that if she stood up and held out her arms her tremors would go. They did.

On the following day she had relapsed completely. Her decision was reviewed, but she insisted on returning to work, though she seemed undecided. Her symptoms were again removed by suggestion, and she was sent home for a month's holiday, and told that her decision could always be reversed in that time.

A month later she rang up the writer from a telephone booth at one of the main London termini. She had arrived to continue her training as a nurse, and her symptoms had relapsed at once on leaving the train. She made her final decision in the telephone booth. She has remained well.

Prognosis.

The prognosis of a case of hysteria is the prognosis of the individual's success or failure in normal adaptation. It is impossible to form an opinion as to the future on a basis of symptomatology alone. If a reliable impression is to be gained, consideration must be given to the strength or weakness of the patient's physical and personality resources as a whole in relation to the social and cultural milieu to which he must adjust himself, and to the stresses he is likely to be called upon to face. If he is to assess the patient's capacity to resist flight into illness, the physician must, in the course of his therapeutic exploration, endeavour to build for himself a living mental picture of his patient's reactions to past and present problems. This will allow him to foresee to some extent his future conduct, at least in response to predictable stress. While emphasis must be laid on this total view, there are certain aspects of an hysterical illness which are of especial importance in prognosis.

If the stress which appears to have determined the patient's illness is not an overwhelming one, or one that has continued beyond normal endurance, the reason must be sought for his retreat from a situation which the average individual is expected to face. Further inquiry may reveal that there are other difficulties and anxieties which have weakened his resistance, and that retreat has only taken place after a genuine effort to overcome them. If, on recovery, return to a less trying environment is possible, the outlook for adaptation to average stress may yet be good. If, on the other hand, the patient has to return after his symptoms have cleared up to a situation as difficult as the one that wore down his resistance and forced him to seek refuge in hysteria, relapse can be expected, however full the insight that has been gained during treatment. It is only when it causes the patient to see his difficulties in a way which allows him to dispose of them that insight is of value and is likely to be retained.

In the same way, if he suffers from some native handicap, physical or intellectual, for which he cannot compensate, which has prevented him from taking a normal place in the community, normal adaptation cannot be expected on his return to it. Such cases do not present themselves with symptoms of recent hysteria unless some sudden additional strain has brought their deficiencies into relief. Even where a solution of the immediate problem is possible, each retreat may, unless some compensation is found, increase the possibility of a permanent adjustment through functional incapacity. Handicaps such as these are more likely to acquire chronic functional superstructures if they are such as not to be easily discerned by others. The blind man is not only excused his ability to avoid collisions, but he is suffered to be more

bad-tempered than the man who can see. The simpleton of intelligent appearance, on the other hand, has his failings attributed to malice, and can hardly be blamed if he learns to explain them to himself and to others as due to his "nerves." Where the disability lies in incapacity for social adaptation it is often difficult even for the psychiatrist to detect and to make allowance for, even though it is a constant, though unsuspected, handicap to the patient. There can be no doubt that, even apart from the group of psychopathic personalities in which the tendency to hysterical mechanisms is the presenting feature, functional illness is common in psychopaths and prepsychotics of all kinds. The presence of such a personality argues a poor prognosis in proportion to its degree.

Since there is much in hysterical illness that is comparable to faulty habit, it is helpful to inquire into the way a patient has been accustomed to deal with minor difficulties. To those who have been able from childhood to postpone and evade their daily responsibilities on pretexts of physical indisposition, the extension of this mechanism in the face of larger issues may come easily. Those who have been encouraged in youth to believe the world at their service may feel the need of retreat more acutely when exposed to the stresses of adult life. The adolescent who has refused to give up his childhood dependence will find himself unprepared for the traumata inevitable at his age, and will be forced to blind himself to their existence; as is seen in the denial of sex knowledge so common in the female hysteric. The frequent occurrence of hysterical illness in the daughter who has stayed with the parents while the other members of the family have made themselves independent is generally recognized. It may be that she has stayed because she was constitutionally predisposed to hysteria and therefore to dependence. The converse is, however, absolute, i.e. that a dependence which has not been sought by the individual predisposes him to make use of hysterical mechanisms.

Often, before breakdown has occurred, the patient will think consciously how his difficulties would be solved by the fortuitous appearance of a disabling wound or illness. It is frequently possible, in the course of treatment, to revive the memory of these thoughts, and to find out to what extent disability was consciously hoped for. In cases in which incapacity has appeared early, it may become evident that since so little effort was made to prevent a thought from becoming a reality, the same process could easily occur again.

During treatment-the appearance of a zest to return and deal with the old problems in a new way is a welcome sign. It is more easily mobilized where the patient has ordered his life to some definite end in which his interest can be renewed. Where he has led an aimless, day-to-day existence without a central ambition, his prognosis is the worse. A history of previous hysteria with each attack, precipitated by a decreasing stress, and preceded by a decreasing amount of anxiety, suggests that unless a radical overhaul of the whole personality is possible, relapse is likely.

The presence of signs of acute anxiety is an indication that solution of the patient's problems by means of functional incapacity has not been too placidly accepted. A history of a fairly prolonged period of anxiety preceding the development of symptoms argues a good prognosis if this anxiety can be mobilized in the course of treatment. In cases where mechanisms of non-realization are prominent anxiety is nearly always evident, and in these cases the outlook is usually good. In general, the prognosis of panic and terror reactions, unless they occur in the course of chronic hysteria, is excellent, while that for transition states is not quite so good. In recent hysteria with functional incapacity anxiety is never so overt, and *belle indifférence* may have made its appearance. Such cases have much in common with chronic hysteria, and their outlook is the less favourable for that reason.

Anxiety is not always readily recognizable as such. It is often masked by aggression, and for this reason the appearance of a belligerent attitude and of resistance to treatment in the early stage is by no means a bad sign. It has been seen that aggression is common in alternation with true anxiety and with non-realization symptoms in transitional states. This favourable aggression has to be distinguished from that seen in psychopathic personalities, and especially in the epileptoids, in whom chronic and progressive hysteria is common. In the same way true anxiety has to be distinguished from the perpetuation of long-inactive anxiety symptoms as a means of functional incapacity (anxiety hysteria). A useful indication of the presence of true anxiety in retrospect is a history that the patient has wished for death rather than disability as a solution of his difficulties.

Perhaps the most important part of this prognostic estimation of the personality is to decide whether or not breakdown has been the reasonable result of stress. If it has, then recovery may be expected. If it has not, the cause may be found in constitutional inferiority, or inquiry may reveal a deteriorative character change which has been taking place for some time before the actual appearance of symptoms. Some patients appear to have an inborn weakness in their resistance to such a change and, in a favouring environment, drift into the habit of blinding themselves to and evading their responsibilities until the evasion amounts to hysterical non-realization and retreat. Others of greater native strength may be forced into the habit of retreat by acquiring some disability, whether it be an injured brain or a cruel husband, for which they are unable to compensate. In a special group, to which the name degenerative hysteria may be given, patients, often of previously good personality, rapidly develop the grossest hysterical mechanisms, many of them closely akin to malingering, together with irreversible personality change. Many such cases follow head injuries and others prove later to have chronic encephalitis, epilepsy or some other organic insufficiency. This group will always need partial protection and a useful life is rarely possible.

The detection of the signs of personality deterioration associated with

progressive hysteria is of great prognostic importance. If they were absent before symptoms appeared, there is always hope of complete readjustment and the effort of treatment will be repaid. The chronic hysteric develops gradually a childish egocentricity. He covers his lack of interest in the common good with showy protestations of self-sacrifice. His affects are shallow, but he attempts to deceive himself and others with displays of emotionality. He is unambitious and is guided by the whim of the moment, and will mobilize all his pathological resources to obtain it. He is shamelessly dependent on others, and demands his full rights from a community to which he contributes little unless it incidentally satisfies his own self-esteem. He seeks by identifying himself with the child to gain his privileges while retaining the dignity of an adult. His facility in such inconsistent identifications is an indication of the development of a chacteristic suggestibility which can at any time change abruptly to negativism. In such a personality hysterical mechanisms flourish, and if it has been present before they appear, the prognosis is less favourable. In recent hysteria similar characteristics may appear while the symptoms are present, but they have not then so serious a significance as when they have been present before.

Though often misleading until all the causative factors are known, the nature of the actual symptoms, apart from their general type, is of great prognostic value. If the form of the illness is that of a true recent hysteria, the immediate outlook is always good. Amnesia and aphonia invariably clear up, and on the first occasion of their appearance are not usually replaced by functional incapacity. A pseudopsychosis, on the other hand, though it usually responds to treatment, occurs in a poorer type of personality, and the form of psychosis imitated may indicate an underlying trend in that direction. In the group with functional incapacity there are a number of symptoms which rarely occur unless there is considerable personality deterioration. Symptoms which bear a strong resemblance to malingering (dermatitis artefacta, puncture abscesses, pseudopyrexia) indicate that this deterioration is a progressive one unless they occur in a setting of prolonged physical illness or severe anxiety.

Patients who appear at first sight to be dull and degenerate may alter rapidly with relief from strain and a knowledge that an attempt is being made to understand their difficulties. In the patient's interest he must be seen at his best, and this may not be possible until a good deal of effort has been spent in therapeutic exploration. If there is doubt as to whether the patient is deserving of an intensive therapeutic attack he should be given the benefit until he is proved undeserving of it. If, however, it is seen that chronic hysteria is inevitable, the effort spent in treatment should be kept for worthier material. The aim in such cases can only be to improve the patient's adjustment to his life rather than radically to alter him.

A relatively small number of cases of recent hysteria become chronic, and of these only a few become complete dependents. The partially dependent

group is, however, a large one, and includes many of the permanent supporters of hospital out-patient departments. These individuals are a permanent burden on the social institutions which must aid them, and mar the happiness and restrict enterprise in the families to which they are attached. In preventing chronic hysteria, the physician is acting at least as much in the interests of the community as of the patient.

Summary.

The manifestations of recent hysteria are due to the retreat from a situation which is beyond the patient's endurance. Reduced awareness of the situation is an essential feature. It is the pathological counterpart of a normal protective mechanism.

Retreat may be attained by flight into—

Irrelevant activity or anger.

Non-realization symptoms.

Functional incapacity.

In recent hysteria the retreat is a blind one. In chronic hysteria the patient has a fuller awareness of his circumstances, and adjusts himself to them by selectively purposive symptoms. This is only possible at the expense of loss of independence as a social unit and of personality changes consonant with permanent dependence on others.

Anxiety is most commonly the state from which escape is sought. This anxiety may arise in fear or from conflict. Signs of anxiety are very frequently in evidence, if in disguised form, among the symptoms of recent hysteria.

Classification of recent hysterical states:

(1) Immediate reactions.

Hyperkinetic—panic reactions.

Hypokinetic—terror reactions.

(2) Hysterical transition states.

(3) Recent hysteria with functional incapacity.

Constitutional and organic predisposing factors are of great importance, both in lowering resistance to hysterical mechanisms and in determining their form. Recognition of such factors and of that of exhaustion is a necessary background to a psychotherapeutic approach.

In recent hysteria the nature of the symptoms themselves is such as to hinder inquiry into their causation. For this reason, and because there is a time factor in preventing further retreat into functional incapacity, it is often advisable to remove the presenting symptoms at an early stage in treatment.

Panic reactions recover spontaneously or respond to reassurance or redirection of the patient's excessive activity. If they do not they may become transition states. Terror reactions and transition states need rest

and security before symptoms can be attacked. Their treatment may be divided into three phases:

Rest and reassurance.
Removal of symptoms.
Therapeutic exploration and re-education.

Suggestion is of great use in recent hysteria. In the group with functional incapacity, especially, preparation is necessary, as unsuccessful suggestion has an adverse effect of rapport. There must be an incentive to recovery, if only an immediate one. The methods of suggestion include:

Simple demonstration and re-education.
Conditioning out.
Suggestion with vehicle.
Dissociative suggestion.

These methods are used in combination rather than separately.

Removal of symptoms does not mark the end of treatment, but it may greatly assist rapport and the development of insight. In the therapeutic exploration which is made at all stages of treatment a vital study is made, with the patient, of his life. Prognosis can only be based on a review of the total personality and equipment of the patient in relation to the problems and stresses he may be called upon to face. A poor prognosis does not threaten life. Lifelong neurosis, the worst result, is a handicap, not so much to the patient as to those upon whom he is dependent.

The main features to be reviewed for prognostic purposes may be summarized in four groups:

Physical and constitutional factors.—Intelligence. Constitutional or acquired organic deficiencies, especially gross disease of the central nervous system. Exhaustion and debilitating factors.

Previous personality.—Presence or absence of drive and ambition. Evidence of personality deterioration. Extent to which mechanisms of retreat were used unchecked in early life. Psychopathic personality. Exclusion of degenerative hysteria.

Nature of stress upon patient.—Its intensity and duration, and whether the patient has attempted to overcome it. Ability of the patient to adjust to it if given help. Extent to which patient can be shielded against similar stress on recovery.

Form of the reaction.—Intensity and duration of anxiety period before breakdown occurs. Acute changes from previous personality, such as panic and terror reactions, have best prognosis. Transitional states usually good if it is the first attack. Acute functional incapacity less so. Non-realization symptoms are of good import. Symptoms resembling malingering occur in poor personalities unless in exhausted states or degenerative hysteria.

Part II.—Reviews.

Mental Disorders in Modern Life. By ISABEL EMSLIE HUTTON, M.D. London: William Heinemann, Ltd., 1940. Pp. ix + 204. Price 3s. 6d.

First published in 1934, under the appropriate title *The Last of the Taboos*, this book is a praiseworthy attempt to inculcate a more enlightened attitude on the part of the general public towards mental illness. The author stresses the appalling fear, secrecy and deception which surrounds the case of insanity and the stigma associated with certification and the mental hospital. These are some of the reasons which prevent the public from regarding the mentally ill with the same compassion as the physically ill or from helping them with the same liberality. In an attempt to eradicate this viewpoint something is shown of the work in a mental hospital, and the various lines along which this could be extended if there were the necessary financial support. Where propaganda is the main object, there are likely to be overstatements. It is an exaggeration to say that "nothing whatever is done by voluntary effort," or that "there are practically no arrangements for the treatment of the slighter forms of mental disorder or the earlier stages of the more serious maladies."

S. M. COLEMAN.

The Sexual Perversions and Abnormalities. By CLIFFORD ALLEN, M.D., M.R.C.P., D.P.M. London: Humphrey Milford, Oxford University Press. Pp. xii + 193. Price 7s. 6d.

A reader unfamiliar with psycho-analysis might be forgiven if he presumed that Dr. Allen's astounding theories are sponsored by Freud, whose name is so frequently invoked. Freud's teaching is, of course, in diametrical opposition to the opinions here expressed.

Dr. Allen tells us that on no account should the sexual instinct be thwarted; even sublimation is not to be recommended. Masturbation might almost be encouraged, for all muscles and glands benefit by use! By the same argument it is insisted that continence is definitely harmful. We are told to go to the "unspoilt" Tuamotuan to find "sex as it should be." Presumably a state of total cultural stagnation is well worth while if premarital promiscuity and complete sexual licence are the recompense. Having read so far it is not surprising to learn that in Dr. Allen's consulting room the sexual pervert is not only allowed to say all that he wishes, but is persuaded to act out his perversion there and then. It is naïvely explained that a deep transference will be accelerated by adopting Dr. Allen's technique.

Karl Menninger has pointed out that Anita Loos understood her Freud much better than the ignorant people who accuse psycho-analysts of advising

or implying the desirability of uninhibited self-indulgence. He reminds us of "her preferred blonde, who had hoped for some psycho-analysis and was advised to use some suppression instead." S. M. COLEMAN.

Hopousia or the Sexual and Economic Foundations of a New Society. By J. D. UNWIN, *M.C.*, Ph.D. London: George Allen & Unwin, Ltd., 1940. Pp. 475. Price 21*s*.

This highly interesting if speculative work is a corollary to the author's *Sex and Culture*. In the latter it was concluded that Freud's theory as to there being a direct relationship between sexual repression and social evolution is a correct one. In this book an attempt is made to formulate the conditions which would have to be fulfilled if a society were to go on displaying maximum energy for an indefinite period. In a critical introduction Aldous Huxley puts his finger on some of the more obvious economic and sociological anomalies in the Hopousian system. The fact that the work was left unfinished, on account of the author's death, does not altogether dispose of these. From the psychological angle the main criticism is that however desirable and however well such a social structure might work among Unwin's Hopousians, the moral nature of the average European is such as to ensure the collapse of the structure even if it were ever achieved. S. M. COLEMAN.

The Inter-relationship of Mind and Body. Vol. XIX of the Research Publications of the Association for Research in Nervous and Mental Disease. Baltimore: The Williams & Wilkins Company, 1939. Pp. xx + 381. Price 36*s*.

This volume represents the proceedings of the Association for Research in Nervous and Mental Disease for December, 1938. The subject of the inter-relationship of mind and body provides a wide range for discussion and this is amply shown in the list of subjects. Foster Kennedy writes the introductory chapter on the relationship between mind and body. This is followed by chapters dealing with the electrical activity of the brain, with the effect of a variety of physical agents on the brain processes, with the manifestations of emotional states, and finally with the physiological effects of various psycho-therapeutic measures.

The book gives a very well-balanced account of mind and body as we see them to-day, looked at from the viewpoint of modern chemistry and physics.

One of the most interesting statements in the book is that chronic barbiturate poisoning is less dangerous than chronic bromide poisoning. Individuals with depressive tendencies appear to have some affinity for barbiturates.

There are some interesting if somewhat vague speculations on the relationship between hypo-vitaminosis and Korsakov's disease. The subject requires a great deal of investigation. In the same way the investigation of conditions of chronic anoxia as a factor in schizophrenia requires urgent attention.

A very sober word of warning comes from Dr. Tracy J. Putnam—"the prospect of solving any but the simplest psychologic problems by physiologic means is far distant." With this view we heartily concur. There is in many quarters a tendency to argue in a facile illogical manner from the particular to the general.

This nineteenth volume of the series lives up to the high standard set previously. G. W. T. H. FLEMING.

The Hypothalamus. Vol. XX of the Research Publications of the Association for Research in Nervous and Mental Disease. Baltimore: The Williams & Wilkins Company, 1940. Pp. xxx + 980. Price 10 dollars.

Volume Twenty of this series is a very fine production and surpasses the very high standard set by previous volumes.

It is divided into three sections, dealing with the anatomy of the hypothalamus, its physiology and a clinical symposium.

In the introduction Fulton reminds us that the hypothalamus is only one of a series of functional levels, and that though it influences more caudal levels of somatic and autonomic functions, the hypothalamus itself is under the direct control of the cerebral cortex.

The anatomical section is extraordinarily well done and very well illustrated. It deals with the development, comparative anatomy and anatomy and leaves nothing to be desired.

The physiological section deals with cardiovascular regulation, temperature and pilomotor regulation, water metabolism, and movement, carbohydrate and fat metabolism, sexual behaviour and gonadotropic function of the hypophysis, anterior pituitary function, gastro-intestinal regulation, vesical activity, and sleep.

Normal sleep appears to be associated with a decreased activity of the hypothalamus, and increased activity of the hypothalamus leads to increased bodily activity.

The clinical section deals with tumours involving the hypothalamus, personality and emotional disorders associated with hypothalamic lesions, cell changes in the major psychoses, temperature disturbances, surgery and medical syndromes of the hypothalamus. The hypothalamus is regarded as one of a series of stations concerned with the emotions principally and intellect and personality incidentally. Its functions are correlated with the cortex, thalamus and probably lower areas. When released from cortical control it is capable of giving rise to primitive emotional reactions in animals and to similar reactions in man, as well as to coarseness and a lack of appreciation of social niceties.

We read that in 96 per cent. of cases of epileptic psychoses and mental deficiency both the substantia grisea and the nuclei tuberis laterales are involved.

The production of the book leaves nothing to be desired.

G. W. T. H. FLEMING.

Nobber and Firth's Hygiene. Tenth edition. Revised by L. C. ADAM and E. J. BOOME. London: Longmans, Green & Co., 1940. Pp. x + 518. Price 12*s.* 6*d.*

This well-known text-book of hygiene needs no introduction. The present revision is a considerable improvement on the 1921 edition. The various Acts introduced during 1936–1938 are all dealt with efficiently and add to the value of the book. It is somewhat of a surprise to read of speech defects in a text-book of hygiene; surely they come under mental hygiene but not under the general title of hygiene. There is a considerable emphasis on the L.C.C. which rather savours of propaganda. G. W. T. H. FLEMING.

Psychology and Psychotherapy. By WILLIAM BROWN. Fourth edition. London: Edward Arnold & Co., 1940. Pp. viii + 260. Price 12*s.* 6*d.*

Here are presented a series of psychological essays on a variety of subjects, including dissociation, psycho-analysis, war-neuroses, hypnotism, the psychology

of peace and war, the body-mind relationship, and psychical research. In the present edition new chapters have been added on sublimation and on the psychological problems of later life. However interesting individual essays may be, the reader will look in vain for the "general plan and purpose" of the book promised in the introduction. Here the authority is Freud or Jung, there it is Coué or Bergson. Even Dr. Brown is unable to obtain a synthesis from such a variety of opinion. Having been informed that the book has been "thoroughly revised and brought up to date," it is unexpected to find the section on psycho-analysis stopping short at a full exposition of the "Electra complex" and the "censor." S. M. COLEMAN.

Part III.—Bibliography and Epitome.

AMER. J. PSYCHIAT.

VOL. XCVI. MAY, 1940.

Bioelectric Responses in Metrazol and Insulin Shock.

1. The bioelectric potentials from the brain of the rabbit have been studied during metrazol and insulin shock. Insulin, administered subcutaneously, causes a marked increase in the slow wave activity during the coma stage. Cortical potentials during the convulsions are masked by the potentials artefacts caused by the violent movements. Except for a few cases of localized spike potentials recorded from the cortex during the pre-convulsive stage, no characteristic cortical potentials are seen immediately preceding the convulsion.

2. The potentials recorded from the cortex following a shock injection of metrazol may be divided into four phases. These phases are correlated with the various stages of the physical shock.

3. Thalamus, midbrain and cerebellum show abnormal electrical activity during metrazol shock.

4. Sections at various levels in the central nervous system show that the electrical response in the cortex due to the action of metrazol is not primarily dependent on the severed pathways. Characteristic shock potential sequences may even be recorded from small areas of neurologically isolated cortical tissue. The physical shock, on the other hand, is altered profoundly by these neurological sections.

5. Minute quantities of metrazol, applied locally to discrete areas of the cortex of the rabbit, initiate a bioelectric response which, although much more localized, resembles closely that seen following intravenous injection. This activity may spread to other cortical or even sub-cortical areas, presumably by facilitation.

6. An attempt is made to explain something of the action of metrazol on the brain, on the basis of what is already known regarding the effects of faradic stimulation of the cortex. (Authors' abstr.)

The Mechanism of Fractures of the Vertebral Bodies. Fractures of the Mid-thoracic Area Complicating Metrazol Therapy : Prevention and Treatment.

1. A study of the anatomy and of the practical considerations of the spine shows that fractures of the vertebral bodies are usual at those areas of the spine that are mechanically weak or exposed to the effects of traumatism.

2. Metrazol acts to cause convulsions attendant with very forcible muscular contractions sufficient to fracture the bodies of the vertebræ in the mid-dorsal region which is anatomically and dynamically vulnerable. The localization differs from the more usual sites of fracture because of a modification of the type of stress and strain peculiar to the muscular contractions caused by metrazol injections and their effects on the anatomy of the parts affected. The degree of injury varies directly with the force of the muscular contractions and inversely with the resistance offered by, or the strength of, the vertebral bodies. The force of the muscular contractions and the energy expended is so great that a convulsion continuing for 90 seconds may exhaust the patient for 8 to 24 hours.

3. The mid-dorsal area of the spine is anatomically vulnerable, and fractures occur at this site following metrazol therapy because the site is midway between the forward physiological curves of the cervical area above and the lumbar below. The degree of flexion occurs through an arc sufficiently small to make the mid-dorsal spine the recipient of its greatest effects. The vertebral bodies are here wider anteriorly while the discs are smaller, less resilient and more narrow anteriorly; and the dynamic centre of the flexor contracting force of the trunk muscles is at this level.

4. The number of metrazol injections has no relation to the number of vertebral bodies fractured or to the degree of wedging. The extent and degree of injury are rather dependent upon the intensity of the muscular contractions, due to any one particular convulsive treatment, and the strength of the spine to withstand the shock. Undoubtedly if a fracture occurs early in the course of treatment and if treatments continue without the prophylactic measures recommended, increased wedging of the vertebræ may obtain.

5. Rupture of the nucleus pulposus with protrusion into the neural canal is most unusual following fractures of the vertebral body.

6. No practical type of mechanical fixation can prevent injury to the vertebral bodies.

7. Prophylaxis is possible, and the use of spinal anæsthesia given prior to the metrazol injections as suggested by Hamsa and Bennett is recommended.

8. If fracture occur, immobilization of the trunk between treatments and reduction of the deformity, if it is present, with fixation in a plaster jacket for six months after the treatments are completed should result in entire healing of the fractures. (Author's abstr.)

ANN. MÉD. PSYCHOL.

VOL. XCVIII. APRIL, 1940.

ARCH. GES. PSYCHOL.

VOL. CIII. 1939.

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ARCH. NEUROL. PSYCHIAT.

VOL. XLIII. MAY, 1940.

Personality Changes Accompanying Cerebral Lesions. I. Rorschach Studies of Patients with Cerebral Tumours.

Examination of the Rorschach records of patients with cerebral tumours has shown that both as composite pictures and as individual records they differ markedly from the normal. Twenty-eight records of 25 patients with tumours of the brain, even when expressed in graphic form only, show restricted and constricted personality, extraordinarily uniform when contrasted with the variety found in the records of the normal subjects.

When considered in terms of the preoperative and postoperative status of the patient, the records of the postoperative group were found to be slightly superior.

When considered in terms of the pathologic character of the lesion, the slowly growing and rapidly growing tumours, the records showed no significant difference.

The location of the lesion was not an important factor. Twenty-six of the 28 records differed so greatly and consistently from the normal records that the smaller differences between records of patients with lesions in various locations

were relatively insignificant. However, further differential studies are necessary and are in progress.

In differential diagnosis, the author finds that the Rorschach method may be useful in distinguishing between a cerebral lesion and conditions with symptoms simulating this condition.

The attempt to differentiate more exactly within the group of patients spoken of in the Rorschach literature as having " organic " lesions can be completed only when this comparatively uniform group of patients with cerebral tumours is compared with groups of persons with cerebral lesions of other types.

(Author's abstr.)

Vascular Bed of the Retina in Mental Disease.

The cross-sectional area of the vascular bed of the retina has been measured in a group of psychiatric patients classified as having either schizophrenia or manic-depressive psychosis. It is believed that these measurements are an index of the developmental status of the general vascular constitution of the patient.

There is no correlation between the capacity of the retinal vascular bed and either of the two diseases studied. Contrary to previous impression, no correlation was found between habitus in the Kretschmerian sense and the capacity of the vascular bed.

In the schizophrenic group there was a high degree of correlation between the clinical status of the patient and the capacity of the retinal vascular bed. When the measurements of the vascular bed are corrected for differences in stature in the group, the correlation between clinical status and the size of the vascular bed becomes even more significant. (Authors' abstr.)

Serum Protein, Non-Protein Nitrogen and Lipoids in Schizophrenic and Manic-Depressive Psychoses.

Long-term studies of 14 patients with schizophrenia, 11 with manic-depressive psychoses and 7 with symptoms of both conditions revealed abnormal variations in the non-protein nitrogen of the blood and in the total proteins, cholesterol and fatty acids of the serum in all the persons who showed marked changes in clinical status. The patients whose symptoms showed little change rarely had abnormal variations in these constituents.

These results demonstrate that there are abnormally large metabolic changes in the blood which accompany the variations in mental symptoms, particularly those symptoms which can be attributed to dysfunction of the brain stem. When changes in nutritional status were not extreme, the serum lipoids rose during the manic or the depressed phase of the illness and fell with recovery.

Manic-depressive patients as a group were found to have high cholesterol and fatty acid values, while, in contrast, the schizophrenic patients had lipoid values that were below the normal average, in many instances being below the normal limits. (Authors' abstr.)

Histologic Changes following Metrazol Convulsions, with Note on a Fuchsinophilic Reaction as an Index of Early Neurocytologic Change.

Seizures and other motor activities produced in a series of experimental animals by injections of metrazol were observed and recorded.

In contrast to the experience of some other observers, serious lesions were found in the brains of all animals in this series which underwent convulsions from metrazol. Strong evidence of chronic neuropathologic lesions, in contrast to changes which might be imputed to lethal seizures only, was observed in animals which had seizures over periods of more than eight days. The degree and extensiveness of the lesions in these experimental animals corresponded in general with the number and severity of the seizures observed. The type of damage to the

brain seemed to be influenced by the length of time during which the animal had seizures.

In the brains of these animals the phosphomolybdic acid-polychrome stain showed a clear correlation with the Nissl stain. The polychrome method appeared, however, to be more sensitive, showing the changes more definitely and vividly and making it possible to detect early pathologic changes more effectively. With the polychrome stain many changes in the nerve tissues which did not appear with the Nissl stain could be noted.

The total convulsive activity experienced by the animals in this experiment was considerably less than that experienced by many patients clinically, and much less than that experienced by the monkeys in the report of Strecker and his associates. The point made by Strecker and his co-workers that perhaps the damage to the brain which they observed could be related to the prolonged total duration of convulsive activity (a much greater total convulsive period than that experienced by patients under treatment) does not apply therefore in the present experiment.

No direct relation between the degree of neuropathologic change and the total amount of metrazol administered, as noted by other observers, can be established in the present experiment. Of course, the total amount of metrazol administered bore some relation to the number of convulsions produced, but when these figures diverged the pathologic changes tended to follow the number, duration and severity of the convulsions rather than the amount of the drug.

The lesions observed in the experimental animals consistently appeared to be secondary to vascular constriction or vascular changes. This might be taken as an indication that the seizure itself is induced by vascular spasm and consequent anoxia rather than by direct influence of metrazol on the neurons.

The consistency with which lesions were produced in the experimental animals strengthens the natural suspicion that serious neuropathologic changes of some sort may occur clinically in metrazol therapy.

Many kinetic activities besides seizures were observed. Some of these were similar in various degrees to the preliminary clonic activities and torsion spasms observed in patients. Others bore little resemblance to anything seen in clinical treatment with metrazol. Persistent hypertonus was seen prior to death in every one of the animals. It is believed that persistent hypertonus is a grave sign when seen clinically.

Although the present findings tend to indicate that metrazol therapy is drastic, they should not be regarded as discrediting such treatment of conditions serious enough to warrant drastic, or even dangerous, measures. (Author's abstr.)

Temporary Arrest of the Circulation to the Central Nervous System.

1. Permanent pathologic lesions may occur in the cerebral cortex of the cat after complete arrest of the circulation for three minutes and ten seconds.

2. Frank necrosis and softening of the cortex have been observed after circulatory interruption for three minutes and twenty-five seconds.

3. Circulatory arrest for periods in the neighbourhood of seven and a-half minutes causes complete destruction and liquefaction necrosis of the cerebral cortex.

4. The motor and visual cortexes sustain the earliest and most profound damage. The olfactory, orbital and temporal regions of the cortex are the least susceptible.

5. Lamina I, and to a lesser extent lamina II, are the least vulnerable of the cortical layers, while laminas III and IV are the most vulnerable.

6. The Purkinjë cells rank next to the nerve cells of the cerebral cortex in susceptibility.

7. The lateral geniculate nucleus is the most vulnerable of the basal nuclei in the cat, and it is followed, in order of susceptibility, by the hypothalamic nuclei, the thalamic nuclei, the globus pallidus and the caudate nucleus.

8. The brain stem and spinal cord are uninjured by periods of circulatory arrest compatible with continued survival of the animal. (Authors' abstr.)

JUNE, 1940.

ILLINOIS PSYCHIATRIC SOCIETY.

PHILADELPHIA NEUROLOGICAL SOCIETY.

CHICAGO NEUROLOGICAL SOCIETY.

MICHIGAN SOCIETY OF NEUROLOGY AND PSYCHIATRY.

Personality Changes Accompanying Cerebral Lesions. II. Rorschach Studies of Patients with Focal Epilepsy.

A group of 24 patients with focal epilepsy, all of whom had undergone operation for the removal of non-expanding atrophic lesions, was studied by the Rorschach method. The patients were studied postoperatively after varying intervals, and 10 were also studied preoperatively to allow a comparison of records obtained before and those obtained after the removal of cerebral abnormalities. A comparison was made of these patients and patients with large infiltrating lesions, as well as of deteriorated patients with cryptogenic epilepsy and of patients on whom craniotomy and " negative exploration " had been carried out.

The author believes that no one typical personality emerges in the cases of the patients with focal epilepsy, but that there is a wide range of personality difficulties. There was evidence in the records of this group of behaviour problems, of neurotic personality and, in one case, of possible psychosis. There were markedly introvert and extrovert personalities and all varieties of mental approach. There were three cases in which Rorschach signs peculiar to Jacksonian (focal) epilepsy appeared, and three in which the records approximated the type of personality already described in the paper on cerebral tumours.

With respect to the difference between preoperative and postoperative Rorschach records, the author has isolated certain components of the preoperative records which seemed to indicate future psychologic improvement if more favourable conditions could be given the patient. This made her hope that such studies might make a contribution to prognosis, for if improved psychologic capacity, as evidenced by the Rorschach test, is in itself an index of improved cerebral function, as is suggested by this study, this method may become a prognostic procedure for the selection of those patients who are most likely to be benefited, both mentally and physically, by operative intervention. While it is not possible to make such a claim from this study alone, it is hoped that the hypothesis may prove of value for the basis of future work. (Author's abstr.)

Neurohistopathologic Changes with Metrazol and Insulin Shock Therapy.

An experimental study of the action of insulin and metrazol in the cat has shown that when insulin produces deep shock leading to death severe damage to the neurons occurs, and that with metrazol little, if any, change in the central nervous system is discernible.

In the brains of animals which died after the administration of insulin, involvement of ganglion cells was manifested by the presence of cell shadows, intracellular neurofibrillar clumping and damage of axis-cylinders. There was also a definite increase of glia.

In the spinal cord and posterior root ganglia of the animals treated with insulin the changes in the neurons were both quantitative and qualitative, the cells often showing severe disease and in some instances actual destruction.

In the animals given metrazol there were no changes comparable with those seen in the animals given insulin. The changes with metrazol consisted essentially of pyknosis of scattered cells of a minimal degree. There were no quantitative changes. The cell pictures compared favourably with those in the control animals.

If the pathologic changes observed in the central nervous system of experimentally treated cats can be regarded as an index of the ultimate effects in the central nervous system of human beings, insulin in large doses should be used with greater caution, and metrazol may be considered the safer drug with respect to the effect on the central nervous system. (Authors' abstr.)

Cerebral Air Embolism and Vital Staining. Contribution to the Experimental Study of the Blood-Brain Barrier.

The two chief hypotheses concerned with the nature of the blood-brain barrier are presented, and reference is made to the use of vital staining in the study of this phenomenon.

Controlled experiments with cerebral air embolization and subsequent intravenous administration of trypan blue are reported, and the gross and microscopic observations are described.

The microscopic changes were: Exquisitely focal, chiefly intracortical, areas showing varying degrees of loss of stainability in sections. The general appearance of the lesions in stained sections appeared to be due primarily to definite changes in the intercellular ground substance, with occasionally no decrease in the number of cellular elements, but with always some degree of acute ischaemic damage to the nerve cells. Blood vessels, on the other hand, appeared intact in almost every instance, showing only some endothelial hypertrophy and occasional hæmorrhages in the larger lesions. All lesions were sharply demarcated from normal adjoining tissue, and appeared to be entirely independent of cortical lamination or other regional peculiarities of the formed elements.

All lesions, apparently, stained grossly with trypan blue, regardless of the presence or absence of histologically determinable damage to the blood vessels.

Despite the extravascular presence of the toxic dye, there was neither anatomic nor neurologic evidence of any invasion of or effect on normal brain tissue adjoining areas damaged by embolization.

These observations are considered to be additional evidence that the peculiar behaviour of the nerve structures toward intravascular trypan blue is an expression, not of the special retentive powers of the cerebral capillary endothelium, but of the peculiar constitution of the intact cerebral tissues, in accordance with King's hypothesis. Moreover, it would appear that the amorphic, colloidal ground substance which constitutes the bulk of the cerebral cortex represents the essential factor in which this peculiarity resides. (Author's abstr.)

Convulsions Associated with Tumours of the Cerebellum.

While fits have been thought to be of unusual occurrence in association with cerebellar tumours, study of 158 cases of verified tumours of the cerebellum disclosed their presence to be not infrequent.

Although the tonic fit is supposed to represent the usual pattern of convulsions occurring in association with cerebellar tumours, study of the literature as well as of our own cases disclosed that every possible variety of fit may occur.

The various theories which have been offered to explain the so-called cerebellar fit are discussed. It is pointed out that although the convulsions are popularly supposed to represent decerebration, there is no evidence that this occurs. In fact, all the phenomena noted in the so-called decerebrate fit can be produced by decortication alone. Decortication may be produced through the medium of temporary cortical ischaemia resulting from transitory alterations in the intracranial pressure.

The physiologic evidence supporting this contention is reviewed. Since cerebral ischaemia may act as a temporary cortical excitant as well as a depressant, the clonic convulsions noted in a number of cases are accounted for. The changes in cerebral blood flow secondary to alternations in the intracranial pressure may account for all varieties of convulsive phenomena observed.

All types of fits may occur in patients having a tumour of the cerebellum, and the presence of focal or generalized convulsions does not exclude the diagnostic possibility of such a lesion. (Authors' abstr.)

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VOL. XXVII. 1939.

AUSTR. J. PSYCHOL. PHIL.

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BRAIN.

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Gower's Tract and Spinal Border Cells.

By methods of cord-section giving rise to chromolytic cell-changes it is shown that:

1. Certain large cells in the ventrolateral fringe of the spinal grey matter of the 12th thoracic and next succeeding six lumbosacral segments (monkey, cat) give axone fibres which, crossing the mid-line at the level of origin, ascend the lateroventral white column of the opposite side and reach the top of the cord. These cells are most numerous in the 4th and 5th lumbar segments; from their maximum there their number declines somewhat steeply in the oral direction, ceasing in the 11th thoracic segment. Their number declines still more steeply in the aboral direction, none being found in the 7th lumbosacral segment. The

cells are all large, and some are very large; in microscopic features they are not clearly distinguishable from the motoneurones of the ventral horn. On the other hand, they are quite unlike the cells of Clarke's column. Characteristic of their topography is that they occur preponderantly in the grey matter bordering the white column. Hence they can be referred to conveniently as "border cells." Chromolysis did not detect analogous cells in other regions of the cord.

2. Clarke's column in these monkeys extended aborally to, but not beyond the 3rd lumbar segment (Mott, 1895). Although very largely uncrossed, it did not appear to be entirely so.

3. In the 2nd cervical level large cells of the median part of the ventral horn give axone fibres which cross the mid-line to descend the opposite half of the cervical cord.

4. The ventrolateral white column at the 5th cervical level contains fibres which have descended from the uncrossed Deiters' nucleus, from the crossed large cell part of the red nucleus, and from large cells of the pontine and bulbar reticular formation both uncrossed and crossed. (Authors' abstr.)

A Study of Cortical Metabolism in Relation to Cerebral Disease.

1. Potassium ions in concentrations down to 0·01 mols per litre stimulate respiration, lactic acid production and glucose consumption by slices of rabbit cerebral cortex in the presence of oxygen.

2. The rates of respiration, aerobic and anaerobic lactic acid production of human cerebral cortex were measured. It was found that deprivation of oxygen stimulates both glucose consumption and lactic acid production of human brain as had previously been found in animal tissues.

3. In former work it had been found that potassium excess combined with anaerobic conditions depress lactic acid production of rabbit cerebral cortex. The rate of glucose disappearance measured directly is also found to be depressed by excess of potassium under anaerobic conditions.

4. Cyanide inhibits respiration but stimulates lactic acid production and consumption of glucose by rabbit cerebral cortex.

5. Excess of potassium ions combined with cyanide, however, depresses metabolism to a low level.

6. Reasons are given for the belief that nervous activity is dependent on glucose consumption with liberation of lactic acid and resultant electrical depolarization at the neuronal surfaces. Conditions, such as excess of potassium ions and deprivation of oxygen, which increase glucose consumption, thus cause increase in nervous activity.

7. It is suggested that normal central reflex activity is due to local liberation of potassium ions with concomitant stimulation of carbohydrate metabolism.

8. It would also follow that pathological cerebral irritation with increased nervous discharge is due to the similar stimulation of neuronal metabolism as a result of deprivation of oxygen. Thus the signs of irritation which accompany intracranial hæmorrhage, traumatic delirium with cerebral œdema, Stokes-Adams attacks and sometimes intracranial neoplasm, are explained as due to increased neuronal metabolism consequent upon oxygen deprivation.

9. The paralysis and cessation of nervous function, which follow irritation in the above pathological conditions, are probably due to subsequent diminution in rate of metabolism. The initial nervous activity, accompanying deprivation of oxygen, causes liberation of potassium ions from the cells. The resulting excess of potassium ions outside the cells, combined with anaerobiosis, actively depresses the previously raised metabolism. Thus two of the cardinal signs of acute cerebral disease, namely, irritation followed by paralysis, are explained on a metabolic basis.

10. The pharmacological action of cyanide, in which convulsions are succeeded by cessation of nervous activity, is accounted for on similar lines as a result of the effects of cyanide on cerebral metabolism. (Author's abstr.)

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VOL. X. JUNE, 1940.

BRIT. J. PSYCHOL.

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The Goodenough Test in Chronic Encephalitis.

Six children, aged 9 to 11, suffering from chronic encephalitis, were found unable to score on the Goodenough man-drawing tests as well as they did in other standardized intellectual tests. There was no evidence of technical disability or of mental defect. It is concluded that this is a specific disability, and that it probably arises from perceptual difficulties in relation to their own body rather than in optic perceptual difficulties. S. M. COLEMAN.

Suicide Among Hospitalized Drug Addicts.

An investigation was made of 28 suicidal patients with drug addiction. These were found to fall into two groups: genuine suicides (15) and theatrical suicides (13). The mental make-up, heredity and maladjustments of these two types are fully described. S. M. COLEMAN.

Study of a Case Involving Homicide.

A case involving homicide is reviewed. Post-mortem findings disclosed hypoplasia of the cerebro-vascular system and of the circle of Willis. The question is raised as to the role of the resultant anoxia in the emotional instability noted in the psychosis. S. M. COLEMAN.

Electrocardiographic Studies.

Electrocardiographic tracings taken soon after one single treatment with metrazol showed no evidence of myocardial damage in three patients. No evidence of myocardial involvement was detected in 36 patients studied electrocardiographically months after termination of both metrazol and insulin treatments. Evidence of improved function was found in 9 patients. S. M. COLEMAN.

The Haemato-Encephalic Barrier.

The usual range of permeability quotients as measured by the modified form of Walter's bromide method is from 2·0 to 4·0 and constitutes a normal "permeability spectrum." An individual's permeability quotient is not an absolutely

fixed quantity. In the absence of specific structural alterations, exogenous infections, abnormal physiological states, etc., the chief factor to influence the amount of permeability is the psychomotor activity. S. M. COLEMAN.

Colloid (Paraphysial) Cyst.

The paraphysis exists in human embryos and may enlarge during post-natal life, producing a cystic enlargement which forces its way through the roof of the third ventricle as a pendulous mass between the foramina of Monro. "Paraphysial" cyst suggests both the origin and embryologic significance of the tumour. The histological appearance and symptoms are described. The first reported case of rupture of the cyst into the brain tissue is here described. S. M. COLEMAN.

Beri-beric Neuromyeloses.

It is concluded that beri-beri is not a mere polyneuritis; that the nerve lesions are degenerative; that clinical and anatomo-pathological manifestations are of central origin; and that the syndrome of neuromyelosis, the frequency of which is stressed in this paper, constitutes the predominant anatomo-clinical form of beri-beri. S. M. COLEMAN.

J. NEUROPHYSIOL.

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Electric Responses Derived from the Superior Cervical Ganglion with Micro-Electrodes.

The electrical activity of the superior cervical ganglion of cats and rabbits has been studied with micro-electrodes. The recording system consisted of a capacity-coupled, push-pull amplifier and a cathode-ray oscillograph.

"Axon-like" spikes are obtained during preganglionic stimulation or as an injury discharge with micro-electrodes of 7 to 10 apertures. The spikes are post-synaptic phenomena and show an all-or-none character and a duration of 1·5 to 2 msec. They are found dispersed over the time range corresponding to the standard ganglionic record.

The brief duration, sharp localization and all-or-none character of the spikes recorded with the smallest micro-electrodes strongly suggest that they are derived from single cells.

Study of the single-spike potential during successive stimuli and with an unaltered position of the micro-electrode has shown variations of latency as great

as 7 msec. In some cases the frequency of response is different from and largely independent of the frequency of the preganglionic stimuli.

The "axon-like" spike is followed by one negative and two positive after-potentials, the last being identical with the slow positive after-potential of the ganglionic record. (Authors' abstr.)

Effect of Cortical Lesions on Affective Pupillary Reactions.

The threshold to pain reaction was studied on suitably trained, unanaesthetized cats after varying amounts of cortex had been removed. The indicator used was the reflex dilation of the pupil caused by inhibition of the Edinger-Westphal nucleus. Cortical areas giving this reaction were also determined. The results are as follows:

1. Ablation of the sensory or sensorimotor cortex does not raise the threshold to pain reaction.

2. Massive cortical lesions lower the threshold to pain reaction.

3. Cortical areas capable of inhibiting extrapyramidal movements also cause inhibition of the Edinger-Westphal nucleus. (Authors' abstr.)

Action of Ether and Nembutal on the Nervous System.

The actions of ether and nembutal on the nerve axon, the synapse, the rhythmically active nerve cell, the spinal cord and the brain have been analysed principally in terms of the action potential changes they produce.

The amplitude and area of the axon spike potential and the negative after-potential are progressively diminished by ether and by nembutal.

The electrical threshold of the axon is raised, its conduction rate is lessened, and its absolutely refractory period is prolonged by ether and by nembutal.

Ether markedly increases accommodation in the axon; nembutal decreases it slightly.

Both ether and nembutal block conduction through a peripheral ganglion. This is interpreted as indicating that they progressively lessen excitation of the soma through the synapse.

With depression by ether or nembutal, the period of latent addition (summation interval) at the synapse is shortened and the effectiveness of temporal summation is lessened. Further, the period of recruitment is shortened by these agents in proportion as they decrease the magnitude of the cyclic variations in amplitude and area of the immediate cortical response.

Ether increases the frequency of discharge of nerve cells possessing spontaneous rhythmicity and nembutal decreases it, often without any initial increase. Both drugs first increase the magnitude of the response of nerve cells and then, with increasing anaesthesia, decrease it. The increase produced by nembutal is considered to be in part a consequence of the reduction of the response frequency.

Ether and nembutal differentially depress the immediate cortical response to saphenous nerve stimulation, the order of final extinction of its constituent waves being third, second, and first. The general cortical excitation produced by spread is eliminated as the late waves are depressed. These effects are interpreted as due to blocking of synaptic stimulation.

The action of ether on the nerve cell or cell group suggests that it first stimulates and then depresses the excitation and response mechanisms. Nembutal has a much feebler preliminary stimulating action. The duration of the cell response under ether is less than that under nembutal, and recovery of responsiveness under ether is more rapid than under nembutal. This may account for the different discharge frequencies induced by these agents.

Present and past researches of this laboratory bearing on the question of excitation and inhibition of neurons are analysed. The facts suggest that excitation is an effect on the soma produced by the summation of brief electrical stimuli which arrive at the terminals of impinging nerve axons. A brief and a prolonged

excitatory state develop in the soma following their action. Inhibition, aside from the well-known rhythmical changes in responsiveness, has not been found to be accompanied by the development of a potential. It results in a lowering or elimination of the potentials associated with activity and presumably would oppose the activation of nerve cells. (Authors' abstr.)

Degeneration and Regeneration of Sympathetic Synapses.

A series of experiments is recorded in which the progressive stages in the degeneration and regeneration of synapses in the superior cervical sympathetic ganglion were studied histologically by silver stains, and physiologically by the cathode-ray oscillograph. Transmission through the ganglion diminished with the progressive experimental degeneration of the *boutons* attached to the preganglionic fibres. Restoration of normal function in the ganglion returned when the regenerating preganglionic fibres re-established contact with the ganglion cells by means of *boutons de passage* and *boutons terminaux*. Evidence is presented which strongly suggests selective regeneration of S_1 fibres to S_1 cells, etc. No histological or electrical evidence was found which would indicate that the ganglion cells suffered in any way from the degeneration of the synaptic contacts on their surface. The experimental results confirm unequivocally the theory of structural discontinuity in the sympathetic nervous system. (Author's abstr.)

Studies of Motor Performance after Parietal Ablations in Monkeys.

1. The alterations in motor performance which follow ablations of the parietal lobe have been compared with those due to ablation of areas 4 or 6. Unilateral removal of any of these three areas produces motor disability, which in each instance is characterized by relative disuse of the operated, as compared with the normal extremity, and by the greater involvement of distal joints and movements, as compared to proximal. The motor syndrome produced by ablation of any one of these areas may, however, be clearly distinguished from that produced by either of the other two.

2. As demonstrated by placing and hopping responses, tactile deficit appears following unilateral or partial ablation of either areas 3-1-2, 1-2 or 5 and 7. Proprioception is much less affected by these parietal lesions, but complete bilateral removal of all parietal tissue permanently abolishes the hopping and the tactile and proprioceptive placing reactions.

3. Absent or diminished knee jerks, together with diminished resistance to passive manipulation, appear immediately after all parietal ablations. Later knee jerks may become hyperactive, but resistance to passive manipulation never becomes increased. (Authors' abstr.)

Somatic and Autonomic Reflexes in Spinal Monkeys.

Spinal cord lesions were made in 14 monkeys. In 9 animals transections were performed at various levels, and observations made relative to the rate and extent of return of somatic and autonomic functions below the level of the lesions. In 3 monkeys the effect of partial lesions of the spinal cord was noted. In 2 such animals observations were made relative to the effect of transverse cord lesions after bilateral lumbar sympathectomy. The term "shock" applies equally well to the autonomic as to the somatic systems following complete lesions of the cord. The return of somatic reflexes precedes the re-establishment of such autonomic functions as piloerection, sweating, and vasoconstriction. Although the autonomic functions return after spinal transection, they do not reach the same degree of efficiency that they exhibit in the normal animal. Cooling of one lower extremity in ice-water normally produces a drop in temperature in the non-immersed lower extremity, but fails to do so during the period of "shock" following spinal

transection, or for a short period of time following lumbar (preganglionic) sympathectomy. This indirect cooling response is temporarily depressed after partial lesions of the cord. (Authors' abstr.)

Nerve Activity Accompanying Fasciculation Produced by Prostigmin.

The fascicular twitching observed in animals following the administration of prostigmin is associated with antidromic nerve impulses which may be recorded from the anterior (motor) roots.

Both the fascicular twitching and the nerve impulses are abolished by small doses of curare.

Similar impulses are observed when a muscle is caused to contract by the intra-arterial injection of acetylcholine.

It is suggested that these experiments provide evidence that acetylcholine has a stimulatory effect not only on striated muscle, but on the terminal portions of the motor nerve as well. (Authors' abstr.)

Effects on Respiration, Blood Pressure and Gastric Motility of Stimulation of Orbital Surface of Frontal Lobe.

From the orbital surface of the frontal lobe in both cats and monkeys an area in the gyrus orbitalis near the olfactory tract was found to give rise upon stimuli of 1-6 V to inhibition of respiration, rise of blood pressure and decrease in the tonus of the gastric musculature. The respiratory effect was obtained nearly always in the cat and always in the monkey; the elevations of arterial pressure were higher and more consistently present in the monkey; the inhibition of tonus in the gastric muscles occurred only infrequently in the cat, but in the great majority of instances in the monkey. (Authors' abstr.)

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VOL. IX. APRIL, 1940.

PSYCHOSOMATIC MEDICINE.

VOL. II. JAN., 1940.

Studies on a Group of Children with Psychiatric Disorders. I. Electroencephalographic Studies.

There was a high percentage (68 per cent.) of abnormal electroencephalograms indicating a physiological disturbance. Apart from a large number presenting diffuse cortical dysrhythmia, 16 per cent. were found to present evidence of focal dysrhythmia.

One-third of the cases with an abnormal E.E.G. had an I.Q. below 80. The average I.Q. of the group of 7 cases with a focal dysrhythmia was 81·7

Of the group of 44 children investigated, 35 showed what the author calls an

epileptoid personality; of these, 25 showed abnormal E.E.G.'s. The writer divides his epileptoids into three groups:

1. Idiopathic epileptoids with a possible biological relationship to epilepsy as indicated by the presence of diffuse cerebral dysrhythmia.

2. Symptomatic epileptoids in which the epileptoid behaviour originates from an organic pathology of the brain indicated by focal cerebral dysrhythmia.

3. Pseudo-epileptoids in which there is a close resemblance in the behaviour to that of epileptics, but in which no abnormal E.E.G.'s was found.

G. W. T. H. FLEMING.

Disorders of Mental Functioning Produced by Varying the Oxygen Tension of the Atmosphere. I. Effects of Low Oxygen Atmospheres on Normal Individuals and Patients with Psychoneurotic Disease.

Variations in the oxygen concentration of the inspired air, beyond that to which the individual is accustomed, result in marked changes in mental functioning. This disturbance in mental functioning takes place in normal and psychoneurotic subjects exposed to inhalation of low oxygen atmospheres, and also in patients with previously existing anoxia exposed to high oxygen atmospheres. In the present study, observation of 17 medical students who breathed an atmosphere of 13 per cent. oxygen (corresponding to an altitude of 12,400 ft.) for three hours revealed marked changes in affective behaviour, with impairment of emotional control, in 59 per cent. elation and flightiness, terminating in lethargy, and in 41 per cent. mental dullness from the beginning. The " retention and recall " test in 15 of the 17 students showed a larger incidence of errors and impaired memory after exposure to 13 per cent. oxygen for 3 hours.

The patients, after inhalation of the low oxygen mixture, revealed an even more marked lack of emotional restraint, with feelings of exaggerated self-esteem and sexual preoccupations. Their mood ultimately changed from that resembling a hypomanic state to dullness and lethargy. Those patients (4 of 9) who did not show elation at the start were dull and lethargic at the beginning. The number of errors in the " retention and recall " test showed considerable variation before and after exposure to inhalation of 13 per cent. oxygen, in 5 of 9 patients being better in the low oxygen atmosphere. The greater degree of relaxation which the low oxygen atmosphere induced appeared to free them from their usual preoccupations, and make for a superficially better intellectual performance. However, in respect to insight, judgment and control of emotions, more marked impairment was uniformly present than in the student group.

The results of inhalation of 13 per cent. oxygen revealed especially that an emotional release, with diminished reason, memory and judgment, follows exposure to moderate oxygen deficiency for a three-hour period, both in psychoneurotic patients and in normal individuals.

The inhalation of high oxygen atmospheres by patients with previously existing chronic anoxia may also produce a profound disturbance in mental functioning. Irrationality, stupor and delirium may take place within three hours' exposure to 50 per cent. oxygen. When these patients become acclimatized to their increased oxygen tension, the mental disturbance disappears, frequently with the appearance of a cheerful and optimistic mental state. (Authors' abstr.)

APRIL.

RASS. STUDI PSICHIAT.

VOL. XXIV. MARCH–JUNE, 1940.

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RIV. PATOL. NERV. MENT.

VOL. LV. JANUARY–FEBRUARY, 1940.

RIV. SPER. DI FRENIAT.

VOL. LXIII. MARCH, 1939.

Deviation of Gait in Cases of Hemianopia.

The author alludes to the symptom of a lesion of the frontal lobe reported by Stenvers and others, the only symptom of which consists of a deviation to the opposite side to that of the lesion when walking with eyes open. He claims to have been able to demonstrate a similar deviation away from the cerebral focus in cases of homonymous hemianopia.

Dyschromia Cutaneopilaris of Nervous Origin.

Following an account of our knowledge of cutaneous and hair pigmentation the author describes a case of dyschromia cutaneopilaris occurring whilst the patient was suffering from a depressive state. A particularly interesting item of the discussion is the reference made to a number of well-authenticated cases of immediate blanching of the hair after shock or acute anxiety.

Hypoglycaemia Causing Convulsive Attacks Caused by Adenoma of the Insula of the Pancreas.

The pathological account of a case of spontaneous hypoglycaemia due to adenoma of the pancreatic insulae. Changes in the cerebral cortex are described concerning particularly the third and fifth strata of the area precentralis giganto-pyramidalis, Broca's area, and the area frontalis granularis.

JUNE, 1939.

On the Biology of Hysteria.

A clinical, experimental and psychological investigation of a patient with an extrapyramidal post-encephalitic syndrome, together with many neurovegetative disturbances due to a hypothalamic lesion. The patient has frequent attacks of lethargy, of catalepsy and of somnambulism with dissociation of memory, consciousness and personality. The attacks of typical psychogenic nature are bound to a hysterical mentality characterized by hypersuggestibility. The author examines the relations between the organic and the functional symptoms. He considers the subcortical theories of hysteria and formulates the following hypothesis. Hysteria and particularly the major syndromes of mental dissociation are conditioned by a congenital or acquired hyperexcitability of the hypothalamus.

A Contribution to Our Knowledge of the Relations between Epilepsy and Heart Disease.

The author, as a result of anatomical and pathological investigations on 171 epileptic patients, fails to find any relation between epilepsy and heart disease.

The Ide Colour Reaction for the Diagnosis of Syphilis.

A comparison of the Ide reaction with the Wassermann shows that it is a little less sensitive but equally specific.

Disturbances of Eye Movements in Chronic Epidemic Encephalitis.

The eye movements were examined in 41 cases of chronic epidemic encephalitis. Twenty-four of the cases showed Parkinson symptoms and 17 suffered from mental disorders without Parkinsonism. Disturbance of ocular movement occurred in both classes.

The Action of Mescalin on the Mental Processes.

Thirty cgr. of mescalin sulphate were administered to each of six subjects. Four showed euphoria, improvement of recent memory and the power of integration with some improvement of attention. In one case the drug caused depression, and in the sixth depersonalization. The author considers the drug is useless for the purpose of eliciting confessions.

Glycaemia, the Takata-Ara Reaction and the Weltmann Reaction in Insulin Therapy.

The authors studied the blood-sugar content during convulsive therapy by insulin. They cite cases in which, when coma persists in spite of sugar injection, further sugar administration fails to awake the patient, although the blood sugar is raised above normal.

The "Cerebro-stimulin" of Pope.

Pope claims to have discovered a specific substance stimulating the cerebral cortex of the frog in cerebrospinal fluid. The author does not consider the technique followed by Pope to be capable of establishing the existence of the alleged specific substance.

SCHWEIZ. ARCH. NEUROL. PSYCHIAT.

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VOL. VI. 1939.

1. Biochemistry, Physiology and Pathology.

Changes in the Brain Resulting from Depletion of Extra-cellular Electrolytes. Yannet, Herman. [*Am. J. Physiol.*, **128**, 683–9 (1940).]

Analyses of the serum and brains of animals whose extra-cellular electrolyte were depleted to varying levels are presented. The data indicate that the brain cells adjust to this depletion by releasing intracellular K in amounts proportional to the decrease in the concentration of extracellular Na. The data are consistent with the view that all the Na and probably all the Cl in the brain is diffusible.

E. D. WALTER (Chem. Abstr.).

Physiology and Pathology of the Hypophysis. II. The Temperature-regulatory Function. Nisi, Naoto. [*J. Chosen Med. Assoc.*, **30**, 1–21 (*German abstr.*, 1–2) (1940).]

In rabbits, completely hypophysectomized, or with only anterior lobe removed (A), body temperature rises much higher than in the normal animal on exposure to heat, and goes much lower on exposure to cold. In A, central pyrogenic stimulants

do not act, but peripheral stimulants like tetrahydro-β-naphthylamine or adrenaline are effective, although the response to the last drugs becomes less as time goes on. The facts that picrotoxin, so-called cold-centre stimulant, and warm-water perfusion over the heat centre, cause a marked decrease in the body temperature in A, and that heat-centre stimulant causes a drop in body temperature, may mean that the cold-centre of Meyer may be stimulated by removal of the anterior pituitary. These abnormal responses to various agents in A will return to normal if the anterior lobe is implanted or its extract is injected.

S. TASHIRO (Chem. Abstr.).

Chronaximetric Analysis of the Vasoconstrictor Effects of the Splanchnic Nerve. Chauchard, A., Chauchard, B., and Chauchard, Paul. [*Ann. physiol. physicochim. biol.*, **15**, 799–804 (1939); *cf. C.A.*, **31**, 5869[9], 6336[1].]

Stimulation of the splanchnic nerve in the dog causes a diphasic rise in blood pressure in the normal state but a lower monophasic rise after adrenalectomy. The vasoconstrictor fibres involved in the first rise in blood pressure normally have a chronaxie of 1–1·5 msec. or more and a summation time of 6 seconds. The summation time is decreased by adrenaline (I) and atropine (II), and increased by acetylcholine (III) and yohimbine (IV). The adrenalino-secretory fibres, responsible for the second rise in blood pressure, have a chronaxie of about 0·5 msec. and a summation time of 4 sec., if the adrenal has not been injured. Their summation time is decreased by I, III and IV, and increased by II; if the concentration of II is sufficiently high, the nerve may become incapable of excitation. The fact that only I affects adrenal secretion and vasoconstriction in the same direction offers new proof of the existence of two different phenomena. I, III and IV, by their action on the cells of the adrenal medulla, favour I secretion, while II inhibits it. The analogy between the salivary and adrenal secretion is pointed out.

RUTH BERGGREN (Chem. Abstr.)

Relation of Potassium to Periodic Family Paralysis. Gammon, G. D., Austin, J. H., Blithe, M. D., and Reid, C. G. [*Am. J. Med. Sci.*, **197**, 326–32 (1939).]

A rapid loss through the urine of K absorbed from the gastro-intestinal tract was found in a patient with periodic family paralysis. Water diuresis rapidly removed K from the patient, with a fall in serum K and the development of a seizure. Attacks of weakness were associated with a falling serum-K and recovery with rising values. K salts were of use in preventing as well as curing seizures.

B. C. P. A. (Chem. Abstr.).

Histidine Detection and Estimation in Urine. Racker, E. [*Biochem. J.*, **34**, 89–96 (1940).]

Histidine (I) was determined in urine by a method based on Knoop's bromine reaction with I (*Beitr. chem. Physiol. Path.*, **11**, 396 [1908]). The urine was treated with Ba(OH) to remove interfering phosphates, and then with H_2SO_4 to remove Ba. The filtrate was mixed with a 5 per cent. Na urate suspension and then with Br until an excess was present. After 10 minutes the Br was destroyed with As_2O_3 and the solution was heated with Na_2CO_3 to develop the colour. Na urate which sensitizes the test was added in excess to make all the samples uniform. Normal urines contained 2·80 mgm. 1/100 ml. with an average of 20. Higher values were not observed in the urines of melancholic patients. Pregnancy urines usually were high in I.

E. W. SCOTT (Chem. Abstr.).

Nervous Humoral Regulation. Chernigovskii, V. N. [*Uspekhi Sovremenoi Biol.*, **9**, *No.* 3, 387–433 (1938); *Khim. Referat. Zhur.*, 1939, *No.* 5, 51.]

Sympathin, which is excreted into the blood during excitation of the sympathetic nervous system, is related to, or is identical with, adrenaline. During excitation of the parasympathetic nerves acetylcholine is formed. Acetylcholine

acts only for a short time because it is split by cholinesterase. The tissues contain a supply of mediators (acetylcholine and sympathin) in the form of inactive promediators. The chemical nature of the promediators has not yet been determined.
W. R. HENN (Chem. Abstr.).

Existence of a Respiratory Neurohormone. Koppanyi, Theodore, and Linegar, Charles R. [*Science*, **91**, 297–8 (1940).]

In addition to acetylcholine, other choline derivatives, muscarine, mecholyl and doryl were assayed for their respiratory stimulating actions in atropinized animals. Muscarine and doryl (0·15–0·5 mgm./kgm. body weight) produced pressor effects and marked stimulation of respiration. Doryl (0·25 mgm. or more per kgm.) produced after a brief stimulation a secondary depression of respiration. The pressor effect of acetylcholine is not abolished by doryl. Mecholyl, except in very large doses (2·0 mgm. or more), does not produce respiratory stimulation. Atropine does not completely block the vasodilator effect of mecholyl. Only choline derivatives with a nicotine-like action stimulate respiration. The choline group in itself is not the causative agent. If effective doses of acetylcholine (0·3–1·0 mgm./kgm.) are injected into atropinized animals via the common carotid artery there occurs (*a*) a slight acceleration of respiration about 5 sec. after injection, and (*b*) the usual panting response about 15 sec. later. Conclusion: There exists a neurohumoral mechanism involving the excitation of the chemoreceptors in the carotid sinus region, which, in turn, causes reflex stimulation of respiration.
FELIX SAUNDERS (Chem. Abstr.).

The Effect of Malonic Acid on the Respiration of Nerve Tissue. Huszak, Istvan. [*Biochem. Z.*, **303**, 349–53 (1940).]

The respiration of muscle tissue is inhibited by malonate (of a given concentration) to the same extent as by 0·001 M KCN while that of nerve tissue is affected very much less or not at all. The effect of KCN on both muscle and nerve is the same. Lactic or pyruvic acid inhibits or even completely counteracts the action of the malonic acid on the nerve tissue. S. MORGULIS (Chem. Abstr.).

Arsenical Encephalopathy. II. Pathogenic Study. Tzanck, A., and Lewi, S. [*Ann. dermatol. syphilig.*, **10**, 893–906 (1939–40); *cf. C.A.*, **34**, 1742$_4$.]

A theoretical discussion of the nature of arsenical encephalopathy. Tzanck and Lewi believe the phenomenon is due to an individual intolerance of the body to the arsenical, rather than to ordinary As poisoning or to reactivation of the syphilitic process. Susceptibility is apparently related to the endocrine system, e.g. the reaction occurs especially frequently in pregnant women.
M. HORN (Chem. Abstr.).

The Cause of Reduction of the Sugar Content of the Cerebrospinal Fluid in Meningitis. Hendry, Esther. [*Arch. Disease Childhood*, **14**, 307–16 (1939).]

Three possibilities were investigated: (1) That no decrease occurs in the permeability to glucose of the blood barrier was concluded from the fact that increases in cerebrospinal fluid glucose (I) after intravenous glucose injection in non-meningitic disease were no greater than those found in tuberculous meningitis. (2) That bacterial consumption of glucose does not usually cause reduction in I was shown by incubation of normal fluid with *Staphylococcus albus* and *aureus*, meningococcus, pneumococcus, and *B. tuberculosis*, without significant drop in I. With *B. coli*, however, all I disappeared (3) That polymorphonuclear leucocytes do cause lowering of I was shown by its marked drop after incubation of normal cerebrospinal fluid and white blood cells with and without added glucose and with adequate controls, while with lymphocytes only practically no change occurred. The course taken by I in various meningitides is discussed in relation to these findings. KATHRYN KNOWLTON (Chem. Abstr.).

Cerebrospinal Fluid in Typhus. D'Ignazio, C., Lombardi, A., and D'Arcangelo, D. [*Minerva med.*, **1**, 76–81 (1940).]

The cerebrospinal fluid of 23 patients with exanthematic typhus was frequently examined. There was always hypertension. In 20 to 30 per cent. the fluid contained blood. The albumin content was about normal, from 0·20 to 0·4 per cent.; in those patients with severe disease it was increased to 0·9 and 1 per cent. There was a parallelism between increased protein concentration and positive globulin reaction.

E. S. G. BARRON (Chem. Abstr.).

Colloid Reaction in the Diagnosis of Cerebrospinal Fluid. Herrmann, Werner. [*Kolloid-Z.*, **89**, 297–301 (1939).]

The preparation of Au sol according to the Fowweather method (*cf. C.A.*, **23**, 405) is described. This sol is more easily prepared than other sols and more sensitive to pathological protein. The collargol reaction of Riebeling (*C.A.*, **32**, 5488[5]) is a valuable contribution to the research methods of colloid chemistry. The Au sol and collargol reactions have different chemical bases. They can be used to determine different pathological constituents of the cerebrospinal fluid. Both methods should be used for complete diagnosis of the cerebrospinal fluid.

FELIX SAUNDERS (Chem. Abstr.).

A Modification of the Mastic Reaction of the Cerebrospinal Fluid. Acél, Dezső. [*Orvosi Hetilap*, **84**, 115–17 (1940).]

In each of 10 small Wassermann tubes is placed 2·6 c.c. of AcOH, varying in concentration from a solution made from 88 parts N/80 AcOH and 12 parts water to a solution made from 34 parts N/80 AcOH and 66 parts water. To each tube is added 0·3 c.c. mastic solution prepared by dissolving 10 gm. mastic in 100 c.c. absolute alcohol, filtering after 48 hours, treating 1 c.c. of the filtrate with 8·5 c.c. absolute alcohol and 0·5 c.c. concentrated Sudan III solution, and adding 10 c.c. of this solution to 40 c.c. twice-distilled water. On addition of cerebrospinal fluid to the ten tubes, sedimentation occurs. The result may be read after 2–3 hours. With normal fluids, complete precipitation can be seen in each tube. The reaction is suitable for the determination of meningitis and progressive paralysis.

S. S. DE FINALY (Chem. Abstr.).

Bisulphite-binding Substances in the Blood and Cerebrospinal Fluid. Wortis, Herman, Bueding, Ernest, and Wilson, Wm. E. [*Proc. Soc. Exptl. Biol. Med.*, **43**, 279–82 (1940).]

Methods are described. The normal range of bisulphite-binding substances for human spinal fluid is 0·42–3·07, and for blood 2·0–5·7 mgm. per cent. (calculated as pyruvic acid). The determination cannot be used as an indicator of vitamin B_1 deficiency; it is often normal in various psychiatric disorders, and it is not an accurate measure of the pyruvic acid level. It is elevated after administration of paraldehyde because deproteinization of the fluids with CCl_3–CO_2H partially hydrolyses paraldehyde to AcH, which binds bisulphite in the determination.

L. E. GILSON (Chem. Abstr.).

Central Action of Gonadal Hormones Tested by Means of the Galvanic Current. Kollensperger, Friedrich K. [*Biochem. Z.*, **304**, 90–104 (1940).]

A galvanic current of a given strength passed along the length of the central nervous system of the frog causes reversible phenomena: with head toward the anode, a true narcosis; while with head toward the cathode, a generalized tonic muscle cramp. Narcotics, hypnotics and sedatives which act centrally have a synergistic effect on the former; and the stronger the drug the smaller is the strength of current required to release this reaction. On the contrary, drugs which stimulate centrally raise the galvanic narcosis and lower it for the galvanic cramp. This method has been applied to the study of gonadal hormones. After the injection of

2 or 5 mgm. per kgm. there is a temporary central sedative effect (at most 2 hours), which manifests itself by a transitory lowering of the galvanic narcosis threshold. The effect is independent of the hormone injected or the sex of the frogs used. Similar effects can be produced by cholesterol. But the gonadal hormones, as well as cholesterol, produce only a lowering of the threshold for the galvanic narcosis without altering the threshold for the galvanic muscle cramp, whereas drugs produce reciprocal effects upon these thresholds.

S. MORGULIS (Chem. Abstr.).

The Parasympathicotropic Action of Corpus Luteum Hormone and Testosterone in the Female Organism. Effkemann, G. [*Arch. Gynäkol.*, **169**, 307–16 (1939).]

Pupillary diameters of the eyes of 12 female cats (3 kgm.) were measured photographically for 3 hours following injections of morphine (0·8 mgm. per kgm.), d-pseudo-ephedrine (40 mgm. per kgm.) and atropine (0·14 mgm. per kgm.). The measurements were repeated 21 hours after intramuscular injection of either 30 mgm. progesterone or 40 mgm. testosterone. The dilatory action of the test was decreased by both hormones in the order: morphine, atropine, d-pseudoephedrine. Because of this order, the parasympathicotropic action of the hormones was thought to be working through the hypothalamic vegetative centres in the brain. Follicular hormone, on the other hand, has a sympathicotropic action.

H. P. G. SECKEL (Chem. Abstr.).

Pyruvate Oxidation in the Brain. VII. Some Dialysable Components of the Pyruvate Oxidation System. Banga, Ilonga, Ochoa, Severo, and Peters, Rudolph A. [*Biochem. J.*, **33**, 1980–96 (1939); *cf. C.A.*, **33**, 8726[8].]

The dialysis of pigeon brain dispersions for short periods greatly reduced their power to oxidize pyruvate (I). Full reactivation was obtained by the addition of inorganic phosphate plus a C dicarboxylic acid plus adenine nucleotide (II). The same was true for dispersions of mammalian brain. In the presence of the other components of the system, II not only increased the oxidative removal of I, but also made the oxidation more complete. Cozymase could replace II and in the pigeon brain was even more active. This effect of cozymase was probably due to enzymic splitting of co-phosphorylase. In rabbit brain dispersions, cozymase could replace II only when the period of dialysis had not exceeded 1·5 hours. Phosphoglycerate was oxidized by pigeon brain almost as readily as I because of its rapid conversion into I and H_3PO_4. Citrate and α-ketoglutarate were much less active than any of the C_4 dicarboxylic acids in catalysing the oxidation of I by brain dispersions. The necessity of fumarate and II for the oxidation of I by kidney cortex dispersions was shown in preliminary experiments.

E. W. SCOTT (Chem. Abstr.).

The Estimation of Vitamin B in Cerebrospinal Fluid. Sinclair, Hugh M. [*Biochem. J.*, **33**, 1816–21 (1939); *cf. C.A.*, **33**, 4625[8].]

The method previously described for blood has been applied to the assay of 1–4 ml. of cerebrospinal fluid. The vitamin in normal spinal fluid was present in the unphosphorylated form. The values for vitamin B_1 in 272 samples ranged from 0·0 to 1·3 γ/100 ml., with a mean of 0·5. Pathological samples tended to give higher values, which showed a positive correlation with the white cell count. Estimation of the vitamin in the spinal fluid has no clinical value.

E. W. SCOTT (Chem. Abstr.).

Experimental Avitaminosis of the B_2-complex Group and Pellagra of Man. Efremov, V. V. [*Acta Med. U.R.S.S.*, **2**, 622 (1939).]

The greatest resemblance between avitaminosis in rats, dogs and monkeys and in man occurred in the nervous lesions. In all the experimental animals there was

an ataxic paresis resembling the symptoms found in pellagra in man. In these animals there was a picture resembling that of subacute combined degeneration. In man and in higher animals (dog and monkey) there was also an affection of the cells of the cerebellar cortex and in the medulla. G. W. T. H. FLEMING.

Actual Vitamin C Content of Cerebrospinal Fluid of Young Infants. Bezssonoff, N., Vertruyen, H., Dietz, E., and Mehl, R. [*Compt. rend. soc. biol.*, **132**, 540–4 (1939).]

Spinal fluid from normal infants 1–12 months old contained 4–18 mgm./1 of vitamin C as determined by the methylene blue method and 3–12 mgm./1 as determined with the Bezssonoff reagent (*cf. C.A.*, **30**, 2221[7]). Dichlorophenolindophenol also gave higher values than did the Bezssonoff reagent.

L. E. GILSON (Chem. Abstr.).

Effect of Ascorbic Acid on Oxidation Processes in the Central Nervous System. I. Effect of Ascorbic Acid Reduction on Oxidation Processes in Guinea-pig Brain. Lakhno, Yu. V. [*Biochem. J. (Ukraine)*, **13**, 461–71 (*in Russian*, 471–2; *in English*, 473–4) (1939).]

The greatest intensity of oxidation processes and also of the catalase activity in the brain of the normal guinea-pig was found in the cerebellum, and less in the hemisphere and medulla. Brain oxidation processes and catalase activity in the separate brain sections of avitaminous guinea-pigs did not change by comparison with those of the central nervous system of normal animals.

B. GUTOFF (Chem. Abstr.).

Calcium and Phosphorus Contents of the Blood of Normal and Mentally Diseased Men. Satterfield, G. Howard, McKimmon, W. S., Holmes, Arthur D., and Tripp, Francis. [*J. Am. Dietet. Assoc.*, **16**, 117–23 (1940).]

The amounts of Ca and P in the blood serum of (1) 20 healthy male college honour students, of (2) 17 mentally deficient, psychotic patients, of (3) 11 mentally deficient patients without psychosis, of (4) 57 patients with dementia praecox, and of (5) 12 patients with miscellaneous mental diseases were determined. Average values for Ca and P (mgm./100 c.c.) and for Ca × P were, respectively: (1) 10·65, 3·93, and 41·85; (2) 10·02, 3·55 and 35·57; (3) 10·65, 3·93, and 41·85; (4) 10·22, 3·67, and 37·51; and (5) 9·55–11·20, 2·46–5·43, and 24·82–59·73. Conclusion: The Ca and P contents of the blood of nearly all of the patients with mental diseases were within normal limits. E. CURZON (Chem. Abstr.).

Lipoids of Human Brains during Development. Schuwirth, K. [*Z. Physiol. Chem.*, **263**, 25–36 (1940).]

Analyses of human brain lipoids by the methods of Klenk (*C.A.*, **34**, 2060[4]) are presented. These include foetal, newborn, child and aged. The water and water-soluble extractives diminish with age, while the fat plus cholesterol and ether-soluble glycerophosphatides and cerebrosides increase (*cf.* MacArthur and Doisy, *C.A.*, **14**, 1706). Foetal and newborn brains contain no sphingomyelin, but do contain ether-insoluble glycerophosphatides. The latter are absent from aged brain. In the children's brains these two fractions could not be separated.

MILTON LEVEY (Chem. Abstr.).

Acid-soluble Phosphates in Rabbit Brain. Omura, S. [*Fukuoka Acta Med.*, **32**, 55–8 (1939).]

The cerebral hemispheres contain the following amounts of phosphate: Inorganic PO_4---, 0·0432 per cent.; creatine phosphoric acid, 0·0040 per cent.; $H_4P_2O_7$, 0·0066 per cent.; residual P, 0·0336 per cent. After injections of Na phenobarbital for 3–6 days, the inorganic PO_4--- and creatine phosphoric acid are decreased, and

the $H_4P_2O_7$ and residual P are increased. After daily injections of sulphonal for 5–8 days the changes are similar, save that the inorganic PO_4 – – – retains its normal value. After injections of insulin and glucose, the inorganic PO_4 – – – increases, the other substances showing no change. After insulin alone, the inorganic PO_4 – – – increases, and $H_4P_2O_7$ decreases. B. C. P. A. (Chem. Abstr.).

The Behaviour of the Blood-liquor Barrier in Experimental Poliomyelitis. Kasahara, Mitio, Kakusui, Tosio, and Nan, S. S. [*S. Kinderheilk*, **60**, *No.* 4, 3 pp. (1938); *Collected Papers Faculty, Med., Osaka Imp. Univ.*, 1938, 31–3 (*Pub.* 1939).]

Fuchsin S solution (1·0 to 3·3 c.c. of a 2 to 10 per cent. solution per kgm. body weight) was intravenously, and in part intramuscularly, injected into monkeys. Forty to 80 minutes later the cerebrospinal fluid was withdrawn suboccipitally, acidified with AcOH, and then analysed colorimetrically for the concentration of dye present. After several weeks, 0·5 c.c. of a spinal cord emulsion containing poliomyelitis virus was intracerebrally injected, and in the preparalytic and paralytic stages experiments on dye concentration were conducted as before. In the controls, the range of concentration was from 0·00002 to 0·0003 per cent., and after infection, from 0·00020 to 0·002 per cent. The passage of the dye into the cerebrospinal fluid was about 3 to 20 times more pronounced in the paralytic stage, and 1·7 to 3 times more pronounced in the preparalytic stage, as compared to normal monkeys. Conclusion: The permeability of the meninges in experimental poliomyelitis is increased even in the early stages. MAURICE M. RATH (Chem. Abstr.).

The Plasma Proteins in Epilepsy. Eef-Olofsson, R. [*Acta Med. Scand.*, **103**, 111–17 (1940) (*in German*).]

The total plasma protein content in epileptic patients is, on the average, somewhat higher than in normal persons—6·40 as compared to 6·19 per cent., with a shift of the mean toward a higher value. There is no difference in fibrin (0·26 and 0·24 per cent.) or albumin (4·09 and 4·08 per cent.), but the globulin content is greater (2·04 and 1·88 per cent.) in the epileptic patients. The albumin/globulin ratio is, therefore, somewhat lower in epileptic patients.

S. MORGULIS (Chem. Abstr.).

2. Pharmacology and Treatment.

The Distribution of Barbital in the Brain in a Case of Acute Barbital Poisoning. Zwikker, J. J. L., and Steenhauer, A. J. [*Pharm. Weekblad*, **77**, 2–5 (1940).]

Analysis of the various organs of the body of a woman whose death was attributed to barbital (I) indicated 66 mgm. I in 150 gm. of the contents of the stomach, 46·4 gm. I in 227 gm. liver (20·4 mgm. per cent.), 31·2 gm. I in 100 gm. kidney (31·2 mgm. per cent.), 12·8 mgm. I in 67 gm. blood (19·0 mgm. per cent.), 15·2 mgm. I in 79 gm. prosencephalon (19·7 mgm. per cent.), 20·2 mgm. I in 109 gm. mesencephalon (18·5 mgm. per cent.), and 28·4 mgm. I in 137 gm. rhombencephalon (20·8 mgm. per cent.). Since the distribution of I in the various parts of the brain was quite uniform, this finding supports the view of Koppanyi (*C.A.*, **29**, 228[4], 7496[4]) that the action of barbital is not restricted to the mesencephalon, and is opposed to the view of Keeser (*C.A.*, **30**, 3078[1]; **32**, 7120[4]).

W. GORDON ROSE (Chem. Abstr.).

Barbiturates. XXIV. Pharmacology of 5-sec-Amyl-5-β-Bromoallylbarbituric Acid. Hazleton, Lloyd W., Koppanyi, Theodore, and Linegar, Charles R. [*J. Am. Pharm. Assoc.*, **29**, 49–56 (1940).]

The 50 per cent. fatal dose of sigmodal sodium (I) for rabbits is 40 mgm. (intravenous) and 90 mgm. (rectal), and for dogs it is about 35 mgm. (intravenous). It is a

depressant of the central nervous system producing, in appropriate doses in rabbits, loss of righting reflexes, motor paralysis, muscular relaxation, and a deep sleep from which the animals cannot be aroused; in the dog it produces true surgical anaesthesia. The onset of action of I after intravenous injection is immediate in all animals, and after rectal administration it occurs within a few minutes in rabbits. The rate of essential elimination of I was found to be 37–47 per cent. of the average fatal dose (15–19 mgm.) per hour as determined by two different methods, the following one of which is new: The maximum dose which permits rabbits to maintain normal posture unsupported and to retain approximate normal motor activity is determined; after ascertaining the average sleeping time of all animals that survived the average fatal dose (i.e. until they regained the stage in which normal body posture was again maintained), the essential elimination of the compound is calculated by the following formula: (50 per cent. fatal dose — maximum dose of hypnotic permitting normal motor activity) /(sleeping time in hours) = essential elimination in mgm. (per kgm.) per hour. A method for estimating sleeping time after rectal, oral and other routes of administration applying the data derived from the intravenous essential elimination determination is described. I given intravenously is a circulatory and respiratory depressant comparable to other short-acting barbiturates. The blood pressure and respiratory rate in animals anaesthetized with I are similar to those obtained under other anaesthetic agents. Even in fatal doses, I does not abolish the cardiac slowing from faradic stimulation of the vagus; the cardiac and vasomotor responses to autonomic drugs are unchanged. I has definite anticonvulsant properties, and, conversely, a central stimulant such as metrazole antagonizes its depressant effects. Large doses of antipyrine do not deepen I narcosis or alter the recovery time. About one-fifth of the dose of I (or its end products) is excreted in the urine within 48 hours following administration.

A. PAPINEAU-COUTURE (Chem. Abstr.).

The Estimation of Barbiturates in Blood. Levvy, G. A. [*Biochem. J.*, **34**, 73–7 (1940).]

The blood (20 ml.) was mixed with 2 gm. of NaH_2PO_4 and then stirred with 40 gm. of anhydrous Na_2SO_4. When the mixture was dry it was ground and extracted with a mixture of ether and petroleum ether (1 : 1) in a Soxhlet for 2·5–3 hours. The extract was then shaken with a charcoal–MgO mixture (Merck's ultracarbon 3, MgO 1) to remove phospholipins. The extract was then filtered and evaporated. The residue was taken up in 2–10 ml. of $CHCl_3$. To 2 ml. of this solution were added 0·1 ml. of 1 per cent. Cobalt acetate in absolute MeOH and 0·6 ml. of 5 per cent. isopropylamine in absolute MeOH and the colour was compared with a standard prepared similarly. Recoveries of added barbituric acids ranged from 83 to 124 per cent.

E. W. SCOTT (Chem. Abstr.).

The Effect of Barbiturates on Digestive Secretion. Coffey, Robert J., Koppanyi, Theodore, and Linegar, Charles R. [*Am. J. Digestive Diseases Nutrition*, **7**, 21–3 (1940).]

Barbiturates in large hypnotic and anaesthetic doses in dogs produce a reduction of the gastric and pancreatic secretions, with a prompt return to normal flow after hypnotic doses, and a delayed return after anaesthetic doses. Barbiturates are excreted in the pancreatic juices in very small amounts, and the maximum postcibal excretion in the gastric juice is approximately 5 per cent.

EDWARD EAGLE (Chem. Abstr.).

The Comparative Mental Efficiency of a Drug Addict Group. Partington, J. Edwin. [*J. App. Psych.*, **24**, 48–57 (*February*, 1940).]

The average mental efficiency of 156 drug addicts, measured with the Babcock test, was — 2·28. The group was significantly below normal in learning and motor

tests, but not in repetition tests. Also, old addicts were significantly poorer than young addicts on learning and motor tests, but not on repetition tests. There was only a small and insignificant negative correlation between efficiency and duration of addiction. M. B. BRODY.

Pulmonary and Urinary Excretion of Paraldehyde in Dogs. Defandorf, James H. [*Am. J. Med. Sci.*, **197**, 834–41 (1939).]

Following rectal injection of 1·8 gm. /kgm., excretion rose to a maximum within 3 hours and fell rapidly after 7 hours. During 7 hours, only 2·8 per cent. of the amount administered was excreted by the lungs and 1·3 per cent. in the urine. The amount in the urine was proportional to urine volume; its elimination by this route can therefore be increased by diuresis. Paraldehyde forms the increment in the increase of non-fermentable reducing substances previously observed in the urine. FERRIN B. MORELAND (Chem. Abstr.).

Pharmacology of the Extrapyramidal System. I. Action of Harmine in Cats with an Intact Nervous System. Beer, A. G. [*Arch. exptl. Path. Pharmakol.*, **193**, 377–92 (1939).]

The motor changes from harmine poisoning appear to be due to direct stimulation of the extrapyramidal system.

II. Action of Harmine in Cats Minus Neocortex. Ibid. 393–407 (1939).

Harmine acts the same in the decerebrate as in the intact animal; this substantiates the direct extrapyramidal point of attack.

J. PINCHACK (Chem. Abstr.).

Effects of Drugs on Vegetative Centres. III. Haas, H. T. A. [*Arch. exptl. Path. Pharmakol.*, **192**, 350–60 (1939); *cf. C.A.*, **34**, 2931[6].]

Paraldehyde reduces the fall in temperature and the rise of blood-sugar level that occurs after intracisternal injection of picrotoxin in rabbits. Paraldehyde has similar effects on the response to pilocarpine, but not on that to acetylcholine, ergotamine or ergometrine. Paraldehyde counteracts the effects of adrenaline (intracisternal or intravenous application) on blood sugar and leucocyte count.

B. C. P. A. (Chem. Abstr.).

Vitamin E in the Treatment of Muscular Dystrophies and Nervous Diseases. Bicknell, Franklin. [*Lancet*, **1**, 10–13 (1940).]

Patients, chiefly children, with muscular dystrophies and amyotrophic lateral sclerosis showed improvement after treatment with 0·5 oz. fresh, dried whole-wheat germ twice daily for 6 weeks or more. The diseases appear to be caused by vitamin E deficiency. Normal human diets may be poor in vitamin E.

E. R. MAIN (Chem. Abstr.).

Passage of Prontosil from the Blood into the Cerebrospinal Fluid. Kasahar, Mitio, and Tarumi, Masayasu. [*Klin. Wochenschr.*, **17**, 354–5 (1938); *Collected Papers Faculty Med., Osaka Imp. Univ.*, 1938, 21–2 (Pub. 1939).]

Acute and chronic meningitis were experimentally produced in rabbits. After prontosil (2 c.c. of 2·5 per cent. solution per kgm. body weight) was intravenously injected it was determined colorimetrically in the cerebrospinal fluid. Whereas in normal rabbits there was only a very minute trace of prontosil in the fluid, the concentration in rabbits with meningitis varied from 0·374 to 1·140 mgm. per cent.

MAURICE M. RATH (Chem. Abstr.).

Chemotherapeutic Studies in the Treatment of Meningococcal and Pneumococcal Meningitis. Chopra, R. N., de Monte, A. J. H., Chatterji, B. C., and Gupta, S. K. [*Indian Med. Gaz.*, **75**, 1–7 (1940).]

The mortality rate in 12 cases of meningococcal meningitis treated orally with diaminodiphenyl sulphone glucoside was 41·7 per cent. In 12 cases treated with anti-meningococcal serum the mortality was 75 per cent. In 22 cases treated with serum and drug the mortality was 27·3 per cent., while the mortality in the corresponding control series (serum alone) was 60 per cent. in 20 cases. In 7 cases of pneumococcal meningitis the mortality after treatment with the drug was 100 per cent. When septicide (sulphanilamide) was given orally to 10 meningococcic meningitis cases the mortality was 40 per cent. Two of 3 cases of pneumococcic meningitis given septicide died. C. RIEGEL (Chem. Abstr.).

Antinarcotic Substance in the Normal Serum of Rabbits. Komao, Ito. [*J. Chosen Med. Assoc.*, **29**, 2639–63 (*German abstr.*, 160–1) (1939).]

The serum of the normal rabbit contains antichloral hydrate (A) and anti-Mg (B) substances as tested with mice, but no antiluminal (C). Normal serum plus anterior pituitary hormone (hypophorin) produces C effect. In serum of pregnant rabbits, A is still present, but not B, while C appears. The serum of the animals freed from sex, pituitary or thyroid glands loses all. If pinealectomized, the serum loses B, but C appears. Parathyroidectomy causes a loss of only B. When the reticulo-endothelial system is stimulated, the rabbit loses both A and B, but produces C, while with blockade of the system, all antinarcotic substances are lost.

S. TASHIRO (Chem. Abstr.).

Pervitin as a Means of Increasing Efficiency. Lehmann, G., Straub, H., and Szakall A. [*Arbeitsphysiol.*, **10**, 680–91 (1939).]

With three men, 21–26 years old, observations were made during rest and work (bicycle ergometer) of body temperature, pulse rate, blood pressure, ventilation rate, O_2 consumption, and R.Q., with and without 5–15 mgm. pervitin (1-phenyl-2-methylaminopropane). In some experiments the subjects worked with constant load and speed, in others with automatically increasing load, until exhausted. No changes in metabolism were observed after pervitin administration either during rest or work. At times considerably more work was performed with, than without, pervitin. After work continued to exhaustion, the efficiency was lowered considerably more when the subjects had received pervitin than when they worked without it. The subject without pervitin discontinued work shortly before reaching the limit of maximum O_2 absorption, whereas the subject with pervitin could work to the limit of maximum efficiency. For workmen and sportsmen working to the limit of capacity, pervitin is dangerous because it suppresses the subjective limits of exhaustion, and leads to consumption of reserves of strength normally retained by the organism as protection against too great exhaustion.

T. M. CARPENTER (Chem. Abstr.).

Influence of Pervitin on Some Psychic and Psychomotor Functions. Graf, O. [*Arbeitsphysiol.*, **10**, 692–705 (1939).]

With four men (two of them blind) a study was made of psychic and psychomotor functions during mental arithmetic, stringing of pearls, and riding a bicycle ergometer, with and without doses of 9–15 mgm. of pervitin (1-phenyl-2-methyl-aminopropane). For comparative purposes, the observations with and without pervitin were made on the same day. The pervitin eliminated the feeling of fatigue and inhibitions and led to increased activity and feeling of efficiency. It lessened the ability to concentrate, but acted favourably on efficiency because it lowered the too high tension of attentiveness which, with fine work, leads to disturbance in bodily movements. Marked euphoria was lacking. The effect of

pervitin is variable and seems to depend considerably on the initial condition under which it is given. Pervitin combined with caffeine has a potent effect in increasing the stimulus to an unpleasant degree. Graf cautions against the use of pervitin except when specially indicated.

T. M. CARPENTER (Chem. Abstr.).

Axon Reflex Responses to Acetylcholine in the Skin. Rothman, Stephen, and Coon, Julius M. [*J. Investigative Dermatol.*, **3**, 79–97 (1940).]

The goose-flesh elicited by acetylcholine (I) occurs by virtue of its nicotine-like action. By eliciting sweat secretion with intradermal injection of I two effects can be distinguished: (*a*) a direct action on the sweat glands (muscarine-like effect), and (*b*) an indirect action through an axon reflex mechanism (nicotine-like effect). Drugs with nicotine-like action elicit a cutaneous vasoconstriction which may be the result of an independent axon reflex or may be associated with the pilomotor action of these drugs. PHILIP D. ADAMS (Chem. Abstr.).

Nature of the Pilomotor Response to Acetylcholine; Some Observations on the Pharmacodynamics of the Skin. Coon, Julius M., and Rothman, Stephen. [*J. Pharmacol.*, **68**, 301–11 (1940); *cf. C.A.*, **34**, 519⁷.]

Intracutaneous injection of very diluted solutions of acetylcholine and other drugs with a nicotine-like action caused a strong, transient pilomotor activity in the vicinity of the injection. In human skin and in the tail of the cat this response was abolished by sympathetic nerve degeneration, remained active in areas anaesthetized by nerve block and could be elicited in extirpated pieces of skin. Local anaesthetics, in dilutions as high as 1 : 200,000, inhibited the reaction. Pitressin and histamine had no inhibitory action. The pilo-erection is apparently effected through an axon reflex involving the terminal ramifications of the post-ganglionic sympathetic fibres supplying the pilomotor muscles. Preliminary observations indicate an accompanying axon reflex involving similarly the terminal branches of the nerves supplying the sweat glands.

L. E. GILSON (Chem. Abstr.).

Effect of Testosterone on Serum Lipides in Schizophrenia. Randall, Lowell O. [*J. Biol. Chem.*, **133**, 137–40 (1940); *cf. C.A.*, **33**, 7901³.]

The injection of testosterone propionate during a period of 3 weeks into 9 schizophrenic subjects produced a continuous rise in serum lipides followed by a return toward the initial level after medication. Sesame oil injections had no significant effect in 10 subjects. It is possible that the male sex hormone affects the low lipide metabolism of schizophrenic individuals by an indirect action on other glands of internal secretion. A. P. LOTHROP (Chem. Abstr.).

Biochemical Studies of Insulin Shock. III. Behaviour of Some Soluble Phosphorus Fractions in Muscular Tissues. Romeo, Filippo. [*Riv. patol. sper.*, **22**, 423–36 (1939); *cf. C.A.*, **34**, 1381⁵.]

In rabbits, after large intravenous injections of insulin, there was a diminution of pyrophosphates, moderate increase of total P and a definite increase of inorganic P and phosphocreatine. HELEN LEE GRUEHL (Chem. Abstr.).

Availability of Various Substrates for Human Brain Metabolism during Therapeutic Insulin Shock. Wortis, Joseph, and Goldfarb, Walter. [*Science*, **91**, 270–1 (1940).]

The relative availability of various substrates for brain metabolism was determined by administering them intravenously during therapeutic insulin shock. The effect of the various substrates on the clinical state of the patient was observed.

Simultaneously, the O, glucose and lactic acid uptake of the brain was estimated from analyses of the arterial and jugular blood. In schizophrenics glucose is readily available to the human brain, lactic acid is not metabolized to any significant degree, and pyruvic acid and alcohol are not metabolized at all.

FELIX SAUNDERS (Chem. Abstr.).

Pharmacologic Modification of the Metrazole Convulsion. Rosen, Samuel R., Ziegler, John B., and Cominole, Bruce. [*J. Am. Pharm. Assoc.*, **29**, 164–6 (1940).]

A standard dosage of β-erythroidin-HCl, about 4 mgm. per kgm., markedly reduced the intensity of the metrazole seizure in dogs. The duration of the convulsion was variable, but in the more prolonged instances there were pauses between brief clonic seizures; in general, the duration appeared to be decreased. Data are presented proving that β-erythroidin has a paralytic action on animals that have received an otherwise convulsant dose of metrazole. No untoward side reactions, such as faecal vomiting or defaecation, were observed.

A PAPINEAU-COUTURE (Chem. Abstr.).

Pharmacologic and Pathologic Effects of Repeated Convulsant Doses of Metrazole. Whitehead, Richard W., Neuburger, Karl T., Rutledge, Enid K., and Silcott, Wm. L. [*Am. J. Med. Sci.*, **199**, 352–9 (1940).]

Contrary to findings of certain other investigators, it is found that convulsant doses of metrazole may lead in dogs and rabbits to organic pathological changes, especially in the cerebral cortex. More or less complete necrosis of the nervous parenchyma is observed in small circumscribed areas. Other changes include mild tubular degeneration in the kidneys, scattered haemorrhages in the lungs and generalized visceral congestion. The cerebral changes are attributed to the anoxia produced by vascular spasm and by the anoxaemia resulting from the convulsions. Human cases are cited showing correlative changes.

FERRIN B. MORELAND (Chem. Abstr.).

Failure of Hypnotic and Convulsive Agents to Alter the Course of Experimental Poliomyelitis. Jungeblut, Claus W. [*Proc. Soc. Exptl. Biol. Med.*, **43**, 464–8 (1940).]

Neither narcotic doses of phenobarbital nor production of systemic shock by insulin or metrazole influenced the course of experimental poliomyelitis in monkeys.

L. E. GILSON (Chem. Abstr.).

The Action of Enterally and Perlingually Administered Metrazole. Kuschel, H. [*Arch. exptl. Path. Pharmakol.*, **193**, 330–1 (1939).]

The detoxicating action of metrazole on Na evipan was studied in cats with various routes of administration. Metrazole is absorbed much the same when repeated doses are given under the tongue, swallowed or injected intravenously. The oral mucosa is more permeable to it than the gastro-intestinal.

J. PINCHACK (Chem. Abstr.).

Elimination of Parenterally Administered Metrazole from the Organism. Hinsberg, K. [*Arch. exptl. Path. Pharmakol.*, **192**, 90–5 (1939); *cf. Esser and Kuhn, C.A.*, **27**, 5815.]

An improved method of extracting metrazole from organs is based on precipitating the $CHCl_3$-extracted material with phosphotungstic acid in the presence of 12·5 per cent. HCl. The difficultly soluble product of constant weight obtained is decomposed and the metrazole in the filtrate precipitated by sublimate and its

m.p. determined; experimental error was about 2 per cent. With this method no more than 5·2 per cent. of the injected metrazole could be recovered from the organs of guinea pigs. The drug was found in the intestine and faeces, but was too firmly combined in the latter to be detectable.

J. PINCHACK (Chem. Abstr.).

Detoxication and Excretion of Benzedrine. Beyer, Karl H., and Skinner, J. T. [*J. Pharmacol.*, **68**, 419–32 (1940).]

A new method for the determination of benzedrine in urine is described. The benzedrine is coupled with diazotized p-nitrobenzene and a colour developed by adding NaOH. Benzedrine seems to be completely absorbed from the digestive tract, but only about 50 per cent. of it appears in human urine in the 48 hours after ingestion. Experiments with dogs indicate that part of it is detoxicated in an unknown manner in the liver. L. E. GILSON (Chem. Abstr.).

Benzedrine Sulphate and the Duration of the Resistance to Acute Anoxaemia. Binet, Le, and Strumza, M. V. [*Bull. mém. soc. méd. hôp. Paris*, **55**, 1264–7 (1939); *cf. C.A.*, **32**, 3822[9]; **33**, 236[1], 737[7].]

The period of resistance of chloralosed dogs to anoxaemia when breathing an artificial gas mixture of normal pressure but containing only 2·4 per cent. O was markedly increased by intravenous injections of 0·025–18 mgm. benzedrine sulphate (I)/kgm.; the optimum dose, 0·25–4 mgm. I/kgm., could double or treble this period of resistance. In non-anaesthetized guinea-pigs in low-pressure chambers, in which the O did not exceed 3·4–4 per cent., the interval before respiration failed was perceptibly prolonged by intraperitoneal injections of 0·2–0·4 mgm. I/100 gm. body weight. After treatment with I the marked asthenia and other symptoms, ordinarily observed in guinea pigs at a barometric pressure of 230 mm. Hg, did not appear until the pressure fell to 142–5 mm. Hg. Intravenous injections of 0·3–5 mgm. I/kgm. into dogs resulted in the rapid disappearance of the deep coma following revival from the syncope produced by living in an atmosphere of 4 per cent. O in the low-pressure chamber. The injurious effects of 10 mgm. morphine-HCl or 0·5 mgm. scopolamine on the respiration were suppressed by 0·05 mgm. I.

RUTH BERGGREN (Chem. Abstr.).

The Reciprocal Pharmacologic Effects of Amphetamine (Benzedrine) Sulphate and the Barbiturates. Meyerson, Abraham. [*New Eng. J. Med.*, **221**, 561–4 (1939).]

The undesirable effects arising from the use of large doses of barbiturates in treatment of epilepsy, depressions and other disturbances can be in part or wholly counteracted by small doses of amphetamine sulphate (I). Similarly, the effects of large doses of I can be mitigated by small doses of barbiturates.

E. R. MAIN (Chem. Abstr.).

The Effect of Amphetamine (Benzedrine) Sulphate and Paredrine Hydrobromide on Sodium Amytal Narcosis. Myerson, Abraham, Loman, Julius, Rinkel, Max, and Lesses, Mark F. [*New Eng. J. Med.*, **221**, 1015–19 (1939).]

The narcosis produced by intravenous administration of Na amytal is prevented or counteracted by amphetamine sulphate, but is unaffected by paredrine p-hydroxy-α-methylphenylethylamine). E. R. MAIN (Chem. Abstr.).

Pharmacological Action on the Vegetative Centres. II. Haas, Hans T. A. [*Arch. exptl. Path. Pharmakol.*, **192**, 117–30 (1939); *cf. C.A.*, **33**, 8787[3].]

The influence of pilocarpine (I), adrenaline (II) and ergotamine (III) on the vegetative centres was demonstrated by their ability to decrease the acetylcholine

(IV) content of the brain stem and cortex of eserinized leeches. This decrease was apparent with large doses of I and II and small doses of III given intracisternally; IV, itself, was inactive. Neither I nor III was active intravenously, as was II.

III. Ibid., 350–60.

The study was continued with intracisternal or intravenous injections of I, II, IV and picrotoxin (V), and intravenous injections of III or ergometrine (VI) in rabbits previously subcutaneously injected with paraldehyde (VII) or intravenously with atropine. The direct central action of I, II and V and the highly improbable one of III, IV and VI were indicated by the fact that VII reduced the fall in temperature and rise in blood sugar after I and V, but not after III, IV and VI, and that it counteracted the effect of II on blood sugar and leucocytes.

J. PINCHACK (Chem. Abstr.).

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Part I.—Original Articles.

INVESTIGATIONS INTO THE SIGNIFICANCE OF THE ENDOCRINES IN INVOLUTIONAL MELANCHOLIA.

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(Received August 20, 1940.)

THE question whether involutional melancholia in females can be regarded as a distinct form of mental illness representing a reaction to bodily changes following the menopause has been amply discussed. It has been held by some that such a melancholia is no more than one phase of the manic-depressive psychosis (1, 2). Others hold the opposite view and justify it on statistical and clinical grounds (3).

The conclusion that forms of mental illness which have their origin at the time when the body is undergoing involutional changes are occasioned by these changes themselves is scarcely justified unless the nature of the involutional changes is thoroughly understood.

The investigations recorded in this paper have been directed towards the elucidation of these changes, and to determining in what measure they contribute to mental illness.

Of the total female population, the majority pass through a period of involutional changes without mental suffering beyond that occasioned by certain well-known somatic disturbances. Only a small minority of women enter mental hospitals at or following the menopause on account of mental illness.

It is clear that the menopause can only be one of several factors, varying in importance in individuals, which may be responsible for the so-called involutional melancholia. It seems fair to attribute some psychogenic importance to the menopause, even in cases subject to recurrent attacks of insanity, where a prolonged and severe melancholic illness has developed coincidentally with the appearance of menstrual irregularities.

Cases of involutional melancholia have been treated in hospitals for many years by endocrine extracts, either so-called polyglandular preparations or pure hormone, on the assumption—apparently—that a correction of the endocrine balance would result from such treatment. Precise indications for hormone treatment have been no more clearly established than the endocrine result aimed at, for quite evidently no patient could be restored to the state of endocrine functioning that existed before the menopause.

Results have in general been discouraging. Many papers testify to this effect, and workers have expressed the opinion that the results of hormone treatment are so unreliable that the treatment is not justified (4, 5). The issue is confused. The empirical method of treatment has, it may be fairly stated, proved of value to the gynaecologist or in extra-mural practice, in the correction of somatic symptoms and their immediate mental sequelae; but these claims in themselves give no promise of success where a grave psychosis has obscured the physical symptoms of a menopausal disorder.

Various other factors contribute to the unsatisfactory position of hormone treatment at present. Until recently the cost of endocrine extracts was too high to admit of their prolonged use in adequate doses in the average mental hospital, and the extracts themselves were not necessarily biologically standardized.

In this paper less importance has been attached to therapeutic than to biological results. The interdependence and interaction of body hormones is so extensive that the endocrine factor in involutional melancholia is more likely to be complex than simple. We have endeavoured to classify endocrine abnormalities in a systematic way, and to ascertain whether there is a type of involutional melancholia in which an endocrine dysbalance is a primary cause, and if types of dysfunction exist the correction of which will lead to amelioration of the mental state. In order to do so, we have examined the response of certain individuals in our series of patients to follicular and other hormones. In assessing the nature of the response, we have been concerned only with a change or passing of symptoms, sufficiently marked to justify being associated with the hormone administered. Although therapeutic conclusions might be drawn from some of our results, we wish to emphasize that they are recorded solely to indicate the immediate response to a form of hormone administration.

We feel deeply our responsibility in making any claims for or against therapy in a field that is so complicated and about which there is so little agreement. The true results of treatment are difficult to evaluate in melancholic illnesses,

where the possibility of spontaneous recovery has always to be borne in mind.

Our investigations are still proceeding as the case material grows, and it is hoped that they will show more conclusive results when the number of patients examined is large enough to justify definite statements.

The case material consists entirely of in-patients of the Bristol Mental Hospital. It has been pointed out that there appears to be a higher incidence of involutional melancholia in rural than in urban districts, thereby pointing to the aetiological importance of environment (3). In assessing the value of statistics, it should be remembered that women of the working class, who usually have heavy responsibilities at home, especially if married, are unlikely to enter hospital unless seriously ill. Our case material, therefore, probably presents the most severe examples of the illness, and our results cannot fairly be compared with those recorded by out-patient clinics, private hospitals, and nursing homes. In addition, the average working-class woman may have been subjected to greater stress and strain and physical hardships throughout her life than the more well-to-do patient—an effect which must be of some importance from a psychological as well as from a physical point of view.

It is the impression of the writers that depressive illnesses of whatever origin are particularly common amongst the female population of the Bristol Mental Hospital, and if this is so, a special environmental or local constitutional factor may be at work.

The case material consisted of 30 female patients who showed symptoms of depressive illnesses of varying severity, with certain individual differences, associated with the menopause or involutional state, and who seemed to present the clinical picture of involutional melancholia. There was a history of previous attacks of depression in 4 cases only. In 2 other patients mild attacks of depression occurred when menstrual irregularities first made their appearance, and this initial illness was followed by a degree of recovery, not complete, with a relapse in a few months to a state of severe depression necessitating hospital treatment.

Therefore, 26 of the 30 cases of depression studied could not have been regarded as belonging to the manic-depressive psychosis, and in these cases the menopause may have been the chief factor of influence. In the remaining 4 cases, although they belonged to the manic-depressive psychosis, the present depression seemed to be so closely associated with the menopause that the menopause could be regarded as of aetiological importance.

Examination of a number of patients showed that in not all cases were the same symptoms of endocrine dysfunction prominent. An attempt was therefore made to group all patients according to the most salient features of any endocrine abnormality. The patients seemed to fall into one of the four groups to be described below. It must be stressed, however, that such a grouping is

in itself rather inexact and that overlapping of types probably occurs. The criteria adopted for the grouping of patients were as follows :

Type 1 : Pure Hypo-ovarian.

Patients in this group showed a disturbance or cessation of menstrual function. The body weight was not reduced, and more usually fat was found to be increased especially in the region of the thighs, lower abdomen and feet. Positive striae, indicative of considerable increase in body weight, were sometimes seen. There was no alteration in the distribution or quantity of hair, nor in the texture or condition of the skin. Somatic symptoms of the nature of hot flushes and giddiness were usually complained of.

Type 2 : Hypo-ovarian Combined with Hypothyroidism.

Cases of this type showed menopausal menstrual irregularities, but complaints of hot flushing and giddiness were infrequent and unimportant. The thyroid was small or impalpable. The hair was reduced in quantity over the limbs and pubis, and there was some loss of hair on the head, commencing at the temples. The hair was brittle, and the skin dry and lacking in lustre. The symptoms of hypothyroidism occurred in various degrees, sometimes amounting almost to the appearance of myxoedema. The capillaries of the fingers showed the typical capillary formation of hypothyroidism. There was no marked reduction in body weight.

Type 3 : Hypo-ovarian Combined with Hyperthyroidism.

Patients of this type on the whole resembled closely those in group 1. They showed menstrual irregularities, and hot flushes and menopausal sensations in the head, neck, and body were prominent. In addition, however, there were certain signs and symptoms of hyperthyroidism. The thyroid was always full, sometimes markedly enlarged. In two cases there was a degree of exophthalmos. The skin was moist and sweaty. The pulse rate increased on slight exertion, and extra-systoles occurred. The capillaries showed the form typical of hyperthyroidism. The impedance angle showed readings characteristic of degrees of hyperthyroidism.

Type 4 : Hypo-ovarian Combined with Hypo-adrenalism.

In this type, in addition to menstrual irregularities or amenorrhoea, a prominent feature was acute loss of body weight—as much as 2 st. in a year, without evidence of concurrent physical disorder. The complexion was sallow, with sometimes a brown pigmentation, most marked round the body and nipples. There was great reduction in size, consistency, and power of muscles.

The skin was flabby and thin, showing negative striae, indicative of rapid loss of body weight. The thyroid was impalpable.

Although patients in type 1 and type 3 were fairly characteristic, those in type 4 frequently seemed to show symptoms of type 2, and in all cases that we have examined which conformed to type 4 the thyroid was very small or even impalpable. We are of the opinion that, while each of types 2 and 4 may exist as theoretical possibilities, from our material it is difficult to say with certainty whether either of these types is seen in pure form.

The agitated and non-co-operative state of a number of our patients made it impracticable to estimate the basal metabolic rate.

Of the 30 patients, 11 belonged to type 1, 4 to type 2, 7 to type 3, and 8 to type 4.

None of the patients of type 1 had had any previous mental illness; of those in type 2, 1 belonged to the manic-depressive group; of type 3, 3 patients had had previous attacks of recurrent depression; no patient of type 4 had had any previous mental illness.

Mental Characteristics of the Four Types.

It is not to be expected that with such limited case-material mental symptoms characteristic of each of these four types of glandular disturbance could be demonstrated, though certain features seemed to be more common in one group than in others. These features may be considered as follows:

Type 1.—All the patients complained of headaches, giddiness, hot flushes. They felt vaguely depressed and lacking in self-confidence. Motor and psychic agitation did not occur. Definite delusional ideas were not expressed.

Type 2.—Motor and psychic agitation were prominent in three of the four patients in this type. These three patients were very querulous, repeating over and over again self-accusations or expressions of despair. They could not be engaged in ordinary conversation. They wandered about wringing their hands, scratching their skin, or pulling out their hair. None of them complained of hot flushes, giddiness, or other well-defined somatic symptoms.

Type 3.—None of the patients showed any consistent psychological feature that could not be observed in some at least of the patients in group 1. One or two of the patients in whom the degree of hyperthyroidism was more marked exhibited a considerable amount of emotional instability, anxiety, and apprehension. On the whole, these patients gave the impression of reacting rather acutely to changes in the environment, in contrast to the isolation and retardation of patients in groups 2 and 4. Four of the patients were abnormally suspicious, and their attitude could almost have been described as paranoid.

Type 4.—The type of depression observed in patients in this group formed a marked contrast to that in group 1. In type 4 motor agitation was prominent, but to a less extent than in group 2. All these patients expressed ideas of insufficiency and ill-defined guilt. Six of the seven patients expressed

delusions relating to imagined disturbances of the alimentary tract, such as that "the bowels did not function," or that "something seemed to be moving round and round continually inside the abdomen." It was impossible to ascertain whether any physical disorder was responsible for this particular symptom, but it may be of some interest, as disturbances of the alimentary tract are a frequent accompaniment of adrenal failure. On the whole, the patients of group 4 exhibited mental symptoms very similar to those of group 2, with the notable exception that all were much less kinetic, and motor agitation was less purposeful and less violent. The asthenia and adynamism found in all patients in group 4 may be responsible for this difference.

Relative Incidence of Child-bearing in the Four Types.

Of the 30 patients, 15 had never borne children. This in itself suggests that child-bearing was not, in our series, an aetiological factor of any importance. However, upon examination of the distribution among the four types of patients who had or had not borne children, we find: Of the 11 patients of the pure hypo-ovarian type, 9 had never borne children; of the 4 patients of the hypo-ovarian with hypothyroidism type, 1 had never borne children; of the 7 patients of hypo-ovarian with hyperthyroidism type, 1 had never borne children; and of the 8 patients of the hypo-ovarian with hypo-adrenalism type, 5 had never borne children.

The total number of patients is too small to justify definite conclusions, but it is striking that of the pure hypo-ovarian type as high a proportion as 9 out of 11 had never borne children, while of the hypo-ovarian with increased thyroid activity, 6 out of 7 patients had borne children, or, disregarding the 3 patients in this group who probably belong to the manic-depressive psychosis, 3 of the remaining 4 had borne children.

Vaginal Smears.

Papanicolaou has demonstrated that smears from the vaginal mucosa provide valuable information about the state of ovarian function. He has shown that characteristic changes take place after the menopause, and that these changes can be reversed to a considerable extent by administration of oestrogenic hormone (6).

Using the technique of Papanicolaou, we have examined the vaginal smears of patients in our series, on various occasions during the course of treatment or spontaneous recovery. The results of these examinations will be seen in the accompanying table.

We have described the vaginal smears as belonging to three categories, namely:

+ in which the smear shows mucus, with squamous cornified cells.
— with no mucus and sharply-defined nucleated cells.
± a transitional stage containing elements of + and —.

Our results show that in the majority of patients, irrespective of the type to which they belong according to our series, the administration of oestrogenic hormone builds up the vaginal mucous membrane, with alteration in the picture of the smear from — to +. This phenomenon appears to be a response to oestrogenic hormone observed in the insane and the sane, and cannot be used as a guide either to diagnosis or to prognosis. The most marked degree of atrophy was observed in the vaginal smears of patients in whom the menopause had occurred several years prior to the examination.

Gonadotrophic Hormone.

The gonadotrophic action of the anterior lobe of the pituitary can be estimated by injection of unconcentrated urine into rats. The Ascheim-Zondek reaction I in our experiments indicated the excretion of more than 180 units of prolan per 1,000 c.c. of urine. It has been asserted that after the menopause and after castration in females, gonadotrophic hormone is increased in blood and urine (7, 8, 9). Injection of folliculin inhibits the production of gonadotrophic hormone (10).

We have investigated the excretion of prolan in the urine of our patients before and after treatment, and that of the untreated patients at various stages of their illness. It was considered that some correlation might exist between the gonadotrophic action of the anterior lobe of the pituitary as indicated by the estimation of prolan in the urine, and features of the mental illnesses. The findings are shown in a table.

It will be seen that increased prolan in the urine after the menopause in cases of involutional melancholia is not a constant finding. In our series it was more commonly found in the types 1 and 3, namely, hypo-ovarian and hypo-ovarian combined with hyperthyroidism. Where increased excretion of prolan occurred before treatment, with one exception it disappeared from the urine after treatment with follicular hormone.

The results shown in our small series do not enable us to say definitely how far the estimation of prolan in the urine can constitute a guide for diagnosis or treatment in involutional melancholia.

Follicular Hormone.

A number of patients were selected for treatment with follicular hormone. There were :

Type 1	. . . . .	7 patients.
,, 2	. . . . .	2 ,,
,, 3	. . . . .	5 ,,
,, 4	. . . . .	5 ,,

Type 1.—Of 7 patients treated 4 showed an immediate and consistent improvement. Of these, 3 recovered sufficiently to leave hospital and return to normal life outside, 4 still remaining in hospital at the time of writing, free from symptoms.

Of the remaining 3 patients, 1 has shown remarkable improvement throughout the whole course of treatment, and is now free from somatic symptoms and much less depressed. The other 2 patients, in whom symptoms had existed for more than two years before the commencement of treatment, have shown practically no change.

Of the 4 untreated patients in group 1, two recovered spontaneously and have left hospital; the other 2 have shown no physical or mental change.

Type 2.—None of the patients in this group, treated or untreated, have shown any change during the period of observation. Two have been treated with follicular hormone, and one of these was also treated with progestin.

Type 3.—Of the 5 patients treated with follicular hormone, 1 had had a previous mental illness. Three have left hospital and are apparently perfectly well; 2 are still in hospital, but are free from symptoms.

The 2 untreated patients in this group have both shown some slight spontaneous improvement.

Three of the patients treated in this group had a considerable degree of hyperthyroidism with exophthalmos; all 3 showed a very rapid response to treatment.

Type 4.—Five patients were treated with follicular hormone and in none of these was any improvement noted. No tendency to spontaneous remission was noted in the untreated patients.

In both group 2 and group 4 the general impression was gained that follicular hormone if anything aggravated the symptoms and increased the degree of depression and motor agitation.

Therefore, reviewing 19 cases of involutional melancholia treated with follicular hormone alone, in 10 complete or partial disappearance of symptoms was observed; improvement was noted only in patients belonging to types 1 and 3, namely, the hypo-ovarian type, and hypo-ovarian combined with hyperthyroidism.

Dosage.

With regard to dosage, three different methods were adopted, namely, high and moderate dosage by injection (combined later with oral administration if necessary), and oral administration supplemented by moderate injection.

The high dosage was 50,000 units daily for 14 days; the moderate dose was 10,000 units daily for 14 days; and the oral administration consisted of 3,000 units daily for the first week, 6,000 units for the second week, and 12,000 for the third and fourth weeks, with two injections of 10,000 units during the fourth week.

The number of patients was too small to permit of any conclusions being drawn regarding the best method of treatment, but, whichever method was employed, any significant improvement which occurred was noted during the first week of treatment. When no improvement occurred after one course of treatment, subsequent courses appeared to be ineffective.

Physical Effects of Treatment.

No unpleasant bodily reactions seemed to result from follicular hormone in any patient, although, as mentioned before, certain patients in groups 2 and 4 appeared to become more agitated. All patients gave the impression of better bodily health, and a slight flushing of the skin of the face was observed in every patient. This may indicate the physiological activity of oestrogenic hormone on the autonomic system, and probably depends upon dilatation of the small vessels of the skin. This agrees with the experimental work of Reynolds and Foster (11), who showed that intramuscular injection of oestrin produced a temporary increase in the volume of the finger, indicating an increase in the blood flow.

Body Weights.

There was no constant alteration in body weight of patients treated with follicular hormone, some showing a gain or loss of one or two pounds.

Luteal Hormone.

The failure to produce any improvement in groups 2 and 4 with folliculin suggested a trial of treatment with luteal hormone. This was administered intramuscularly to five patients, in the form of progestine, 5 mgm. daily for ten days. It was without effect upon symptoms.

Corticotrophic Hormone.

In view of the apparent hypo-adrenalism, desoxycorticosterone acetate was administered by intramuscular injections of 1 c.c. containing 5 mgm. for 20 days to one patient in group 4, in whom emaciation was most pronounced. It was without effect on the mental or bodily condition, or weight.

This patient, as well as two others of group 4, were selected for further treatment with corticotrophic hormone. It was administered intramuscularly, 1 c.c. daily (50 units) for six days, to each of these three patients.

In one patient there seemed to be some gain in strength and some slight alleviation of the mental symptoms, and there was a gain in weight of 12 lb., from 5 st. 10 lb. to 6 st. 8 lb. Unfortunately this patient developed pulmonary tuberculosis and became seriously ill, rapidly losing more than a stone in weight.

The second patient, who had failed to respond to desoxycorticosterone acetate, showed no gain in weight, but some mental change. She appeared to be less depressed, and, while formerly idle and inactive, she occupied herself with ward work. Her appetite improved and she no longer expressed ideas of unworthiness, nor the delusion that she was "not entitled to eat" which she had had for more than a year. Ten further injections of corticotrophic hormone administered one month later failed to produce any further improvement.

It is necessary to describe the third case in some detail. This patient had been confined to hospital for over two years. She had been treated with two courses of follicular hormone and small doses of dry thyroid extract. She had lost weight, and her mental and physical condition showed progressive deterioration. At the time corticotrophic hormone was administered, she was confined to bed, deeply depressed, agitated, would scarcely eat, and expressed many ideas of unworthiness, saying that she had neglected her duty and disgraced her husband and family, and that she could neither be forgiven nor recover. A remarkable improvement was observed almost immediately after the first injection of corticotrophic hormone. She became brighter, her agitation ceased, and she no longer expressed melancholic ideas.

She asked to be allowed to get up and occupy herself. She gained 5 lb. in weight in two weeks. This improvement was rapid and sustained, and she is now—six weeks after treatment—entirely free from mental symptoms. She asserts that she feels better than she has done for some years. She has been home with her family for several week-ends, and is to leave hospital shortly.

Discussion.

These investigations emphasize how complex is the whole problem of glandular changes in involutional melancholia. The assumption that an ovarian dysfunction operating by itself can be held responsible is incorrect. The evidence seems to point to a complex derangement in which the anterior lobe of the pituitary plays a considerable part.

Our investigations suggest that cases which could be described as involutional melancholia may be subdivided into four types, according to the predominating glandular disturbance.

The intimate relationship between the pituitary and the thyroid through the thyrotrophic principle may be responsible for what we have observed, namely, cases in which hypo- or hyperactivity of the thyroid co-existed with symptoms of ovarian failure.

In our series we noted that the cases which seemed to derive the greatest benefit from treatment with follicular hormone were those in which a considerable degree of hyperthyroidism existed. The administration of follicular hormone has been shown to inhibit the thyrotrophic action of the pituitary,

TABLE OF FINDINGS.

Case No.	Borne children.	Prolan. Before.	Prolan. After.	Vaginal smear. Before.	Vaginal smear. After.	Treatment.	Result.
Type 1:							
15	No	+	−	−	+	Follicular hormone	Recovery.
26	,,	+	−	−	+	,, ,,	,,
52	,,	+	+	+	+	,, ,,	,,
31	,,	−	−	±	+	,, ,,	Partial recovery.
18	Yes	+	−	−	±	,, ,,	Not improved.
49	No	−	−	+	−	,, ,,	,, ,,
53	,,	+	−	±	+	..	Improving; treatment incomplete.
23	,,	−	..	−	..	None	Recovery.
42	,,	−	..	−	..	,,	,,
56	,,	+	..	−	..	,,	Unaltered.
57	Yes	+	..	−	..	,,	,,
Type 2:							
2	Yes	+	−	−	+	Follicular hormone and progestine	Not improved.
32	,,	−	−	−	−	Follicular hormone	Ditto.
21	,,	−	−	±	±	Progestine	,,
22	No	−	−	+	±	,,	,,
Type 3:							
4	Yes	−	−	+	±	Follicular hormone	Recovery.
5	,,	−	−	−	−	,, ,,	,,
8	No	+	−	±	+	,, ,,	,,
12	Yes	+	−	−	+	,, ,,	,,
24	,,	+	−	±	±	,, ,,	,,
3	,,	−	−	−	−	None	Slight improvement.
36	,,	±	−	+	−	,,	Ditto.
Type 4:							
9	Yes	+	+	+	+	Follicular hormone Corticotrophic hormone	No improvement. Recovery.
44	No	−	−	+	+	Follicular hormone Corticotrophic hormone	No improvement. Temporary improvement.
25	,,	+	−	−	+	Follicular hormone	Not improved.
38	,,	−	−	±	±	,, ,,	,, ,,
13	,,	−	−	±	±	,, ,,	,, ,,
14	,,	−	−	±	−	Corticotrophic	Slight improvement.
34	,,	−	..	−	..	None	Not improved.
46	Yes	−	−	−	±	,,	Ditto.

and some workers have found that follicular hormone can lower the basal metabolic rate in normal guinea-pigs and hypophysectomized rats (12); the antagonism existing between thyroid and ovary has also been established in animal experiments (13).

It is possible that the impression that follicular hormone tended to aggravate the symptoms of patients in whom the thyroid function was diminished, may indicate that follicular hormone can inhibit still further an already insufficient thyroid mechanism.

In one patient, Case 14, Type 4, it should be noted, no thyrotrophic hormone could be detected in the urine.

Failure of the pituitary to supply corticotrophic hormone may be responsible for adrenal insufficiency observed in the fourth group of our cases.

Under certain conditions it may be possible to correct this insufficiency by administration of corticotrophic hormone, with a remarkable change in the physical and mental state of the patient, as occurred in Case 9. This patient may provide an example of a case of involutional melancholia in which an endocrine disorder was the primary factor of causation.

We are unable to say whether a primary disturbance of individual glands is responsible for the production of the types into which we were able to classify our patients, or whether all are derived from an original ovarian or pituitary dysfunction.

As far as we have been able to judge, arterio-sclerosis and other bodily diseases have not been operative to any extent in the patients in our series. It is possible, of course, that secondary changes in the anterior lobe of the pituitary, or even in the adrenals, may arise from vascular disease.

It is hoped that further investigations in the field of involutional states will be possible. We are of the opinion that with increasing knowledge of the functions of the anterior lobe of the pituitary, many of the difficulties of this problem will be solved. Until this is done, great caution should be observed in the choice of appropriate hormones in the treatment of complex glandular disturbances arising out of the menopause.

SUMMARY.

Certain investigations have been made regarding the state of endocrine function in 30 cases of depression occurring at the menopause.

It was ascertained that symptoms of ovarian, thyroid and adrenal dysfunction were present in different individuals in varying degree, so that the cases could be classified according to the predominating glandular disturbance. Physical and mental symptoms conforming to each type have been described.

Comment has been made on the incidence of child-bearing amongst the various types.

The excretion of prolan before and after treatment was estimated; its significance has been discussed.

Vaginal smears were examined; their value in diagnosis and treatment was considered.

The response of a number of patients to follicular, luteal, and corticotrophic hormone was tested. Favourable results with follicular hormone were observed only in patients of two groups, namely, hypo-ovarian, and hypo-ovarian combined with hyperthyroidism.

The importance of adrenal insufficiency, perhaps as a result of failure of the

corticotrophic principle in the anterior lobe of the pituitary, in certain types of involutional melancholia is emphasized.

It is pointed out that indiscriminate use of follicular hormone may be harmful if thyroid insufficiency is present.

The opinion is expressed that disturbances of the activity of the anterior lobe of the pituitary are largely responsible for the protean characteristics of involutional melancholia.

Our thanks are due to Prof. F. L. Golla, Director of the Burden Neurological Institute, through whom these investigations were made possible; and to Dr. J. J. B. Martin, Medical Superintendent of the Bristol Mental Hospital, for his interest and for permission to utilize the case material of the Bristol Mental Hospital.

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PALAEOPHRENIA: A RE-EVALUATION OF THE CONCEPT OF SCHIZOPHRENIA.

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SCHIZOPHRENIA may conservatively be listed among the greatest scourges of present-day society, yet the average citizen has scarcely heard of it.

"The etiology . . . is unsettled; its pathology unknown and its clinical limits in dispute and yet it is a more serious problem than either tuberculosis or cancer. There are twice as many hospital cases of schizophrenia as of tuberculosis. Each year not less than 30,000 to 40,000 individuals, soon after adolescence or in the first flush of manhood or womanhood, fall victims to this condition. Annually 75,000 new patients are admitted to state hospitals and at least one fourth are schizophrenics. . . . They are condemned to a veritable living death, devoid of emotional life as others savour it and barred from participation in the normal activities and affairs of living"(1).

INADEQUACIES OF CLASSIFICATION.

Any plan for co-ordinated research on schizophrenia is confronted by a very serious dilemma. There is at present no generally accepted set of criteria which will satisfactorily delineate and differentiate the clinical constellations representing this disorder (2). The modified Kraepelinian system of classifying psychoses has failed; half the cases are atypical for its divisions (3).

As a reaction against this rigid descriptive grouping the past few decades have witnessed a growing nihilism in general psychiatric classification. For example, Rosanoff (4) drops the diagnosis of schizophrenia completely, describing clinical pictures associated with it under the heading of "chaotic sexuality," thus committing himself to an opinion that the nucleus of schizophrenia lies in the psychosexual field.

Despite the expansion of psychiatric thought and the realization of present inadequacies, diagnostic criteria must not be regarded as obsolete and useless. Classification must be placed on more secure foundations. The validity of the classification "schizophrenia" is doubtful. No unitary theory has ever been made to fit; no diagnostic test yields uniform results. Its heterogeneity may indicate that it is not a class at all; or it may be a genus embracing many species, where one cannot expect the specific properties of a genus. A relevant classification will either discard schizophrenia as a class, or it will make the construction of a theory possible by segregating those entities which constitute a legitimate genus (5)

Dementia Praecox or Schizophrenia.

The term "dementia praecox" was first used by Morel in 1856. Kahlbaum in 1863 isolated what is now hebephrenia and in 1869 catatonia. Hecker described it in 1871. Kraepelin, in 1895, elaborated the preceding work and brought the hebephrenic, catatonic and paranoid types together under "dementia praecox" (6). However, the term is unsatisfactory for there may be neither dementia nor precocity of onset; the hopeless prognosis suggested by the term is not borne out (7).

Bleuler, in 1911, synthesized and sharply outlined the class; he (8*a*, *b*, *c*) used the term "the schizophrenias." But Bleuler's analysis has not been used in the way he meant, although the term "schizophrenia" has been appropriated and inaccurately used as a synonym for dementia praecox. Bleuler considered a personality split as the prime symptom in the group he designated as schizophrenia; but this dissociation is seen in disorders other than dementia praecox (2). It has been suggested that the association disturbances described by Bleuler as splitting can be interpreted as the opposite of splitting (9).

Bleuler (10) believed that the basic disturbance in schizophrenia is an organically determined change in association in which two unrelated ideas are connected; different ones are combined with free use of symbols; there is generalization instead of specificity; associations are determined by alliterations and mediates, modified by unimportant partial identities. On this basis complexes have a free sway and secondary symptoms appear, such as hallucinations, negativism, autism, etc.

The terms "dementia praecox" and "schizophrenia" when used indiscriminately and interchangeably create additional confusion in a situation already exceedingly complicated.

Failure of the Kraepelinian Types.

The group of simple schizophrenia serves as a diagnostic waste basket into which undifferentiated problems are relegated. In this group Lewis finds borderline cases of feeblemindedness, deteriorated hebephrenics, psychopaths, peculiar character fixations, mild aborted forms, and a variety of endocrinopaths. It is evident that here is no one type, but a poorly palpable multitude.

The paranoid type.—It is inevitable, as long as the paranoia concept itself is so poorly defined, that the paranoid forms of mental disease should also be difficult to classify (11). Kraepelin himself, in the last edition of his text-book, dropped the group of dementia paranoides and placed all cases showing disturbances principally in the intellectual field, without changes in affect and will, and not followed by personality dilapidation, in the group of "paraphrenia."

Many of the cases now called paranoid schizophrenia were originally grouped with the paranoias. Some now diagnosed paranoid schizophrenia should

remain with the paranoid states for they do not show deterioration. Others are misclassified catatonic or hebephrenic types. During the early stages of these syndromes there are paranoid trends, delusions and hallucinations, as well as irritability, projection and combativeness. They are diagnosed paranoid schizophrenia ; a few months later the diagnosis is obviously hebephrenia. It is extremely unlikely that any mental disorder changes its type so fundamentally. Paranoid reactions are caused by deeply rooted, life-long specific constellations of psychic development and do not shift into other types of reaction (2).

The catatonic and hebephrenic groups.—Some cases of schizophrenia are ushered in with such an obvious catatonic colouring that a diagnosis of catatonic schizophrenia is made unhesitatingly ; yet later an unmistakable hebephrenia develops. Further, there may be periodic catatonic features in chronic hebephrenia.

In addition, catatonic symptoms may have different significances. A typical catatonic reaction in a first attack of schizophrenia carries with it a relatively good prognosis (7) ; the regression is a deep one, but transient. Catatonic episodes become more malignant as the periodicity increases, and when they occur in hebephrenia do not carry the hopeful prognosis of first attacks of pure catatonia. In my opinion post-partum catatonic reactions are also deep malignant regressions which carry a poor prognosis. There is thus a qualitative or quantitative difference, or both, in different types of catatonic reactions. Lewis prefers to lump the hebephrenic and catatonic classes into one group.

Thought Processes.

The aetiology of schizophrenia is still unknown, but psychopathology offers a partial understanding of the nature of the derangement of thought processes in the syndrome.

Although the symptoms and clinical picture in schizophrenia are extraordinarily varied, what is striking and usual is the bizarre nature of the illness, the absurdity, strangeness and unpredictability of affects, ideas, and their connections. We cannot empathize.

Some psychotic symptoms have a meaning. This important discovery was first made by Jung (12) and Abraham (13) ; Freud (14*a*, *b*, *c*) later verified it. The psychotic breaks with reality and escapes a conflict with it ; he represses the perceptions which stand in the way of his wishes, but does not repress the instinctual impulse. The break with reality follows a regressive path ; the patient sinks back into that state in which he lived before acquiring the function of reality testing. Schizophrenia may represent a regression to a stage of predifferentiation of the ego, or very early ego development. This coincides with the usual impression of a regressive dissolution of personality.

The archaic qualities of schizophrenic thought.—The apparent similarity

among schizophrenics, primitives and children has long been known (15*a–m*). Freud (16) long ago indicated the strong relationship between dreams and primitive thought. Jung (17) demonstrated the similarity of schizophrenic thinking and normal dream activities; his view was endorsed by Bleuler. Many contributors (18*a–p*) have since substantiated the view that schizophrenic thought processes are primitive.

Schizophrenia has been conceived of as a regressive psychosis, characterized by thinking on an earlier genetic level, one of a different kind, with a lower order of abstraction.

Storch (18*a*, *b*) has pointed out that in schizophrenia there is a regression from reasoning, differentiation and abstraction to feeling, concreteness and perception. This is very different from disintegration and dementia.

Thus the chief finding in the thought processes of schizophrenics is a regression to an earlier type of thinking. This symptomatic expression is so definite and characteristic that psychological tests have been devised and employed to detect the change from abstract to concrete thought. This is a measurable deviation.

Psychological Tests.

Bolles, Rosen and Landis (19) find in schizophrenics an impairment of abstract behaviour or conceptual thinking and a tendency to respond in a concrete way. Kasanin and Hanfman (20) describe the Vigotsky test which attempts to develop an artificial concept through the use of sorting of different kinds of blocks. The Weigl test (21*a*, *b*) and the BRL sorting test are used to test capacity for abstract behaviour by sorting objects in general categories and recognizing the basis of these groups. By means of the tests Vigotsky (18*p*), Kasanin and Hanfman (20) and Bolles and Goldstein (22) have shown differences between normals and schizophrenics. Bolles, Rosen and Landis use the three tests for their prognostic implications before insulin therapy; they find that in general patients doing poorly on these tests show no improvement under insulin therapy. Bolles and Goldstein (22), testing schizophrenics and normals, found that the characteristic defect of the schizophrenics was an impairment of the capacity for abstract behaviour.

Goldstein (23), Goldstein and Gelb (24) and Weigl (21*a*) have shown that education does not influence capacity for abstract behaviour; although poorly educated persons tend to react concretely, they can react abstractly as well. But schizophrenics are unable to show any abstract behaviour at all. Hanfman (25), working with Healy's picture completion tests (26), found that the schizophrenic seems unable to keep apart the sphere of personal wishes or fears, the sphere of objective reality, and the system of symbolic representation by picture or by word. Cameron's (27*a*, *b*) work shows that schizophrenic thinking is neither childish nor that of ordinary organic deterioration. Levin (28) also concludes that in schizophrenia there is a characteristic inability to

distinguish abstract and concrete concepts. Shipley (29) has devised a simple, quick, self-administering test for reduction in the capacity for abstract thinking. I have found it to be a helpful, reliable, corroboratory test in clinical work, particularly in early psychoses.

Suggested New Classification.

Thus, study of schizophrenic thought processes points to an apparent conclusion that there is a regression from abstract to concrete thinking, a type found in primitive peoples and possibly used by now civilized man before he developed his complex culture. In schizophrenia there is a "functional decortication," a regression to an earlier reaction pattern. We have seen that the terms "dementia praecox" and "schizophrenia" have many objectionable features. It is therefore suggested that the term "*palaeophrenia*" (Greek παλαιός, ancient, old; φρην, mind), indicating the regression to a more primitive level, be adopted.

I have already indicated that the present classification of schizophrenia into four sub-types is invalid and hinders rather than contributes to clarification of the syndrome.

What Does Palaeophrenia Embrace?

The term "*palaeophrenia*" should be used to include only those cases of *simple schizophrenia* which give symptoms, or a history, of archaic thought; in some there are transient delusions and fleeting hallucinations of a disagreeable nature; there may be mannerisms and bizarre behaviour as well as negativistic manifestations. Abstract thinking is diminished. Many cases at the present time classified as simple schizophrenia have few or no schizophrenic symptoms; such cases, which do not show the symptom cluster here described, should be classified more appropriately under other headings ranging from psychopathic personality to primary behaviour disorders.

There can be distinguished in those cases now called *paranoid schizophrenia* two main subdivisions: (1) There are cases which do not show archaic thought but are characterized by aggressive, irritable, combative behaviour, and projection, without hallucinations and deterioration. They show fixed suspicions and persecutory ideas logically elaborated after a false interpretation of an actual occurrence. Emotional reactions are consistent with the ideas held. (2) The second group comprises those with poorly systematized delusions, hallucinations, archaic thought, illogical thinking, affective dissociation, and regression.

In the first group the mechanism underlying the marked projection is entirely distinct from the mechanism at work in flagrant schizophrenia. In projection the patient disowns his unconscious instinctual impulses and, unable to repress them adequately, ascribes them to another person; he will not and

cannot admit them as his own. In the second group the instinctual impulses are no longer held in check because of the regression ; the patient has regressed past the stage of ego-differentiation, and the unconscious drives, perhaps connected with Freud's primal phantasies or Jung's archetypes, well up at will with nothing to hinder them. Thus expectedly the personalities of patients of the first group remain relatively intact and behaviour is not deteriorated, while the second group shows degraded behaviour.

The second group of course belongs with those cases newly designated "palaeophrenia," while the first group belongs to a better organized form of paranoia. The latter would then include those cases now described as "paranoia," some of those called "paranoid condition," and a few of those designated "paranoid schizophrenia."

The hebephrenic and catatonic types show the archaic thought indicated by the term "palaeophrenia." The attack may announce itself by confusion and a pseudo-depression without retardation. Auditory and visual hallucinations and delusions of a disagreeable nature are prominent ; suicidal attempts are frequent. Following the active first stage a plateau is reached in which one of three patterns is followed :

(1) There are fleeting, often pleasant, hallucinations and bizarre, phantastic, changeable, silly delusions, often with a paranoid colouring ; the delusions are unsupported by logic or reason. There is marked dissociation of affect from ideation, with emotional blunting and apathy. There may be looseness of thinking, inadequate association and poverty of ideas. Behaviour is silly and manneristic, with listlessness and disinterest. Frequently there is disjointed scattered utterance with neologism formation.

(2) There may be stupor, negativism, and muscular tension, with mutism and facial grimaces ; these primary symptoms may be accompanied by suggestibility, echolalia, and echopraxia. Waxy flexibility may be seen, but it is much less frequent than commonly believed.

(3) A condition of excitement may follow. There is constant vocalization, increased psychomotor activity, absurd, stereotyped, repetitive, with attitudinizing. There is verbigeration and noisy incoherence. The patient is inaccessible. Perseveration and stereotypy are common. Impulsive acts are characteristic and dangerous, leading to homicide or suicide.

Any one of these groups may lead into another or alternate. All show the signs of regression to the level of palaeophrenia.

Summary.

1. There is no generally accepted set of criteria for the diagnosis of "schizophrenia."

2. There has been a growing nihilism in psychiatric classification in reaction against this condition.

3. The Kraepelinian system has failed; half the cases are atypical for its divisions.

4. Bleuler's analysis has not been used in the way he meant; he considered a personality split as the prime symptom of the schizophrenic group; but this dissociation is seen in disorders other than dementia praecox.

5. The terms "schizophrenia" and "dementia praecox," used interchangeably and indiscriminately, create additional confusion.

6. A relevant classificatory system will either discard schizophrenia as a class or will segregate sharply those entities which constitute a legitimate genus.

7. The archaic qualitites of schizophrenic thought are indicated.

8. Psychological tests show a definite impairment of abstract behaviour or conceptual thinking and a tendency to respond in a concrete way, a characteristic of archaic thinking.

9. A new classification is suggested. The impairment of the capacity for abstract thinking is a measurable deviation. The term "*palaeophrenia*," suggesting the regression to a more primitive level, is offered to embrace a distinct syndrome which is described.

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COMPENSATORY ENLARGEMENT OF THE POSTERIOR COMMUNICATING ARTERY FOLLOWING ARTERIO-SCLEROTIC CHANGES OF THE POSTERIOR CEREBRAL ARTERY.

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WHILE a vast literature refers to anomalies in various arteries of the brain, there are only a few reports concerning anatomical changes of vessels following altered circulatory conditions. Critchley mentions in his study of the anterior cerebral artery and its syndromes, an observation in which an arterio-sclerotic anterior cerebral artery of one side was so small as to be incapable of maintaining an adequate circulation, so that by way of an abnormally large anterior communicating artery the opposite anterior cerebral supplied both hemispheres. Critchley adds to that case several similar observations from the literature. The application of arteriography to circulatory disturbances has directed attention to analogous cases. Thus Moniz reported several observations in which a closure of the carotid artery of one side led to a distension of the anterior communicating in order to establish collateral circulation. The same mechanism appeared to be effective in the following two cases which we met in the course of our studies on brain vessels.

The first specimen (Fig. 1) came from an old woman, aged 70, H. B—, who suffered for about three years before her death from an increasing confusional state with disorientation, loss of memory, agitation, and hallucinatory phenomena, and who died from pneumonia. The brain shows a very marked atrophy of the whole cortex. Confining my remarks to the vessels which alone interest us just now, the specimen shows a basilar artery of normal size ; on the right side the posterior cerebral artery of normal size and appearance takes origin, while the same artery on the left side is diminutive, and about one-third the diameter of the right artery. The whole wall of the left posterior cerebral artery is of white colour, and is flattened along its origin from the basilar to its junction with the posterior cerebral artery. The retro- and pre-mammillary branches, as well as the quadrigeminal and choroidal artery, which arise from the altered part of the left posterior cerebral show no alterations, and do not differ significantly in size or origin from those of the right side. Both posterior communicating arteries join, at unsymmetric points, the posterior cerebral arteries. While the posterior communicating artery of the right side is of normal size, the left is almost as large as the large vessels of the circle of Willis. Tracing the left posterior cerebral artery distally from the junction with the posterior communicating artery it will be found to be of the same size as the posterior communicating artery ; this part appears therefore as a continuation of the

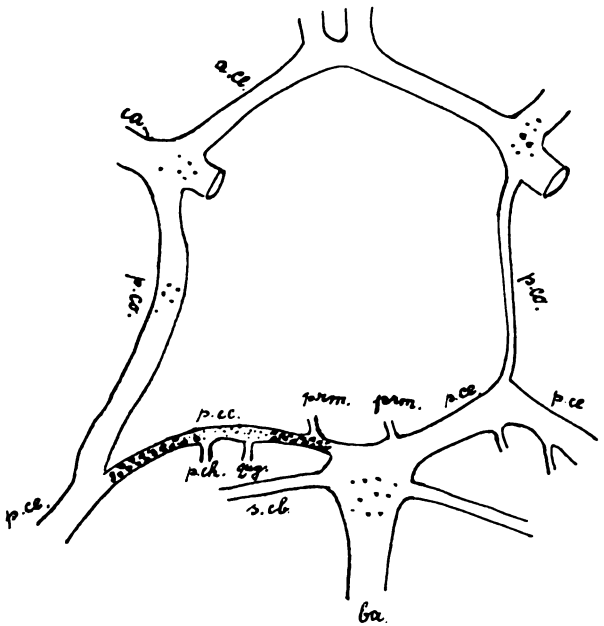

FIG. 1.

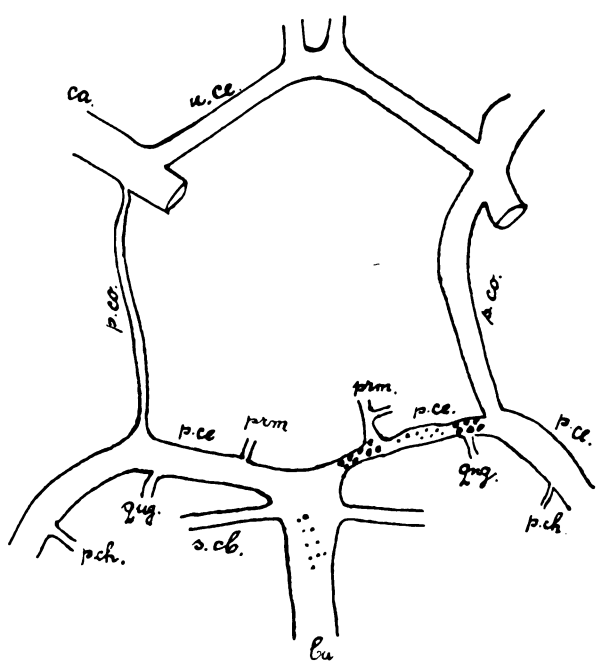

FIG. 2.

a.ce., anterior cerebral artery; *ca.*, carotid artery; *p.co.*, post communicating artery; *p.ce.*, posterior cerebral artery; *prm.*, premammillary artery; *qug.*, quadrigeminal artery; *p.ch.*, posterior choroid artery; *s.cb.*, superior cerebellar artery. • severe vessel-wall changes. . slight macroscopic vessel-wall changes.

posterior communicating artery. Apart from the very marked alterations of the posterior cerebral artery described, there are several smaller arterio-sclerotic patches spread over the large basal arteries, no appreciable narrowing of the walls can, however, be observed in these affected vessels.

The second specimen (Fig. 2) came from a man, aged 51, J. T—, with the diagnosis of mental deficiency; he died from myocarditis. In this case the right posterior cerebral artery, from its origin to the junction with the posterior communicating artery, is much smaller than the left; it shows several arterio-sclerotic patches along this line, most marked at its point of origin, where the narrowing of the wall is especially pronounced. Distally from the junction with the posterior communicating artery the size of the posterior cerebral increases so that it becomes as large in size as the left. The abnormal conditions of the right posterior communicating correspond generally to those observed in the first case on the left. The enlargement is to a lesser degree and extent than in the previous case. Its anterior part at the junction with the carotid artery is distinctly larger than elsewhere. The other large brain vessels show only slight arterio-sclerotic changes.

Comment.

There are cases described as congenital anomalies consisting of an enlarged posterior communicating, or having a diminutive portion of the posterior cerebral, and also the simultaneous occurrence of both variations mentioned in the literature. Foix and Hillemand quote the latter as the most frequent and important anomaly, and add that in these cases the posterior cerebral only supplies the peduncular branches, while all other branches are taken over by the posterior communicating. Stopford found in 6 per cent. of 105 specimens the posterior communicating to be larger than the posterior cerebral near its origin. According to this author the enlargement of the posterior communicating which appears to be compensatory to an abnormally small part of the posterior cerebral is only a persistence of the embryonic condition, since during the early weeks of intra-uterine life the posterior communicating represents the origin of the posterior cerebral from the carotid artery. Moniz mentions this occurrence as an anomaly in his arteriographic studies. Apart from the alterations of the vessel walls one might therefore consider the above two cases as further examples of this type of anomaly. In view of the marked alteration in just that proximal part of the posterior cerebral which doubtless limits the blood circulation from the basilar to the posterior cerebral, so that at the point beyond its junction it receives little if any supply, it seems to be more likely that in the two cases I have described, the enlargement of the posterior communicating is a compensatory measure to this insufficiency.

An arterio-sclerotic alteration might, of course, occur in the narrowed part of a congenital type, although there seems to be no reason why just that narrow part of the artery which is functionally least important should become the site of a severe and almost isolated arterio-sclerotic pathology; but apart from that, such possibility can hardly be accepted for these cases, one of which shows a moderate number of isolated patches spread over the proximal area of the posterior cerebral, with a general moderate narrowing, most marked on the

site of the most intensive patch, which with a further progression of the arterio-sclerotic degenerative process might very well resemble that already developed in the other case with its uniform and very marked arterio-sclerotic alterations and narrowings of the wall in the proximal part of the posterior cerebral. It is highly probable that we have here two different degrees and stages of the same pathological happening in the two respective cases.

Such a compensatory mechanism occurring in an analogous case concerning the relationship between the anterior cerebral and anterior communicating has already been accepted, as mentioned above (Critchley, Moniz). The circulatory conditions in the two cases here described are, however, much more complicated, as a substitution of blood takes place between two entirely different vessel systems. The older assumption that the posterior communicating functions by keeping the blood-flow equalized between the carotid artery and basilar is no longer accepted. Experimental investigations as well as arteriographic studies indicate that the communication between the basilar and carotid system is under normal circumstances more an anatomical than a physiological one. Thus Kramer found by injecting methylene blue into the carotid artery of dogs and apes, that the fluid was distributed only in those parts of the brain supplied by the anterior, middle cerebral and posterior communicating arteries. The arteriographic studies of Moniz, Elvidge and others show that in spite of the pressure employed, only in a relatively small percentage of the cases is the posterior cerebral filled by injection into the carotid artery. In agreement with these findings the anatomical facts demonstrate that the posterior communicating cannot be considered functionally as solely a communicating artery since it has its own field of supply (in contrast to the anterior communicating which is an intrinsic communicating artery). Considering all these facts one would infer that the posterior communicating artery is functionally a branch of the carotid artery (comparative anatomy, in accordance with the ontogenetic development above mentioned, demonstrates that the posterior communicating retains its communication between the carotid and basilar in lower animals. It may be that it develops with a higher phylogenetic scale from a solely communicating artery to an artery with its own field of supply). It may finally be mentioned that in apes (Le Gros Clark) and also in humans according to my own observations, anastomoses may appear between branches of the posterior part of the posterior communicating and the posterior cerebral. The very close connection of the capillary field of both these arteries in that area may perhaps indicate that the posterior part of the posterior communicating receives its blood-flow from the posterior cerebral; thus two different sources of main arterial supply would maintain the circulation in the posterior communicating.

Though the physiological significance of the posterior communicating does not seem to be altogether clarified, the observations here described prove that not only under anomalous conditions, but also under pathological circum-

stances, the posterior communicating artery may function as a real communicating artery when the circulation to vast parts of the brain becomes deficient by progressive pathological changes.

The two cases described were chosen from 16 unselected brains investigated ; this is too small a number to permit any general conclusions concerning frequency of such cases ; but it directs attention to the curve of the posterior cerebral, i.e. the line from its origin to its junction with the posterior communicating, as to a place in which relatively isolated arterio-sclerotic processes may appear. That occurrence becomes more understandable and also of more significance in view of the remarkable findings of D. G. Williams, who was able to demonstrate that the perivascular nerves of the posterior cerebral from its origin to its junction with the posterior communicating are derived from the basilar plexus, whilst all that part of the posterior cerebral distally from this point receives nerve fibres from the carotid plexus, such fibres arriving by way of the posterior communicating.

We are thus dealing apparently with a well-defined pathological happening. Since the part of the posterior cerebral proximally from the junction with the posterior communicating supplies, by way of the pre- and retro-mammillary arteries, the quadrigeminal and posterior choroidal arteries (the latter is included when the junction is distally from the point of origin of the posterior choroidal) important regions of the brain stem, we may expect as a consequence of the arterio-sclerotic alteration in the curve of the posterior cerebral a well-defined associated clinical syndrome. I regret that the history and the clinical-neurological examination of the cases were insufficient to trace this aspect.

Summary.

Two cases are described in which an arterio-sclerotic alteration with narrowing of the proximal part of the posterior cerebral artery occurred together with an abnormally large posterior communicating. Whilst the anatomical condition of a narrowed curved part of the posterior cerebral together with an abnormally large posterior communicating artery had been described as an anomaly not infrequently occurring, the two cases here analysed demonstrate that a progressive narrowing of the curve of the posterior cerebral of arterio-sclerotic nature may lead to a compensatory enlargement of the posterior communicating artery.

It is probable that we are dealing with a well-defined pathological happening which may be associated with a clinical syndrome of some importance.

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Part II.—Reviews.

Intelligence and Crime: A Study of Penitentiary and Reformatory Offenders. By SIMON H. TULCHIN. Chicago: The University of Chicago Press, 1939. Pp. xii + 166. Price $2.

This important investigation is based on psychological tests applied to all Illinois State Reformatory and State Penitentiary offenders over a seven-year period. The tests were applied to more than 10,000 males and 150 females; no valid deductions can be drawn from the latter on account of their small number. The essential result obtained from this statistical survey is that the proportion of criminals with inferior mentality is no higher than in the general population, as indicated by using exactly the same tests and assuming the Illinois draft army to be representative of young men in that state. It is therefore concluded that criminologists must look to other factors than differences in intelligence for an explanation of crime.

There is, however, some evidence to suggest that intelligence may play an important role as a contributing factor in determining the type of crime. It was found that the highest median scores were made by the men committed for fraud and the lowest for men committed for sex crimes. Intelligence is also considered in relation to race, recidivism, age, height, weight, educational record, marital status, employment status and religion. S. M. COLEMAN.

Medical Diseases of War. By Sir ARTHUR HURST, M.A., D.M., F.R.C.P. London: Edward Arnold & Co., 1940. Pp. viii + 427. Price 16s.

In this book it is interesting to note that the first half is solely concerned with the psychoneuroses of war and allied conditions. The second section provides chapters on those general diseases commonly met with by medical officers in the last war. Here are included Trench Fever, Typhoid, Dysentery, Epidemic Jaundice, War Nephritis, Skin Diseases (by Dr. H. W. Barber), and Gas Poisoning.

Much of the first section is devoted to a detailed study of the varying manifestations of hysteria in soldiers. The author has been able to draw on a very wide experience in the last war and there are numerous excellent case-histories. It is pointed out that the slow methods of treatment used in civilian practice are neither necessary nor practicable in war-time. At first much use was made of suggestion with or without hypnosis, but experience showed that the method of choice is explanation, persuasion and re-education. Details in treatment vary with the symptomatology, but the essential principles remain the same. Judging by the case reports, the method of treatment given in such detail in this book is justified by its results. This section also contains a chapter on anxiety neuroses by Dr. Ross.

First published in 1916, a second edition was called for in 1918. The

present edition has been thoroughly revised in the light of more recent experience. It should prove a valuable handbook for medical officers called upon to treat civilians and soldiers during the present war, and can be especially recommended to those engaged upon war-time psychotherapy.

S. M. COLEMAN.

Shell-Shock in France 1914–1918. By CHARLES S. MYERS, *C.B.E.*, F.R.S. Cambridge University Press, 1940. Pp. xii + 146. Price 4*s.* 6*d.*

This little volume contains short chapters on the causes, symptoms and treatment of "shell-shock" cases and also on their disposal both in France and in this country during the last war. While condemning the term "shell-shock," as a "singularly ill-chosen term," it seems curious that the author should attempt to perpetuate it in the title to his book. Dr. Myers is fairly catholic in his methods of treatment of the psycho-neuroses. For cases of war hysteria, he favours explanation, persuasion and re-education, though admitting that certain cases do better with deep analysis, hypnosis or strong suggestion with the aid of ether or electrical stimulation.

Unfortunately the objective value of Dr. Myers' book is to some extent marred by the constant and unwarranted intrusion of irrelevant subjective matter. It is admitted that the preparation of this work brought to the surface certain unpleasant personal difficulties and private animosities of those times, but there seems to be no valid reason why references to these should not have been kept out of the printed text. Exhibiting a mechanism well known to psychiatrists, the author is pleased to contrast the self-seeking and jealousy of the Harley Street specialist with the mild scholar from the "quieter backwaters of a University town." S. M. COLEMAN.

A Psychologist's War-time Diary. By ANTHONY WEYMOUTH. London: Longmans, Green & Co., 1940. Pp. 300. Price 12*s.* 6*d.*

Journalist, novelist, Harley Street doctor, psychologist and wireless commentator—the author, in diary form, tells us something of the people with whom he has made contact during the first six months of the war. In his varied capacities, he has had the opportunity of hearing the views and the experiences of all classes and types, ranging from Cardinal Hinsley to George Robey, and from Lord Horder to Bernard Shaw. There are numerous amusing anecdotes and interesting side-lights on war-conditions. Interspersed are little chats on popular psychological topics, such as sleep and dreams, memory, heredity, "shell-shock," the psychology of charm, etc. It is clear that it is the journalist and commentator, not the doctor and psychologist, who are responsible for this book. S. M. COLEMAN.

New Facts on Mental Disorders. By NEIL A. DAYTON, M.D. Baltimore: C. C. Thomas, 1940. Pp. xxxiv + 486. Price $4.50.

The problem of mental disorders is tackled as a single problem and from a statistical point of view based on an analysis of some 90,000 admissions to mental hospitals. The work is really the result of the labours of a team of investigators. A number of interesting facts are revealed. There was a definite increase in the incidence of mental illness for some time before the depression of 1929–30 started, and this did not increase during the depression.

The admission rates of re-admissions were decreasing steadily from 1917–1933. Amongst male admissions, abstinence, temperance and intemperance supply exactly the same numbers. Amongst female admissions 74 per cent. were abstinent and 19 per cent. temperate. Future mental patients did not turn to alcohol as a means of escape from unemployment and depression. The senile psychoses and the arterio-sclerotic psychoses show a higher incidence than all other psychoses combined.

The author points out that prohibition produced a decrease of 20 per cent. in female admissions from dementia praecox, of 29 per cent. in involutional psychoses and 68 per cent. in female alcoholic psychoses.

"Mental disorders in Massachusetts are increasing so slowly that all apprehension as to the seriousness of the situation may be discarded." It was found that "society has been unable to absorb recovered patients ready for discharge to as great an extent in recent years as in past years."

This is a very interesting book and a very useful model for research on similar problems. G. W. T. H. FLEMING.

Beyond the Clinical Frontiers. By EDWARD A. STRECKER, M.D. London: Chapman & Hall, 1940. Pp. 210. Price 9*s.* 6*d.*

This book presents the sixth of the Salmon Memorial Lectures, a memorial to the late Thomas William Salmon.

The first five lecturers all set a very high standard in their work, and Dr. Strecker, who is Professor of Psychiatry at Pennsylvania University, has certainly kept up the standard.

The book is divided into nine chapters dealing with massive retreat from reality; common evasions of everyday life; first aids to reality evasion; the mental patient, the "normal" man and the mob; the crowd man at close range; lessons to be learned from mental pathology; the need for mental hygiene; the feasibility of mental hygiene and mental hygiene planning.

This is mental hygiene at its best, and most charmingly written. The sentence "Our hope lies in the socially-minded person who is sufficiently in touch with reality to be also a non-crowd man" contains a great truth. As Nietzsche said: "Mankind has a poor ear for best music," but the music contained in this book may well prove to attract mankind in time to save him from complete devolution. Mass psychosis needs mental hygiene to prevent it. G. W. T. H. FLEMING.

Psychological Studies in Dementia Praecox. By ISABELLA KENDIG, Ph.D., and WINIFRED V. RICHMOND, Ph.D. Michigan: Edwards Brothers, 1940. Pp. x + 211.

This book is divided into three parts, dealing with (1) Dementia Praecox and General Intelligence, (2) Patterns of Mental Function in Dementia Praecox, and (3) Dementia Praecox and the Concept of Deterioration.

The authors find that the dementia praecox mind is blunted and dulled. This intellectual inferiority is not due to deterioration, but is mostly the product of emotional maladjustments which later play an important part in the precipitation of the psychosis.

The general impression is that deterioration has not been shown to take place in many cases of dementia praecox. No matter how great the regression, intellectual ability remains intact. There is a functional impairment of intellect, but no permanent loss. G. W. T. H. FLEMING.

The Physiology of Sex and its Social Implications. By KENNETH WALKER, F.R.C.S. Pelican Books: Harmondsworth, Middlesex, England, 1940. Pp. 157. Price 6*d*.

In a characteristic preface the author apologizes for adding to the noisy interlude which has followed the Victorian silence on sexual matters. The book provides a useful introduction to the subject, the author's viewpoint being well balanced and tolerant. The truth, we are reminded, has many facets, and in judging on such vexed social problems as marriage, prostitution, sexual deviation and sex education it is as well to steer a middle course between the extreme reactionary and progressive. By the arrangement of his subject as well as by the many references it is clear that the author is a disciple of Havelock Ellis. S. M. COLEMAN.

The Idea of the Soul. By WILLIAM ELLIS, Ph.D. London: George Allen & Unwin, Ltd., 1940. Pp. 314. Price 12*s*. 6*d*.

This inquiry into the fundamental metaphysical question, the psycho-physical relationship, is written by a biologist. The author's survey starts with the beliefs of primitive man, passes on to the metaphysical speculations of the Greeks, then to Renaissance philosophy and so up to modern philosophical behaviourism and the theories of Bertrand Russell. The author writes with exceptional clearness on a subject unique for its abstruseness. Particularly to be commended is his ability to throw into relief the essential contribution made by each philosophical school. Coming to modern speculation there is an excellent chapter in which he reduces neo-Cartesian dualism and the epi-phenomenalism of philosophical behaviourism to a series of paradoxes.

The author's own contribution is derived from Leibniz's theory of monads. Briefly all Nature is regarded as psychical, there being the following grades in the spiritual hierarchy: animation, life, consciousness, self-consciousness. It is shown that there is no sharp discontinuity between life and the rest of nature, for example between the unconditional reflex of an organism and the sensitivity of wax to fire. The same physico-chemical sensitivity pervades the whole of the material universe.

Psychologists may find in this book a valuable metaphysical foundation, scientists an equally valuable corrective. S. M. COLEMAN.

Part III.—Bibliography and Epitome.*

ALLG. ZTSCHR. F. PSYCHIAT.

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* A number of abstracts in this section are reproduced from *Chemical Abstracts* and *Psychological Abstracts*. To the Editors of these two Journals we extend our grateful thanks.

The Respiratory Response of Psychoneurotic Patients to Ideational and to Sensory Stimuli. Respiratory Response in Psychoneuroses.

1. A series of experiments was carried out on a group of psychoneurotic patients and of normal controls, in which was studied the effect on the respiration of the administration of a painful stimulus and of its subsequent recall. The changes in minute respiratory volume are reported as an index of respiratory response.

2. Of 32 experiments on 27 psychoneurotic patients (Group I) with diagnoses of hysteria, anxiety neurosis and phobia, an increase in minute respiratory volume appeared during the painful period in 79 per cent. of the experiments, and during the period of recall in 77 per cent. of the experiments. The increase obtained for both periods, especially for the pain period, was on the average significantly greater than the variability of this group of patients as shown in a preliminary period.

3. Of 14 similar experiments on 12 psychoneurotic patients (Group II) with diagnoses of hypochondriasis, compulsion neurosis, reactive depression, questionable schizophrenia, the changes in minute respiratory volume during the periods of pain and recall were not significantly greater than could be expected from the variability of this group during the preliminary period. Furthermore there were almost as many cases showing a decrease as showing an increase.

4. In 24 similar experiments on 15 control subjects, an increase for the periods of pain and recall appeared in about 80 per cent. of the cases. The increase found was greater than the variability of this group during the preliminary period.

5. The response of the three groups of subjects to a painful stimulus and its recall appeared to be closely parallel to the response to an unpleasant ideational stimulus as previously reported. (Authors' abstr.)

A Survey of Mental Illness Associated with Pregnancy and Childbirth.

(1) Contrary to many previous reports, the majority of the patients of this series were found to have manic-depressive psychoses, a large number were cases of dementia praecox, and only 3·6 per cent. were considered to be toxic-exhaustive deliria. The tendency in the last decade seems to have been to classify fewer of these cases as "psychosis with other somatic disease," as apparently the great majority vary little if at all from the usual pictures of the non-puerperal psychoses.

(2) The present writer failed to find as high a proportion of the depressive type of manic-depressive psychoses as did Kilpatrick and Tiebout, although this was the

most frequent type in the series studied. Also, their finding that the presence of physical factors related to childbirth makes for more frequent confusion in the depressive type was not substantiated.

(3) Contrary to Kilpatrick and Tiebout's finding that puerperal schizophrenias are all of paranoid reaction, this study shows a greater number of catatonics than of the paranoid type.

(4) The writer failed to substantiate the claim of Strecker and Ebaugh that something is added to the ordinary symptomatology of puerperal manic-depressive psychoses by the intrusion of low-grade infectious and exhaustive factors.

(5) However, this series does corroborate the findings of Strecker and Ebaugh that schizophrenic reactions associated with the puerperium frequently show pronounced manic-depressive symptoms, clouding of the sensorium, and a tendency to remissions; that these cases tend to slow deterioration, and that a high percentage of post-partum psychoses occur in the Jewish race. It seems probable that the slow deterioration noted is due to the predominance of catatonic types rather than to modification of the schizophrenic process itself by the reproductive process.

(6) The study shows a considerably greater morbidity in the heredity of the manic-depressive group than in the schizophrenic and toxic-exhaustive groups, and still greater morbidity in the heredity of the psychoneurotic and psychosis with psychopathic personality groups.

(7) The present series of toxic-exhaustive reactions, admittedly a small number from which to draw any conclusions, failed to show the comparatively large number of personality deviations reported by Strecker and Ebaugh in such cases, and considered by them to throw some doubt on the validity of infection and exhaustion as the sole specific etiological agents.

(8) Although hostility to the child, which Zilboorg considers to be the "nodal point" of puerperal depressive reactions, was noted in a high percentage of the manic-depressive cases in this study, and although it was twice as frequent in the manic-depressives as in the toxic-exhaustive group, it was not found to be any more characteristic of the depressive types than of the other forms of manic-depressive psychosis, or of the puerperal schizophrenias.

(9) The same finding was noted with regard to antagonism to the husband, as the percentage showing this character was even greater in the other types of manic-depressive psychosis than in the depressive forms.

(10) Ambivalence toward the husband, child and self also was found to be no more characteristic, in this series, of the depressive reactions than of the other forms of manic-depressive psychosis, although it was almost twice as frequent as in the schizophrenic series.

(11) The authors were unable to find a high percentage of the incest ideas and homo-sexuality considered so typical of the puerperal depressive reactions by Zilboorg.

(12) Chronic masturbation and excessive eroticism were noted commonly in the schizophrenias of the series, but by no means to the extent found by Zilboorg, who failed to find eroticism in only one of his cases.

(13) The same author's claim of evidence of an unresolved Oedipus situation in most puerperal schizophrenias was not entirely substantiated by this study; in fact, a slightly greater number of the cases seemed to show a mother preference.

(14) The study does tend to corroborate, at least to some degree, Zilboorg's claim that the aloof, shy woman with little previous contact with men and prolonged courtship tends to develop puerperal schizophrenia. His statements that these women marry in the latter part of the third decade of life, and that their persistent frigidity points to the impending development of puerperal schizophrenia could not, however, be completely verified from this survey.

(15) Although Zilboorg's findings regarding almost constant antagonism to the husband were confirmed by the present study, the writer found little evidence to support his claim that the women patients had become hyper-sexed for a short interval before resuming their frigidity post-partum; nor did this survey reveal

the claimed consistent happiness during pregnancy. The antagonism toward the child, as expected from Zilboorg's hypothesis, was present.

(16) Homosexual tendencies were rarely noted, in contrast to the findings of Zilboorg.

(17) With few exceptions, the psychoses did have their onset post-partum.

(18) The schizophrenias reported by Zilboorg developed predominantly in multiparae, while those of the present series were slightly more frequent in primiparae. In the multiparae here reported, his findings of an assumption of the masculine role in the interval between pregnancies was strikingly lacking.

(19) Again, a sense of guilt was found much more commonly than one was led to expect from Zilboorg's studies. (Author's abstr.)

Dynamic Disturbances in the Handwriting of Psychotics, with Reference to Schizophrenic, Paranoid and Manic-depressive Psychosis.

1. The handwriting of psychotic patients shows definite characteristics.

2. The basic disturbance in the psychotic handwriting is expressed by the drastic disturbance in the dynamic relationship.

3. The fundamental dynamic disturbance finds different modifications in the handwriting of the schizophrenic, the paranoid and the manic-depressive patients.

4. These different modifications are characterized by an emphasized disturbance in one of the graphic spheres.

(*a*) The dimension of breadth in schizophrenic writings.

(*b*) The dimension of depth in paranoid writings.

(*c*) The dynamic relationship implicating the dimension of height in manic-depressive condition writings. (Author's abstr.)

The Treatment of Delirium Tremens with Insulin in Sub-shock Doses.

Insulin with carbohydrates seems at this time to be the only method of treating delirium tremens which has improved upon the statistical results reported by Kraepelin, who used diet, support and paraldehyde for rest.

Insulin is effective because it rapidly re-establishes normal carbohydrate metabolism. It likewise quickly replaces deficient glycogen reserves in the liver. These two factors, which are part of the same process, re-vitalize the liver and re-establish normal protein and fat metabolism. During the period of deficient carbohydrate metabolism and deficient liver function, toxic intermediate products of abnormal protein and fat metabolism have become so concentrated that they have produced the pathology and symptoms of delirium tremens. Re-establishment of the liver function advances the progress of metabolism, and these products are carried forward to their ultimate normal, less noxious end products. This reduces toxic concentrations, removes the " irritative " factor, the cerebral pathology reverses itself by natural processes, and the delirium is quickly relieved.

Insulin therapy is rapid, effective and simple to administer. The series presented by Steck and by the author had a combined time for complete clearing of the delirium of 2·5 days. (Author's abstr.)

A Study of Insight of Psychiatric Patients.

1. The insight of 100 patients discharged from a private sanitarium has been studied.

2. Among those diagnosed as depressions there was a greater proportion of patients who showed good insight on admission than among those with other psychoses. Psychoneurotics all showed fair to good insight.

3. All but one of the patients discharged as " much improved " or " recovered " showed some insight and most of this group showed good insight.

4. Absence of insight on admission did not impair the prognosis for recovery, but patients with partial insight showed a poorer recovery rate than either those with no insight or those with good insight.

5. Lack of insight was frequently associated with such manifestations as disorientation, poor comprehension, irrelevance, memory impairment, hallucinations, delusions, conduct disorders and retardation. (Author's abstr.)

Prognostic Criteria in Dementia Paralytica.

1. One hundred cases of dementia paralytica treated at the Worcester State Hospital between the years 1925–1938 were studied to determine criteria useful in the prognosis. An inquiry into the cause of failure of one-half to two-thirds of paretics to undergo remission under pyretotherapy was also undertaken.

2. These patients were treated by one of four methods: malaria, standard diathermy, modified diathermy and tryparsamide. Thirty-three per cent. of the total group underwent remission.

3. The following criteria are found to be of value in the determination of the prognosis: age of the patient, duration of the paretic process, previous therapy, extent of neurological dysfunction, history of epileptiform seizures, degree of defects in sensorium, tendency toward spontaneous remission, type of psychopathology exhibited, and degree of adjustment of the preparetic personality.

4. Most important prognostic criterion is the degree of adjustment in the preparetic personality. All of the patients with well-integrated personalities prior to the onset of dementia paralytica underwent remission no matter what type of therapy they were given. Only three out of 63 patients with poorly adjusted personalities experienced remission.

5. Of the other criteria, the most significant are the extent of neurological dysfunction, degree of defect in sensorium and type of psychopathology. Patients in the delirious, apathetic and agitated groups had the best prognosis, those in the demented and schizophreniform the worst.

6. There is found to be a strong correlation between the degree of adjustment in the preparetic personality and the other prognostic criteria. Well-integrated individuals tended to have milder neurological and sensorium defects, slower progress of symptomatology before therapy, and a tendency to spontaneous remission as well as a better prognosis.

7. Three cases of dementia paralytica are cited to show how a relatively accurate prognosis can be formulated.

8. Causes for the greater resistance to the progress of the paretic process and the better response to therapy in the previously well-integrated individual are discussed. (Authors' abstr.)

A Comparative Study of Thinking in Schizophrenic Children and in Children of Pre-school Age.

An analogy is frequently drawn between schizophrenic and child thinking. In order to check the validity of such analogy, verbal productions from protocols of fifteen normal children of pre-school age (two to five years) and three schizophrenic children (with ages varying between seven years ten months and fourteen years seven months) are presented and compared. These productions were obtained under very similar conditions, i.e. favouring the spontaneous expression of phantasy, allowance being made for differences in ages, clinical needs and situational contingencies.

The systematic investigation of the phantasies of young normal children with regard to the evaluation of reality shows that responses fall within three categories: denial of character of reality, which is the most common type of response; evasion; and finally, reiteration with apparent belief. The latter category, containing the smallest number, includes those responses in which a strong emotional component is evident, chiefly fears, but also wishes. It is not possible to demonstrate in normal children true delusions and hallucinations or disorders characteristic of schizophrenic thinking. Experiences which come closest to these belong to the third category, i.e. reiteration with apparent belief, but are not appreciably different from similar experiences initiated in the adult by some strong emotional stimulus.

It is recognized, however, that the child shows a greater emotional lability and greater susceptibility to somatic changes than the adult. In one instance, where a confusion between reality and phantasy seemed apparent, the child showed emotional immaturity and a lack of social adaptation which point to a relation between the coincidence of such experience and a tendency toward faulty integration and adjustment in the future. Follow-up studies of the children's later adjustment should throw light on this point.

From the present records it appears evident that experiences which most closely resemble those found in the schizophrenic are dependent upon emotional factors and not upon characteristics inherent in child thinking. (Author's abstr.)

Set in the Schizophrenic as Measured by a Composite Reaction Time Index.

Twenty-five schizophrenic patients and ten normal subjects were used in an experiment on reaction time employing preparatory intervals of 1, 2, 4, 7·5, 15 and 25 seconds in length. Two procedures were used. In the regular warning procedure each particular interval was presented a number of times in succession. In the irregular warning procedure the various preparatory intervals were presented in a systematically random fashion. The principal findings were:

1. Normals showed significantly shorter reaction times than did the patients, although there was a small degree of overlap. The shortest reaction times of the normals occurred at the 2-second interval in both procedures. The patients on the other hand showed their minimum times with somewhat longer intervals.

2. In the normal subjects the reaction times of the regular procedure are significantly shorter than those of the irregular procedure at each interval except the 25-second, at which point the two curves crossed. The differences between the two procedures diminished with increase in length of interval. The schizophrenics gave shorter times in the regular procedure at only the 1-, 2- and 4-second intervals. At the longer intervals the times of the regular procedure were actually longer than those of the irregular procedure.

3. A composite index was constructed on the basis of these differences between patients and normals, which effectively separated the two groups with practically no overlap. This composite index, which can be expressed in terms of a single number, is more effective in differentiating the two groups than is simple reaction time level.

4. The suggestion is made that such an index has practical value as a clinical device. (Authors' abstr.)

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Pneumo-encephalography and Cerebro-spinal Fluid Reactions after Air Replacement in Epileptics.

Twelve cases were observed. In all cases an increased cell count followed air-replacement and was at its maximum after 24 hours. There was some protein increase in four cases, the increase affecting both the albumen and globulin fractions.

The Chlorides of the Cerebro-spinal Fluid.

Fifteen hundred determinations of the chlorides in normal liquors gave values between 7·02 and 7·55 gm. per thousand.

ARCH. ARGENT. DE NEUROL.

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ILLINOIS PSYCHIATRIC SOCIETY.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY.

Cystometric Studies in Cases of Neurologic Disease.

Objective study of bladder function in cases of neurologic disease adds greatly to an understanding of the various abnormalities of bladder function encountered. Such studies yield most information when made in the form of a continuous graphic record of bladder pressure during filling of the bladder.

In normal patients the desire to void usually occurs with from 100 to 300 c.c. of filling, the average being about 150 c.c. A bladder contraction usually occurs with between 300 and 500 c.c. of filling, the average being about 350 to 400 c.c. Voiding about the catheter may or may not be associated with the contraction.

Bladder contractions are essentially reflex, and the primary reflex centre is in the second, third and fourth sacral segments of the spinal cord. Normally they are inhibited until several hundred cubic centimetres of filling has been accomplished. In the infant a bladder contraction occurs with a relatively small amount of filling. This is also the case, but to a less marked degree, in cases of enuresis in children.

With complete chronic transverse lesions of the spinal cord an " automatic "

or, better, reflex bladder is developed, which essentially functions in the same manner as the bladder of the infant.

Diffuse lesions of the central nervous system above the sacral portion of the spinal cord produce a variety of types of bladder dysfunction. Examples of such lesions are tumour of the cord and brain, injuries of the brain, multiple sclerosis and vascular accidents.

Cystometrograms of patients under spinal anaesthesia or with acute transverse lesions of the spinal cord or cauda equina show a progressively higher peak of pressure with each injection and a progressively higher resting level after each injection. This is due to a neuromuscular reflex (stretch reflex), and depends on the activity of the post-ganglionic visceral motor neuron. A high resting level of pressure is maintained after filling in these cases. Patients with chronic lesions of the cauda equina show at some stage of filling small, irregular, poorly sustained bladder contractions.

In cases of tabes dorsalis and in some cases of chronic overdistension there is atonicity of the bladder wall with a late desire to void, and absence of bladder contractions or any rise in bladder pressure even with 1,000 c.c. or more of filling. There appears to be a marked reduction of afferent impulses from the bladder wall in these cases.

A constantly high resting level of pressure is seen in cases of hypertrophy of the bladder musculature due to obstructive lesions at the neck of the bladder. It is usually about 10 mm. of mercury and remains constant during filling. It depends on the degree of hypertrophy of the bladder musculature that is present and does not represent a neurologic lesion. (Authors' abstr.)

AUGUST, 1940.

Philadelphia Neurological Society.

Primary Cortical Centres for Movements of Upper and Lower Limbs in Man.

It has long been commonly accepted in the literature and in the standard textbooks of anatomy that the primary cortical centres for the lower extremity in man were situated on the lateral convexity of the cerebral hemisphere. A critical review of the literature, however, indicates that this concept became established on the basis of a wholly inadequate number of observations made on the human brain—in fact, largely on observations made on the brains of experimental animals.

Observations made by the author as a result of electrical stimulation along the superior mesial border of the human cerebrum in 14 consecutive cases indicate that the primary motor area for the upper extremity commonly extends upward on the lateral surface of the cerebral hemisphere as far as its superior mesial border, while the leg, as a rule, is represented only on the mesial surface of the cerebrum.

An upward " migration " of the primary motor strip, unique in man, is implied by the observations reported here. It seems probable that this has been influenced by two factors: (1) " Liberation " of the upper extremity from the routine burden of locomotion, with its consequent elaboration of new and highly complex functions, and (2) acquisition of speech and other forms of symbolic expression. These new functional acquisitions have been accompanied by corresponding expansion of the cortical areas representing the tongue, mouth, lips and upper extremity, with the result that the cortical representation for the leg has been crowded farther and farther upward on the lateral surface of the hemisphere until it was finally pushed " over the top " on to the mesial surface of the hemisphere.

Focal contractions of the rectal sphincter, produced by stimulation of the mesial surface of the cerebral hemisphere, are here reported for the first time.

(Author's abstr.)

Relation of Intracranial Tumours and Symptomatic Epilepsy.

The slowly growing neoplasms have a higher incidence of secondary epilepsy than the rapidly-growing tumours, probably because death terminates the history sooner in cases of the latter type. Seizures form a first symptom also more frequently in cases of the slowly growing tumours. Infiltrating and encapsulated

tumours, if they are equally slow growing, have an incidence of seizure twice as often in cases of encapsulated tumours as in cases of infiltrating tumours. In our clinic the percentage of "cure" of seizures by operative removal of encapsulated tumours is about the same as that from excision of focal cerebral scars for the relief of epilepsy.

Abscesses of the brain are apt to produce seizures at an early stage and again after the formation of a healed scar. Subdural haematomas have a relatively low incidence of seizures, and the attacks even then seem to be due to cerebral injury that may have resulted from trauma rather than to the haematoma itself.

(Authors' abstr.)

Relation of Experimental Histamine Headache to Migraine and Non-migraine Headache.

(1) Headache may be produced by sudden intravenous injection of minute amounts of histamine phosphate in from 30 to 40 per cent. of patients subject to chronic recurrent headache.

(2) The same procedure fails to cause headache in those who are characteristically free from this complaint.

(3) Apparently the threshold for histamine headache is lower in persons subject to chronic recurrent headache than in those not so afflicted.

(4) The threshold for histamine headache is somewhat lower in patients subject to migraine headache than in those subject to non-migraine headache.

(5) In patients subject to migraine attacks the type of headache produced by histamine is frequently similar to migraine headache.

(6) In patients subject to other types of chronic recurrent headache the type of headache produced by histamine is only occasionally similar to the patient's habitual headache.

(7) No evidence was discovered that the cranial vascular tree in patients subject to hemicranial migraine headache is unilaterally hypersensitive to histamine.

(8) Further evidence has been presented linking migraine and histamine headache.

(Author's abstr.)

Inhibitory Functions of the Corpus Striatum.

(1) Stimulation of the caudate nucleus inhibits spontaneous movements of the skeletal muscles, probably induced by the cortico-spinal system. The effect is best noted on the ipsilateral side.

(2) Stimulation of the caudate nucleus inhibits bladder tone and tends to depress respiration and reduce activity of the sweat glands.

(3) Little evidence for somatic localization of these effects within the corpus striatum has been found. (Authors' abstr.)

Electro-encephalographic Studies of Injury to the Head.

Clinical and electro-encephalographic studies of 64 cases of cerebral trauma due to injury to the head are presented, in 37 of which the condition was acute. The principal results may be summarized as follows:

(1) In cases of acute injury to the head, cerebral trauma was indicated in the electro-encephalogram by (*a*) random or regular delta waves varying in frequency from less than 1 to 6 per second; (*b*) poor regulation or disorganization of the alpha rhythm; (*c*) epileptiform discharges.

(2) The severity, type and localization of cerebral traumas judged by the electro-encephalogram corresponded closely, in cases of more severe injury, with the results of clinical, roentgenologic and serologic studies and of examination of the spinal fluid, as well as with operative findings. In cases of mild injury the electro-encephalogram appeared to be the most sensitive indicator of cerebral injury.

(3) The electro-encephalogram provides a sensitive objective measure of recovery. Electro-encephalographic abnormalities were gradually replaced by normal activity

as the patient showed clinical improvement, but persisted longer in some cases than did other clinical signs of cerebral disorder.

(4) In some of the cases of more severe injury delta and epileptiform waves and disorganized activity were observed in the electro-encephalogram several years after the injury. These were associated clinically with changes in personality, epileptic seizure, irritability, disorder in thinking or, in a few cases, with no remarkable clinical abnormality.

(5) Post-traumatic syndromes due to malingering or hysteria are clearly evident from the electro-encephalographic examination, since in such cases none of the characteristic abnormalities associated with genuine cerebral trauma are obtained.

(6) Electro-encephalographic indications of subdural haematoma or effusion, epidural haematoma, intracerebral haemorrhage and focal as contrasted with generalized trauma provide an aid to surgical therapy. (Authors' abstr.)

Prevention of Dislocations and Fractures in Metrazol Convulsions.

Metrazol therapy has been threatened with abandonment because of fractures and dislocations which have been caused by the convulsions. These have consisted of injuries to the mandible, humerus, femur and thoracic vertebrae.

Prevention of these complications depends on knowledge of the anatomic mechanisms involved in their production. These are described. The preventive methods of other workers are discussed.

A technique to prevent mandibular dislocation and fractures of the humerus and femur is described. Vertebral injury is prevented by a method of spinal hyperextension.

By proper manual restraint, fractures and dislocations due to metrazol convulsions may be prevented. (Author's abstr.)

Relation of Age to Motor Impairment in Man and in Sub-human Primates.

In primate infants (man, chimpanzee or monkey) the development of paresis and spasticity has been shown to be related to defects in the functional and anatomic development of the central nervous system. Evidence obtained from experimentation on sub-human primates shows that the central nervous system of the infant is potentially different from that of the adult, as manifested by the motor deficits which appear after known cortical ablations. This is corroborated by clinical evidence obtained by the study of the human infant.

1. The absence of cortical motor areas is not accompanied by any marked and noticeable motor deficit in the infant before complex skilled motor activity has developed.

2. Paresis is first seen after ablation of motor cortical areas in the infant at a time when normally skilled co-ordinated movements should appear.

3. Spasticity (increased resistance to passive manipulation) begins to appear much later than paresis, possibly at the time when there is functional organization of certain subcortical motor pathways.

4. In the monkey the greater adequacy of motor function which develops after precentral ablations in infancy is due in part to reorganization of cortical function, since additional motor deficit appears in such animals after subsequent ablation of post-central or frontal association areas.

5. The paresis, and to a much greater extent the spasticity, is always less severe in all primates if the causative lesion occurred in infancy.

(Author's abstr.)

Human Behaviour after Extensive Bilateral Removal from the Frontal Lobes.

In the case reported a traumatic injury had destroyed somewhat less than one-third of each frontal lobe and left a scarred zone in each hemisphere, giving rise to continuing abnormal electrical potentials and to recurring epileptic seizures.

Surgical removal of scars and a zone of grossly normal cerebral tissue, in such a way as to insure a minimum of scar, resulted in comparative freedom from attacks (two seizures in the 15 months following operation, as compared with weekly seizure before). Although after operation a third, and possibly more, of the total volume of each frontal lobe was lacking, there was a striking post-operative improvement in personality and intellectual capacity, with the same medication as before the operation. After the initial post-operative period no clinical or psychometric evidence of deterioration was detected.

It is obvious that abnormal areas of brain may produce, in a positive sense, both decreased mental capacity and abnormalities of behaviour, and that absence of these areas may allow other parts of the brain to recover their normal functions. It is concluded that removal of a third of both frontal lobes, uncomplicated by pathologic change in the rest of the brain, need have no grossly deteriorating effect. The significance of this finding for the study of function of the frontal lobes is discussed. (Authors' abstr.)

BULL. MENNINGER CLIN.

VOL. IV. JULY, 1940.

CANAD. J. OCCUP. THER.

VOL. VII. APRIL, 1940.

War Neuroses and Psychoses.

A brief account is given of the aetiological factors and symptomatology of the various types of malingering, neuroses and psychoses met with in war-time. It is pointed out that in peace psychoses far outnumber neuroses (8 to 1, U.S. Army, 1915), while in war the relations are reversed, neurotic reactions making up 50 to 60 per cent. of the total nervous and mental disabilities. Regarding treatment it is insisted that success depends more upon the personality of the physician than on the method employed. S. M. Coleman.

Rehabilitation.

It is concluded that in dealing with the nervous invalid, the types of treatment and training must be determined not alone by the nature of the neurosis as such, and the work to which, suitably or unsuitably, the patient may have been accustomed; but pre-eminently by his original mental constitution, its capacity and mode of reaction. If the neurotic patient is also a defective or a psychopath or otherwise constitutionally handicapped, as is the case more often than not, it is useless to prescribe treatment or occupation for him simply as a patient suffering from a neurosis without regard to these fundamental and permanent mental limitations. S. M. Coleman.

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INDIAN J. PSYCHOL.

VOL. XIV. 1939.

INT. J. PSYCHOANAL.

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J. APP. PSYCHOL.

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VOL. LXXIII. AUGUST 15, 1940.

The Medial Thalamic Nucleus: A Comparative Anatomical, Physiological and Clinical Study of the Nucleus Medialis Dorsalis Thalami.

1. The nucleus medialis dorsalis is composed of two well-defined parts, a parvicellular and a paralamellar, and a poorly defined medial portion, the nucleus medialis dorsalis pars magnocellularis.

2. The dorsomedial nucleus receives fibres from the adjacent lateral and ventral thalamic nuclei, and from the midline structures along the third ventricle. Cortico-thalamic fibres enter it from the prefrontal cortex.

3. A well-organized system of fibres passes from it to the cortex of the convexity and orbital surface of the prefrontal lobe.

4. Physiological studies of the nucleus have added little to the knowledge of its function.

5. Although softenings of both nuclei dorsalis mediales in the human have been associated with mental defects and dementia, it is doubtful whether the damage to the dorsomedial nuclei alone is responsible for this condition.

6. The probable function of the nucleus medialis dorsalis is to integrate the somatic and visceral impulses and to relay them on to the cerebral cortex.

(Author's abstr.)

Thalamic Connections of the Frontal Cortex of the Cat.

The positions of the areas of the frontal cortex of the cat in which end the axones of the cells of the main sensory nuclei of the dorsal thalamus have been determined by comparing the locations of cortical lesions with the disposition of the resulting thalamic degeneration. Twenty-five experiments were made with 19 cats.

The medial thalamic nucleus degenerated after lesions involving the gyrus proreus. Of the parts of the ventral nucleus, the arcuate is connected to the cortex about the lower end of the coronal sulcus, the ventrolateral to the cortex about the upper end of the coronal sulcus and the lateral part of the post-crucial gyrus, the ventral anterior to the motor area in the lateral part of the precrucial gyrus and in the crucial sulcus, the ventromedial to the cortex immediately lateral to the precrucial sulcus. (Author's abstr.).

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VOL. XXX. AUGUST, 1940.

J. EDUC. PSYCHOL.

VOL. XXXI. 1940.

J. EXP. PSYCHOL.

VOL. XXVI. 1940.

Facilitation of the Alpha Rhythm of the Electro-encephalogram.

In this study of occipital and pre-central alpha rhythms, facilitation was exhibited by an increase in amplitude and regularity of the potentials, usually appearing as a series of bursts. Stimuli eliciting facilitation were similar to those reported as eliciting the PGR. They were characterized by a change in the general psychological state of the subject from relaxation to readiness, attentiveness, or awareness, and from these states back to relaxation. The states were induced by putting sudden questions to the subject, presenting ready signals indicating the beginning of some task, giving instructions, etc. Facilitation was found to undergo a process of adaptation. Individual differences in ease and regularity of eliciting facilitation were obtained. Facilitation of the occipital and pre-central rhythms could at times be elicited independently. H. W. KARN (Psychol. Abstr.).

The Effect of Benzedrine Sulphate on Syllogistic Reasoning.

Twenty S's were given a syllogistic reasoning test at four different experimental sittings. At two of the sittings the S's were under the influence of 10 mg. of benzedrine sulphate: the other two sittings involved a capsule of lactose. Test scores were taken at each sitting, together with records of mood ratings, fatigue ratings, blood pressure, and heart rate. The following conclusions are drawn: (1) The drug had no statistically significant effect on the reasoning scores of the S's as a group in terms of either their accuracy, their speed, or their efficiency alone. However, all the changes were slightly in favour of the influence of the drug. (2) The drug had a slightly greater effect on the women's reasoning scores than on the men's. (3) The S's who were lighter in weight obtained a slight increase toward significance due to the drug, which change was not as well shown in the heavier S's. (4) Benzedrine had no statistically significant effect on the self-ratings of the S's as to mood and fatigue. (5) There was no statistically significant change in the rate of the heart beat due to the effects of the drug. (6) There was a significant rise in systolic blood pressure due to the effects of benzedrine.

H. W. KARN (Psychol. Abstr.).

J. GENET. PSYCHOL.

VOL. LVI. JUNE, 1940.

J. NERV. MENT. DIS.
VOL. XLI. JUNE, 1940.

Psycho-analytic Procedure in the Hospital.

In this paper some of the problems and difficulties encountered in establishing a hospital routine based on psycho-analytic concepts are considered. In order to provide for each individual patient the optimum conditions under which recovery may take place the following advice is given: (1) The fostering of a 24-hour a day appreciation of the patient's illness, (2) the provision of a teaching programme for all who come in contact with the patient, and (3) the analysis of nurses.

S. M. COLEMAN.

Paraphysial Cysts.

The writer suggests that not enough attention has been paid to the early symptoms of these tumours, whose presence may be suspected from a history of sudden onset with severe headache followed by hypersomnia, visual disturbances, epileptiform seizures, and frequently by the onset and relief of symptoms by a change in posture of the head. The diagnosis can be confirmed by ventricular air studies. It is pointed out that with earlier recognition it will be possible for a greater number to be successfully removed. S. M. COLEMAN.

The Treatment of Cryptorchidism.

The paper consists of psychiatric observations on 21 cases of cryptorchidism treated with gonadotropic hormones. Of these cases 11 were bilateral, 2 unilateral, 3 scrotal, and 5 were pseudocryptorchids. Antuitrin S and antophysin were used. These hormones were administered intramuscularly in doses of 200–300 units two or three times weekly.

It was concluded (1) that descent of the testicles does not mean necessarily change or improvement in the mental status. (2) The behaviour of the patient could not be ascribed to the cryptorchidism alone. (3) There are various types of conditions in which undescended testicles may occur and there is apparently no psychiatric entity associated with them. (4) The occasional improvement in the mental status could not be ascribed to the endocrine therapy alone. (5) When the total picture is evaluated, the restricted clinical value of the hormone therapy becomes apparent. (6) The pseudocryptorchids should be differentiated from the true. (7) In true cryptorchids descent was noted in only 3 of 13 cases.

S. M. COLEMAN.

Intradural Spinal Lipomas.

A case of intradural spinal lipoma is presented, upon which laminectomy and later autopsy were performed. The lipoma appeared histologically to arise from the pia arachnoid and to grow out from rather than to invade the cord substance. Reference is also made to another tumour of mixed mesodermal derivatives, one of which was fat, occurring between the two corpora mammillaria.

S. M. COLEMAN.

J. NEUROPHYSIOL.

VOL. III. JULY, 1940.

Hypothalamic Lesions and Pneumonia in Cats.

1. Forty cats were operated upon in three series. Bilaterally symmetrical lesions were placed in the rostral (5 cats), middle (26 cats) and caudal (9 cats) regions of the hypothalamus.

2. Characteristic changes in the motor behaviour and the emotional responses of the animals are described.

3. All animals with rostral lesions (anterior commissure to optic chiasm) survived. Sixteen of the 19 animals with middle destructions (chiasm into mammillary bodies) succumbed to bilateral bronchopneumonia in one to eight days. Two of the 8 animals with caudal lesions (mammillary bodies and portions of the mesencephalon) died of pneumonia on the 7th day.

4. Animals with rostral lesions retained the ability to prevent an abnormal fall in body temperature; those with caudal lesions showed occasional disturbances of temperature regulation; whereas animals with middle lesions showed marked poikilothermia. All animals responded to infection with fever, but those with middle lesions could not maintain the hyperthermia in the presence of fluctuating environmental temperatures. A close correlation existed between the degree of poikilothermia and the incidence of pneumonia, but important exceptions occurred.

5. The following possible contributory factors were studied and found to be of little or no significance in the aetiology of pneumonia in the animals with middle hypothalamic lesions; distemper, anaesthesia, basilar haemorrhage, peritonitis, aspiration, laryngeal obstruction, pulmonary emboli, gastro-intestinal disturbances and exposure to extremes of temperature. Destruction of the central region of the hypothalamus therefore causes a high incidence of fatal pneumonia in cats, but the specific aetiologic factors in this relationship require further investigation.

(Authors' abstr.)

Progression Movements Elicited by Subthalamic Stimulation.

In cats anaesthetized with nembutal, alternating movements of the legs similar to those of normal walking and running were elicited by 60-cycle alternating current stimulation of the subthalamus in the region dorsal to the mammillary body. The sharp localization and low threshold of the response indicate that the subthalamus contains a specific centre which directs the order of movement of the legs in locomotion. (Author's abstr.)

Electrical Activity of the Lateral Geniculate of Cats following Optic Nerve Stimuli.

1. Four groups of fibres in the optic nerve produce four potential waves after conduction. The geniculate and cortex are activated chiefly by the first group of fastest conduction, with one radiation spike only following each nerve volley. Paired shocks exciting these fibres in the optic nerve, even when maximal, show facilitation of the second responses at intervals of 2 to 15 or more msec. The same applies to successive synapses traversed in the cortex, the results being cumulative.

2. The homolateral response of the optic cortex in cats varies from 15 to 70 per cent. of the contralateral. No facilitation can be detected at the geniculate level by simultaneous or successive stimulation of the two optic nerves, and little, if any, at the cortical level.

3. Slow potentials of the order of after-potentials in their time relations can sometimes be demonstrated at electrodes thrust into the cell layers of the geniculate. They seem to be non-conducted, and are interpreted tentatively as slow decay of cell body or dendritic excitations.

4. The cortical activity shows a depression followed by facilitation having a phasic relationship to the alpha rhythm, after a single volley in the optic nerve. The short-period facilitation occurring at geniculate and cortex counteracts this depressive phase so that with light anaesthesia responses of the cortex will follow up to at least 100 per second. Fluctuations of amplitude in these responses still follow the alpha wave set up by the first stimulus of the train, until temporal dispersion of alpha processes occurs.

5. Fibres from the optic tract spread in a thin surface sheet over much of the area bounded by the medial and lateral geniculates, the pretectal area, and superior colliculus. From regions not usually assigned optic function, post-ganglionic responses can be recorded. In general, the larger fibres with faster conduction rate and lower threshold synapse are in the anterior regions of the optic tract distribution, the smaller in the posterior regions.

6. The chief conclusions we can draw from these findings lead to further hypotheses to be tested rather than to an explanation of visual function.

(Authors' abstr.)

Integration of Locomotor Behaviour Patterns of the Hagfish.

1. The California Hagfish, *Polistotrema stouti*, was subjected to operational procedures designed to illustrate the nature of the locomotor behaviour patterns. Visual impressions of the deficiencies produced were used for interpreting the results.

2. Simple cord section produces a disintegration of the total behaviour pattern which can be re-established under strong external stimulation.

3. That the behaviour studied is a total pattern is indicated by the fact that isolation of a segment of the cord causes an immediate formation of a new site of initiation of the waves, and also in that the wave length of the undulations integrated by isolated segments varies with the length of the segments.

4. The undulatory waves represent moving sites of nervous integration, and their speed and direction may be experimentally altered.

5. Stimulation of the posterior end of the body and particularly of the tail results in the usual head-to-tail undulations. Stimulation of the gill region initiates waves of reverse direction.

6. Single hemisections of the cord do not incapacitate the animal for forward

locomotion, though backward swimming becomes impossible. Paired contralateral hemisections act as complete sections except that with strong stimulation the pattern was more easily restored to normal.

7. It is possible, with properly placed hemisections, to dissociate the undulatory pattern into right and left-sided halves. Direct faradic stimulation of the sides of the cord also produced this fractionation. (Author's abstr.)

Effects of Heating Hypothalamus of Dogs by Diathermy.

Small gold foil electrodes, 3 by 6 mm. in size approximately with insulated thermocouple wires attached, were placed on either the anterior hypothalamus or the posterior hypothalamus of dogs by a subtemporal approach to the base of the brain. The free ends of the electrode wires were brought to a subcutaneous position on the skull, and the dog allowed not less than one month to recover from the operation. Tests were made to determine if the temperature regulatory functions of shivering, panting and peripheral vasoconstriction and vaso-dilation were normal. When these functions were normal the brain was heated locally by diathermy current from the brain electrode in a controlled environment. Heating the anterior hypothalamus caused inhibition of shivering and vasodilation. Heating the posterior hypothalamus produced sleep and a slight decrease of shivering intensity. Panting was not induced by local hypothalamic heating. The results prove the existence of centres for shivering inhibition and thermal vasodilation in the anterior hypothalamus which are motivated by local brain temperature changes without changes of general body temperature or peripheral temperatures. Post-mortem examination of the hypothalamus revealed that no hypothalamic structures had been injured in any way by the experimental procedures.

(Authors' abstr.)

Role of Neocortex in Regulating Postural Reactions of the Opossum (Didelphys virginiana).

Electrical stimulation of the neocortex in 17 opossums revealed various areas from which movements of the contralateral facial, fore leg and hind leg musculature could be obtained.

The placing and hopping responses of the opossum are much slower and less exact than those of phylogenetically higher forms.

These postural responses are controlled in part by the electrically excitable areas of the neocortex. Ablation of this sensori-motor area of one hemisphere produces deficiencies in the responses of the contralateral foreleg and hindleg.

The deficiencies in postural adjustment resulting from cortical lesions are less extensive than those resulting from ablation of similar areas of the cortex in higher forms.

Visual responses are affected by removal of the visual cortex, but with this exception lesions in non-excitable portions of the cortex cause no deficiency of the postural responses studied.

Extirpation of a portion of the sensori-motor area produces deficiencies which are less extensive than those resulting from ablation of the entire area. Bilateral ablation of electrically excitable cortical areas results in bilateral deficiencies.

Unilateral removal of the electrically excitable area alone produces just as great deficiencies in the placing and hopping responses of the contralateral legs as does ablation of the entire neocortex of one hemisphere. (Authors' abstr.)

Chemical Constitution and Anaesthetic Potency in Relation to Cortical Potentials.

The cortical electrical response to anaesthesia from eleven alcohols has been studied in cats in regard to the effects of an increase in carbon atoms in the alcohols and an increase in potency, to the total frequency per second of cortical waves: the frequency becomes progressively slower with increasing molecular weight (increased number of carbon atoms) of the alcohols.

The rate of change of the frequency curve is the reciprocal of that of the potency curve. That this slowing is due to an increase in anaesthetic potency rather than to an increase in molecular weight *per se* is shown by the fact that the total frequency is also slower when the secondary or tertiary forms of the alcohols are compared with the primary; thus frequency appears to bear a definite relationship to the anaesthetic potency of the alcohol, even when molecular weight and atomic composition (but not structure) are maintained unchanged. A new approach to study of the meaning of anaesthetic potency is presented. (Author's abstr.)

Ocular Movements from the Occipital Lobe in the Monkey.

Contralateral conjugate deviation of the eyes with lateral or with either upward or downward components was obtained by stimulation of the occipital cortex. When the exciting electrodes were applied to the cortex of area 17 superior to the calcarine fissure, the movements tended to be lateral and downward. When applied below the same landmarks, the deviation was lateral and upward. The relationship of this finding to the projection of the retina on the cerebral cortex is discussed. (Authors' abstr.)

Nature of the First Visible Contractions of the Forelimb Musculature in Rat Foetuses.

The earliest visible contractions of skeletal muscle in the living, intact rat foetus were produced by electrical stimulation during the 16th day of gestation. These involved a variety of forelimb movements.

The movements typically exhibited high threshold, relatively long duration (especially of the phase of relaxation), tendency toward rapid fatigue, and long time factor (suggestive of both long latent period and long chronaxie of the muscles).

The limb at this stage is in a state of early differentiation, including not only muscle-fibres, but also fascia, tendons and joints. This strongly suggests that extramuscular factors may be influencing the nature of the muscular response, whose visible properties thus may be more apparent than real. It is concluded, therefore, that the somatic movements cannot be unequivocally accepted as reflecting the physiological capacities of the muscles involved.

Evidence is presented indicating that potentially effective neuromuscular transmission, on the efferent side at least, exists in 16-day rat foetuses, although the nerve-endings themselves are primitive in form.

The theory of a " myogenic " developmental phase of muscular activity is discussed, and it is concluded that no valid evidence for such a phase exists. (Authors' abstr.)

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Topographic Studies of Disturbances of Sweat Secretion after Complete Lesions of Peripheral Nerves.

Colorimetric investigation of sweat secretion shows that after total interruption of a peripheral nerve the loss of sweating is complete only within the autonomous zone of the nerve.

The mixed or intermediate zone is revealed by more or less marked hypohidrosis. Following the administration of pilocarpine this zone shows an area of hypohidrosis.

The maximal zone of a peripheral nerve may be demonstrated (*a*) after section of all adjacent nerves (the area of residual sweating), or (*b*) by incomplete lesions of the nerve, characterized by pain and cutaneous tenderness and spontaneous sweating.

In the area of residual sweating the autonomous and mixed zones can be distinguished from each other by differing degrees of sweating.

The demonstration of the different zones in the sweat picture shows that there is great variability in the area of autonomous supply of each peripheral nerve and in the extent of overlap of adjacent peripheral nerves with one another.

(Author's abstr.)

Alzheimer's Disease.

Six cases of Alzheimer's disease are recorded with pathological findings.

A plea is made for a wider conception of this disease, at any rate until such time as more is known about it, and that this conception should be founded on the pathological histology.

It is suggested that two factors may be involved in any given case, the one endogenous or constitutional and the other exogenous. The former is represented by familial cases; the latter by those examples of subacute toxic-infective psychosis with dementia which present the characteristic histology of Alzheimer's disease. Between these two all gradations may be expected, but most cases, and especially the classical type which presents a fairly typical clinical picture, approximate to the endogenous variety.

The importance is stressed for the need for more complete histological examinations of the other organs of the body. The possibility of extracerebral factors must ever be in mind. (Author's abstr.)

A Study of Pure Word-deafness.

A case has been described in which there was a syndrome consisting of pure word-deafness, and what has been described as asymbolia for pain, following a head injury. The inter-relationship of these two disorders has been discussed, and it has been pointed out that pure word-deafness and asymbolia for pain have the common feature of a disturbance in the relationship between the individual and his environment. The localization of the responsible lesions has been discussed. Consideration has been given to the problem of the position of pure word-deafness in the system of aphasias. (Authors' abstr.)

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On Mass Psychoses.

Masses or crowds are formed mainly in periods of national or social tension. In the crowds individuals lose their personalities, and their moral or educational inhibitions disappear. The actions of crowds often manifest pathological signs. Mass psychosis is present when the mental basis of crowd formation is pathological, or when the behaviour of the crowds results in unreasonable exaggerations. The most frequent mass psychosis is mass hysteria. Among its manifestations there are vehement explosions caused sometimes by a single person's pathological reactions; primitive, unrestricted motions, similar to convulsions; blind imitations of peculiar habits; escapes into illness or even temporary deficiency of sense organs; belief in fantasy pictures as real existences; and uncritical worship of mysterious phenomena. The leader of the masses has a tremendous influence which can be used for construction as well as destruction. The lasting capacity of mass psychoses is different; explosive reactions are terrible, but they may quickly disappear; escapes and intentional neuroses stop when the aim is attained, or becomes hopeless; fantastic ideas generally last longer, at least for the duration of the basic excitement; and, finally, mystic suggestions can be suppressed only when their originators can be stopped. M. ERDÉLYI (Psychol. Abstr.).

MED. J. AUSTR.

VOL. XXVII. JUNE 29, 1940.

Cerebral Compression.

As an intracranial lesion expands, it does so primarily at the expense of the more easily compressible constituents of the brain, namely, the subjacent venous

and cerebro-spinal fluid channels. If the lesion is removed at this stage the brain will expand promptly, as it is forced out by the return of the blood and cerebro-spinal fluid to their normal channels and to a slight extent by the natural elasticity of the cerebral substance. If, however, the lesion should become very large and exert its pressure over a relatively long time, additional fluid is expressed from the interstitial tissue of the brain and perhaps also from the various cells. In such cases, when the lesion is removed there will be a certain degree of expansion due to the return of blood and cerebro-spinal fluid and to elasticity. Complete expansion will depend on how much interstitial fluid has been expressed by the lesion. If the amount is small the brain will soon resume its normal contour; but if it is large, several hours may elapse before the brain expands fully. The rapidity with which the lesion expands also seems to influence the rate of expansion. In the case of a slowly-expanding lesion, the brain apparently accommodates itself so that very little interstitial fluid is expressed, while if the lesion expands rapidly a relatively large amount of fluid is expressed from the interstitial tissues.

Thus it can be seen that the length of time the brain is compressed, the degree of pressure exerted and the rate of expansion of the lesion are the primary or indirect factors controlling the rate of expansion of the brain after the compressing agent has been removed. The loss of fluid from the interstitial tissues and possibly from the cellular elements is secondary to the influence of the above three factors, and is the direct factor influencing expansion of the brain.

It is not necessary that all three should be present to the same pronounced degree, for if one is slight the same result may occur when the other two factors are more pronounced. This is demonstrated in the two clinical cases that have been reviewed. In the first the lesion was very large, rapidly expanding, and exerted its pressure for less than two hours. In the second case the lesion was also large, but slightly less so than the first. It expanded slowly, but exerted its pressure for several hours longer.

The physico-chemical factors controlling this exchange of fluid as the result of pressure are another problem, and have not been considered in this study. Further presumptive evidence in support of the above conclusions may be obtained from the two clinical cases described. In each case the blood-pressure readings did not fall below normal until just before death, and the pressure of the cerebro-spinal fluid was elevated in both cases during the post-operative course; but even these factors were not sufficient to force the brain out to its normal contour when the lesions were removed.

This condition must be very uncommon, and to be brought about it seems necessary that the lesion should compress the brain for some hours, that it should be large and exert a considerable degree of pressure, and that it should expand rapidly. This study, applied clinically, supplies another reason for the surgical removal of an intracranial expanding lesion at the earliest opportunity in cases in which such a removal is possible. (Author's abstr.)

OCCUP. THER. AND REHABIL.

VOL. XIX. APRIL, 1940.

Conjuring and Occupational Therapy.

The value of conjuring in the field of occupational therapy is considered and the technical methods for teaching conjuring to patients in classes are indicated.

In an interesting section on the psychology of conjuring it is stated that 10 per cent. depends on manual dexterity, 10 per cent. on apparatus, and 80 per cent. upon the successful application of psychological principles. "Gestures, expressions and dramatic patter are intentionally planned, not only to entertain, but also to mislead deliberately the spectators' senses, and to confuse their perceptions." Despite the popular theory, it is the mind, not the eye that is deceived, for the hand is quicker than the eye only because the latter is engaged elsewhere. All magicians concede that a highly educated person is the easiest to fool, because he has learnt to reason logically. Children, on the other hand, are the most difficult because of inattention and undeveloped reasoning power.

The psychological principles involved include two main groups. The first concerns misdirection of attention and is discussed under the following subheadings: (1) diversion of attention, (2) distraction of attention, and (3) relaxation of attention. The second category is concerned with misdirection by the creation of illusions of perception, based upon the principle of association of ideas.

S. M. COLEMAN.

VOL. XIX. JUNE, 1940.

Outlets for the Propitiation of Guilt.

In this paper it is shown how occupational therapy is able to provide means for guilt atonement by offering acceptable means of self mutilation, lessening in this way the demands of the super-ego. S. M. COLEMAN.

PROC. AMER. ASSOC. STUD. MENT. DEF.

VOL. XLIV. 1939.

A Contribution to the Study of the Influence of Heredity on Mental Deficiency. The Genetics of Phenylpyruvic Oligophrenia.

Two hundred cases of phenylpyruvic oligophrenia were studied. The disease is characterized by an alteration of the metabolism of phenylalanine. Clinically, anomalies of the motor system are demonstrable and pronounced intellectual retardation is present in all cases. Over 20,000 inmates of 14 state institutions for the feeble-minded were examined. The family of each case of phenylpyruvia was visited and all living parents and siblings and relatives of some were examined. These data were examined to determine whether the disease was caused by environmental factors, but seemingly it was not. Then the material was examined for evidence of genetic mechanisms. The data were found to be consistent with the quantitative requirements of the theory of monomeric recessivity. Apparently the disease is determined by an autosomal recessive gene.

M. W. KUENZEL (Psychol. Abstr.).

Research in Progress upon the Electro-encephalogram in Mental Deficiency.

Studies have been directed principally to the determination of whether differences in intellectual level tend to be associated with differences in characteristics of the electro-encephalogram. To facilitate control of the chronological age variable one study was concerned with subjects over 16 years of age; another dealt with patients of the Mongolian type; a third with subjects of the non-differentiated familial type. Thirteen individuals with phenylpyruvic oligophrenia have been examined. Another mixed group of 30 individuals ranging in age from 2·5 to 10 years are being followed through at regular intervals in order to study the relation of developmental changes in the electro-encephalogram with other measurable changes in growth. Still another study is concerned with pairs of identical and fraternal twins. The new technique is said to be leading to the discovery of some of the physiological factors on which intelligence and its deficiencies depend.

M. W. KUENZEL (Psychol. abstr.)

The Conditioned Habit Treatment of Nocturnal Enuretics.

Six males and one female from an institutional population of mental defectives were selected for a preliminary investigation of the usefulness of Mowrer's technique for nocturnal enuretics. The experiment is described. Initial voluntary awakenings occurred as early as the fifth night in one case and as late as the twenty-first night in another. Successful therapeutic results were obtained in six of the seven cases.

M. W. KUENZEL (Psychol. Abstr.).

PROC. ASSOC. RES. NERV. MENT. DIS.

VOL. XIV. 1939.

The Electrical Activity of the Brain: Its Relation to Physiological States and to States of Impaired Consciousness.

A review of selected investigations in the field of electro-encephalography, with particular emphasis upon the author's research in individual differences and their inheritance, in the relation of alpha rhythm and personality type, in the modifications during sleep, and in the effects of abnormal conditions such as anoxia, various drugs, and pathological conditions. It is concluded that a general correlation exists between characteristics of the electrical activity of the brain and the state

of consciousness of the subject—" a closer relationship, it is believed, between consciousness and an objective physiological phenomenon than has been obtained by any previous method." D. G. MARQUIS (Psychol. Abstr.).

Effects of Vitamin Deficiency on Mental and Emotional Processes.

The role of vitamin deficiency in brain function is shown by the recently discovered relationship between nicotinic acid deficiency and pellagra, a syndrome characterized by nervous and mental manifestations. Evidence from a series of 51 patients with Korsakov psychosis indicates that recovery is many times more frequent under treatment with massive doses of vitamin B_1 (thiamin chloride), although definite conclusions must await more extensive evidence. Another series of patients with encephalopathic syndromes showed a reduction in mortality from 89 per cent. (47 cases) to 12 per cent. (16 cases) when treatment with nicotinic acid was introduced. In the recovered patients improvement was noted within 24 hours after treatment. D. G. MARQUIS (Psychol. Abstr.).

The Effects of Barbiturates and Bromides on Mental and Emotional Processes.

Bromide and barbiturate intoxications not only provoke characteristically different neurological syndromes, but also quite specific psychiatric pictures. Delirious and hallucinatory episodes with marked disorientation and confusional states are typical in bromide psychoses, which may also bring out deep castration fears and individual problems. In the barbiturate cases the stupor is followed only by a short period of confusion and there is a definite disturbance in the mood, usually in the direction of euphoria. Taken together with the known specific symptoms of alcohol, marihuana and mescal intoxication, these results indicate that drugs produce characteristic psychological changes which are specific to the nature of the drug, and presumably depend upon its site of action in the nervous system. D. G. MARQUIS (Psychol. Abstr.).

Effects of Benzedrine in Altering Mental and Emotional Processes.

Experimental investigations of the physiological, psychological, and clinical effects of benzedrine are reviewed. In speculating on its mechanism of action, the author suggests that benzedrine acts directly on central neurons in a manner antagonistic to acetylcholine, and is probably similar to, if not identical with, a substance which is elaborated within the body. Such a substance might be closely related to the sympathins. D. G. MARQUIS (Psychol. Abstr.).

The Effects of Marihuana.

The symptoms which follow the smoking of marihuana cigarettes are increase in motor activity, a feeling of exhilaration and excitement, or of languor, mental confusion, disorientation, accelerated perception, elementary visual illusions and hallucinations, euphoria and talkativeness. Subjectively there are feelings of accelerated thought processes and of intellectual brilliance, changes in time perception, various somatic feelings, dizziness, hunger, swelling of the head, lightness of the extremities, a sensation of walking on air, lengthening of the limbs, and sexual illusions and excitement. D. G. MARQUIS (Psychol. Abstr.).

Central Nervous Mechanisms for Emotional Behaviour Patterns in Animals.

A review of the experimental study of the mechanism of emotional behaviour leads to the conclusion that anger, fear, pleasure and sexual excitement in animals are specific kinds of behaviour which are distinguishable from one another and from all other forms of activity. With the possible exception of the full display of pleasure, each of these modes of response is effected by central neural mechanisms which are subcortical and suprabulbar. Future work should determine the various channels involved in the arousal of emotional behaviour. In the case of sexual

behaviour, one of the factors is definitely hormonal, and in the absence of the cortex the number of emotional stimuli is greatly reduced.

D. G. MARQUIS (Psychol. Abstr.).

Levels of Autonomic Function with Particular Reference to the Cerebral Cortex.

Redefinition of the autonomic nervous system so as to include the central mechanism of control permits the concept of functional levels to be applied to autonomic as well as somatic functions. The possibilities of reflex and integrated control of autonomic functions at the spinal, bulbar, hypothalamic and cortical levels are reviewed. Comparative studies in various animals indicate that there has been a progressive encephalization of mechanisms of emotional expression and of autonomic control in the ascending evolutionary scale.

D. G. MARQUIS (Psychol. Abstr.).

Behaviour of the Newborn Infant and Early Neuro-muscular Development.

The development during the first two years may be grouped into four stages: (1) The first four months period is marked by a diminution of the atavistic reflexes and rhythmical movements of the newborn. (2) The period between four and eight or nine months is characterized by the development of voluntary movements in the upper spinal region. (3) From eight to fourteen months there is increasing control of activities of the lower spinal region. (4) The remaining ten months are marked by the rapid development in associational processes, conditioning, and symbolic associations, including language. D. G. MARQUIS (Psychol. Abstr.).

The Brain Structure of the Newborn Infant and Consideration of the Senile Brain.

Experimental studies of the correlation between neural development and behaviour in animals are reviewed in relation to the author's investigations of the histological structure of the brain of the newborn infant. Whether any part of the cerebral cortex can function at birth is a matter of speculation. There is no myelin anywhere in the cortex, but animal studies have shown that myelin is not essential for neural activity. Throughout the cortex a neuropil is present in sufficient quantity to afford a means for contacts between afferent and efferent fibres.

D. G. MARQUIS (Psychol. Abstr.).

Physiological Changes in Emotional States.

The biological function of the acute emotional experience is the precipitation of an internal crisis, in which habit is interrupted and the primitive facilities for biological adjustment are mobilized—both the visceral and the intellectual facilities. The so-called emotional states of many neurotic and psychotic patients, on the other hand, represent merely the stereotyped and conventionalized expression of a pattern of behaviour sometimes associated with emotional experience. In studies of excited and " emotional " patients, no evidence of increased blood sugar or of cardiac acceleration was found. Emotional experiences, with the usual visceral accompaniment, can of course be induced acutely in such patients.

D. G. MARQUIS (Psychol. Abstr.).

PSYCHIAT. QUART.

VOL. XIV. JULY, 1940.

Psychometric Study of Insulin-treated Schizophrenics.

A comparative psychometric study of the mental efficiency of schizophrenic patients immediately before and after insulin treatment suggests the possibility of a psychological test battery capable of forecasting the probable effects of insulin therapy to a considerable degree. A test battery consisting of a vocational interest blank, tests of counting by 3's and naming words in three minutes, a similarities and a directions test, gave a correlation of ·73 and a percentage of correspondence of 87, with a clinical appraisal of the patient's condition 6 to 18 months after termination of treatment. This correspondence was closer than the correspondence between the psychiatrists' ratings at the time of termination of treatment with clinical findings recorded after a 6 to 18 month period. Analysis of the psychometric findings suggests the possibility that certain patients may be harmed rather than improved by the insulin treatment. (Authors' abstr.)

The Prevention of Metrazol Fractures by Beta-erythroidin Hydrochloride.

A group of 37 patients was treated, consisting of 17 schizophrenics, 10 manic-depressives, 7 suffering from involutional psychosis, and 3 from compulsive neuroses of long standing. A total of 156 separate treatments were given, with 139 resulting seizures.

Roentgenograms of the vertebral column were taken in 26 cases, and found to be entirely negative. In all the 11 remaining in which circumstances did not permit the expense of plates, careful clinical evaluation revealed no evidence of fractures. The important question whether the considerable modification of the severity of the convulsion interferes with the therapeutic efficacy of metrazol can be answered by stating that of the 37 patients treated, 29 have been discharged in satisfactory remission. The average number of treatments per patient was 4·2. The average hospital stay was 19·3 days. No fatalities occurred. Three patients who relapsed within a three month interval after therapy all responded well to further treatment. (Authors' abstr.)

The Mode of Action of Ergotamine Tartrate in Psychotic Patients.

One mgm. doses of ergotamine tartrate given daily to a group of long-standing aggressive and destructive patients were sufficient to restrain temporarily many of their troublesome symptoms, the result being shown in improved emotional response and thinking ability. Six of the cases that failed to retain their improvements with ergotamine later were insulin or metrazol failures likewise. There were only significant changes in peripheral autonomic effects, a slight depression of the sympathetic mechanisms being shown as is demonstrated by the increased weight, appetite and rectal temperature, and decreased pulse pressure, blood sugar and calcium. These physical changes are so slight that it does not seem possible that they could be in any way responsible for the great psychic and behaviour changes seen. In the one case which recovered, the autonomic effects were more marked. Because of the slight effects on the sympathetic mechanism seen in these cases under ergotamine therapy, it appears that the effect obtained in the behaviour of aggressive cases may be attributable to some action on the central nervous system, not related to its peripheral effect. (Author's abstr.)

Preliminary Report on the Results of the Treatment of Schizophrenia by Nitrogen Inhalation.

1. A group of 17 patients, 16 suffering from schizophrenia and one from manic-depressive psychosis, was treated by nitrogen inhalation.

2. The following results were noted: 5 completely remitted, 4 greatly improved, 1 improved (now in remission), which makes improvement in different degrees in 10 out of 17 (2 were slightly improved, 5 unimproved); one relapse after a five months' remission.

3. A follow-up study of cases in remission one year and longer indicated that these patients tend to remain improved.

4. The advantages of the nitrogen treatment are briefly as follows:

(1) The procedure is simple and does not always require hospitalization.

(2) It has been relatively free from complications in over 400 treatments.

(3) The method is constantly controllable. (Author's abstr.)

Report on 441 Cases Treated with Metrazol.

1. These results with metrazol therapy in schizophrenia have been much poorer than the results observed by many other authors. This may be due to the indiscriminate choice of patients, the lack of facilities for intensive psychotherapy, and the over-enthusiasm of early observers in interpreting their results.

2. Metrazol therapy gave no better results in this series than most observers have seen in non-specifically treated cases. In many instances the results with the latter method were much better.

3. Metrazol therapy has many inherent dangers, some of which are now known. It took four years to find such a simple condition as a fractured dorsal vertebra. In addition, there have been complicating fractures, dislocations, torn muscles and broncho-pneumonia.

4. Some cases of schizophrenia have shown dramatic improvement with metrazol therapy. It is difficult to predict which would show such improvement. It is apparent that in isolated instances and early in the disease, improvement may occur shortly after treatment. In some of these same cases, late follow-up results have shown regression to the original psychotic condition. (Author's abstr.)

Some Observations on Treatment of Institutional Epileptics with Dilantin.

1. Dilantin sodium seems to be a more effective anti-convulsant than drugs previously available.

2. There was little correlation between decrease or complete control of seizures and corresponding mental improvement.

3. A substantial percentage of patients showed an adverse reaction to the substitution of dilantin for phenobarbital, with marked increase in delusional trends and other psychotic manifestations.

4. Because of its potent anti-convulsive action, epileptic patients who are otherwise organically sound should be given the benefit of an adequate trial with dilantin.

5. Unless further investigation shows that this drug can act synergistically with a sedative such as luminal in controlling psychotic symptoms, its most satisfactory results will be obtained in non-psychotic rather than in mentally impaired individuals. (Authors' abstr.)

The Treatment of Epilepsy with Sodium Diphenyl Hydantoinate.

1. Sodium diphenyl hydantoinate is an effective anti-convulsant.

2. In a series of institutionalized chronic epileptics who had been receiving other anticonvulsant previously, it produced significant improvement in 50 per cent., some improvement in 26·3 per cent., and no improvement in 23·7 per cent.

3. Toxic reactions of various types are caused by dilantin. None of these seem to be serious in nature, and all can be controlled by decrease or withdrawal of the drug. However, careful observation of the patient during treatment is advisable.

4. A combination of phenobarbital and dilantin is advisable in some cases. (Authors' abstr.)

The Response of Various Types of Epilepsy to Dilantin Therapy.

Study of the above series seems to show that sodium diphenyl hydantoinate (dilantin) is a relatively non-toxic drug when used in doses up to 0·6 gm. a day. Frank cardiorenal disease appears to be the chief contra-indication to the use of this drug. Minor complications were found to clear up rapidly when the drug was withdrawn for two or three days. In most cases, even the rather frequent toxic dermatitis does not preclude further treatment after an adequate rest period. The complications are sufficiently severe, however, to call for an adequate and well-trained nursing personnel. Although the number of these cases is too small to draw infallible conclusions, the markedly different response of the various subgroups opens up interesting avenues for further clinical investigation. (Author's abstr.)

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Hand Usage and Angleboard Dextrality Quotients of Adult Stutterers and Non-Stutterers.

This study was designed to check the hypothesis that stutterers are characterized by ambilaterality of central nervous system organization as indicated by measures of handedness. Two modifications of procedure differentiate the present

investigation from previously reported pertinent researches. First, the 98 stutterers, average age 21 years, and the 71 non-stutterers, average age 22 years, who served as subjects, were unselected with regard to hand usage. In previous studies by Van Riper, Jasper and others, unselected stutterers were compared with right-handed, left-handed and ambidextrous non-stutterers, selected on the basis of hand usage data. Second, the three tests of handedness which were used were scored by means of the dextrality quotient (DQ) formula, which makes possible the intercorrelation of tests and representation of relatively fine degrees of difference from 0·00 per cent. to 100 per cent. right-handedness. Two parts of the Van Riper angleboard test were used, and after these were administered each subject answered a hand usage questionnaire. Correlations between scores computed by two independent scorers for the two parts of the angleboard test, and for stutterers and non-stutterers, respectively, ranged from ·94 ± ·008 to ·99 ± ·002. Correlations between the various tests of handedness ranged from —·15 ± ·08 to +·29 ± ·06, with the exception of one coefficient of +·62 ± ·05. Frequency distributions of DQ's were markedly similar for the stutterers and non-stutterers on each test; the distributions of the angleboard scores approximated a normal curve, and those for the hand usage DQ's were skewed to the left, but were essentially unimodal. No statistically significant differences between means were found. (Author's abstr.)

An Evaluation of the Postulates Underlying the Babcock Deterioration Test.

The standardization and the explanation for the validity of the Babcock deterioration scale have been based on the assumption that vocabulary is an old habit which fails to deteriorate in proportion to the acquisition of more recent material. This assumption, however, is untenable, since it has been shown that vocabulary develops up to the age of 18 years and is, therefore, in no manner an older habit than the abilities which the test measures on the items which show the effects of deterioration.

The thesis is advanced that the Babcock test for deterioration is valid not because recently acquired behaviour is compared with old habits, but because goal activity which can be carried to completion with only one set of acts is compared with goal activity where the end results can be achieved by a number of separate and qualitatively different acts of unequal difficulty. The memory, etc., items of the Babcock test require specific methods of completion, whereas on the vocabulary test the subject has a number of choices with which to define a word, and even if the more difficult conceptual organization has deteriorated, the correct response can still be given on a " lower " conceptual level. Analyses of qualitative studies of vocabulary tests presented in the literature show that the difficulty of defining a word is a function of the number and kinds of correct definitions which can be used.

To test the above hypothesis a one-alley maze has been devised which can be solved by seven appropriate, but different, methods. The results show that there is a qualitative difference in the methods used to solve the problem which is related to the general level of ability of the subjects. (Author's abstr.)

A Scale for Evaluating Prognosis in Schizophrenia.

The findings of the many psychiatric studies on prognosis in schizophrenia have been organized into a weighted scale and used in differentiating " process " schizophrenia from the schizophreniform psychoses. Differential weights were given to the various malignant and benign scale items in proportion to the importance ascribed to them and the frequency with which they were mentioned in the more than 50 psychiatric studies that have been made on prognosis in schizophrenia.

The initial use of the scale has been in classifying the schizophrenic patients treated with either metrazol or insulin therapy. The results clearly differentiated those who were classified as " in remission " or greatly improved at treatment staff conference from those who were considered only slightly improved or unchanged.

These findings suggest that the high percentage of "remissions" in schizophrenia reported for both metrazol and insulin therapies is related to the inclusion of a disproportionately large number of schizophrenic or so-called "dementia praecox" patients selected for therapy. This agrees with Langfeldt's speculation concerning shock therapy results, and also explains the individual differences in reaction to shock therapy among the schizophrenics treated.

(Authors' Abstr.).

A Comparison of Two Techniques for Measuring Intellectual Impairment and Deterioration.

This study was concerned with extending the method of measuring mental deterioration employed by Babcock. Her method is to contrast a relatively enduring function with a group of disintegrating ones. More specifically, she contrasts the patient's mental age as determined by the Terman vocabulary test with his mental age as determined by a group of memory, motor, and learning tests. Deterioration is indicated by the efficiency index, which represents the extent to which the latter falls short of the former.

With a view to enhancing the value of the method, the authors have been searching for even more rapidly disintegrating functions to contrast with vocabulary. The present study is concerned with an evaluation of the function of abstract thinking in this connection.

The Babcock examination and a pencil-and-paper test of abstract-thinking ability were given to 160 patients in a private mental hospital. The patients were then grouped according to degree of deterioration, as indicated by the Babcock efficiency index. Mean mental-age scores for the two tests were practically identical in the group showing no deterioration. In all the remaining groups the abstract-thinking scores were considerably the lower. The results indicate that the abstract thinking test, when used in conjunction with a vocabulary test, constitutes a sensitive measure of intellectual impairment. (Author's abstr.)

Differential Functional Loss in Certain Psychoses.

The Wechsler-Bellevue Intelligence Test was administered to 100 patients at Elgin State Hospital. The purpose of the study was to determine differential patterns of, and variability in functional loss for, various psychoses. Comparison is possible in terms of standard scores on the ten subtests of the scale. Scatter for patients was compared with Wechsler's norms and scores of another control group. Scatter was about 35 per cent. greater for the psychotics.

Intercorrelations for the psychotics were markedly different from those of the controls. Wechsler's highest intercorrelation was between "similarities" and "comprehension"—·721; the lowest, between "object-assembly" and "digit-span"—·155. Corresponding psychotic correlations were ·55 and ·17 respectively. The highest psychotic intercorrelation was ·70 ("digit-symbols" and "picture-arrangement"), and the lowest, ·13 ("digit-span" and "comprehension"). Wechsler's intercorrelations between these were, respectively, ·444 and ·372.

Therefore there are significant differences in variability and pattern of scores between psychotics and normals. (Author's abstr.)

Pathology of the Figure-background Relation in the Child.

Goldstein and Gelb have described a disturbance in the differentiation of figure and background in brain-injured adult patients. We have attempted, in various experimental situations, to demonstrate the presence of this disturbance in brain-injured children. Two groups of mentally-retarded children were used. The members of the one group showed symptoms of brain lesion, but these were not present in children of the motor and tactile-motor tests, and their reactions to patterns presented tachistoscopically. One of the tests consists of copying patterns made up of marbles placed in the holes of a cardboard background. Both the

marbles and the holes have a definite configuration. The child must construct the patterns in spite of the influence which the background (hole-) configuration exerts. A tactual-motor test was constructed on similar principles. The pictures used in the tachistoscopic test were drawings of objects embedded in a clearly structured homogeneous background. The child was asked to tell what he saw. The results of the various tests demonstrate that, for the brain-injured child, the characteristics of the background have strong stimulus value, whereas they exert little influence on the reactions of the children having no brain lesion.

(Authors' abstr.)

The Effect of Metrazol Shock upon Habit Systems.

The hypothesis tested was whether a single metrazol convulsion weakened more recently acquired habits to a greater extent than older habits which had previously been repressed or extinguished, with the result that the latter then became dominant. Twenty schizophrenics undergoing metrazol therapy were compared with a control group. The technique involved setting up a simple motor habit and then training in another habit which was similar to, but incompatible with, the first habit, thus necessitating the suppression of the first habit. The experimental group was then subjected to metrazol shock, and both groups tested for retention of the habits. It was found that a statistically significant higher number of reversals to the older habit occurred in the group subjected to metrazol shock than in the control group.

(Author's abstr.)

Emotional Factors in Gastric Neurosis and Peptic Ulcer.

The purpose of this investigation was to determine to what extent induced affective states were accompanied by changes in gastric function in patients suffering from gastric neurosis and peptic ulcer. While the subject rested, motility and secretion of the stomach, finger temperature and respiration were recorded. Affective states were induced by discussing emotionally charged life situations with the subjects over prolonged periods. To date, 55 experiments have been conducted on nine patients. In affective stress, particularly anger, the gastric motility increased ; the acidity values at times after an initial fall, rose ; respiration became more frequent and shallow, but with sighs ; the finger temperature fell, and in patients with peptic ulcers blood occasionally appeared in the stomach contents. Similar changes appeared in gastric function during sleep, if the subject, prior to the observation, was subjected to affective stress. (Authors' abstr.)

Studies in Electrically Induced Convulsions in Rats.

In several European countries schizophrenia is currently being treated by convulsions electrically induced. To obtain data on the possible effects of this type of treatment, and to study allied problems, a series of 50–100 convulsions were induced in a group of 55 white rats by passing a current of 4·5 milliamperes through the intact brain. The present report covers the four following points :

(1) Description of attack : Convulsions are of the typical "*grand mal*" type, and closely resemble the " neuroses " produced by air blasts and other methods.

(2) General behaviour changes : After 5–10 convulsions the rats become extremely passive, inactive and submissive. Many exhibit a waxlike flexibility. This behaviour is not limited to the experimental situation. Motility records indicate that after 50 convulsions rats are about 65 per cent. as active as control animals. Over a three-week period, convulsed animals show only one-half as great a gain in weight as control animals. Convulsion-free periods of from two to three weeks tend to " normalize " the experimental animals.

(3) Effect of drugs : Neither the subcutaneous injection of alcohol (·25–1·25 c.c.), nor of adrenalin (·10–50 c.c., concentration 1 in 1000) affected the threshold of shock necessary to produce a convulsion. Both drugs, however, resulted in behaviour changes.

(4) Conditioning : All animals gave evidence of some conditioning, but no

true " conditioned convulsion " was ever obtained. One possible explanation is the finding in human studies that convulsions produce a complete and permanent amnesia for events immediately preceding the attack. (Author's abstr.).

Electro-encephalographic Aspects of Migraine and of the Common Headache.

This is a first report on an electro-encephalographic study of the common and the migraine forms of headache.

Multiple-channel recording is employed, and the electro-encephalograms during headache episodes are compared with those taken during normal periods in the same subjects. Illustrative " brain wave " records of differing types will be shown of patients before and during headache episodes and during the course of development of an individual attack. The records seem to indicate that the migraine subjects thus far used give a characteristic wave-form differing from the general run of normal subjects. (Author's abstr.)

Brain Potentials during Sleep: An Investigation of Electro-encephalographic Individual Differences and their Constancy.

This study is an investigation of the degree to which constancy of individual differences in the EEG is exhibited in three general conditions, one during sleep and two during waking. In the sleep experiments multiple-area all-night EEG's were recorded from 20 individuals distributed throughout the alpha index range and were analysed categorically. As additional evidence, 82 samples of record were obtained from six of these subjects and were analysed as Fourier transforms with the Grass wave analyser.

The continuous all-night sleep records were analysed according to the amount of time any of several wave " categories " was present. Though rather marked individual differences were found to exist, these differences were apparently unrelated to any specific aspect of the waking record. Groups formed on the basis of per cent. time waking alpha similarity showed no consistent mean group trends for any of the sleep wave categories, although there was a tendency for subjects with a strong waking alpha rhythm to show more sleep alpha rhythm, and for subjects with a rare alpha rhythm to show more random sleep potentials. These differences were not great.

Rank difference correlations computed between alpha index when awake and any of the sleep categories, and between the several sleep categories, showed no significant relationship other than between waking and sleep alpha activity, and between spindles and spindles plus random.

The Fourier transforms also failed to reveal any distinguishable differences in the sleep records that could be related to the waking records. (Author's abstr.)

Differences in the Electro-encephalograms of Normal and Behaviour-problem Children.

Electro-encephalograms from occipital, central and frontal regions in 36 normal, 50 behaviour-problem and 22 " constitutionally inferior " children, and in a control group of 30 college students, were analysed in terms of frequency, amplitude, and per cent. time measurements.

Three abnormal factors in the electro-encephalograms differentiated the behaviour-problem cases from the normal children: greater prevalence of 2–5 per second waves, 5–8 per second waves, and the " hyperventilation effects." The " constitutionally inferior " children resembled the behaviour-problem children with respect to the two latter types of abnormality. The college students showed practically none of the abnormal characteristics.

The slow waves and the latent signs of abnormality induced by hyperventilation in the behaviour-problem children are interpreted as disturbances of cortical function which appear to be important factors in the inability of this group to adjust to environmental conditions, particularly when such conditions are unfavourable.

(Author's abstr.)

An Analysis of Frontal Lobe Function in Monkeys by Means of Two "Delayed Response" Methods.

An attempt has been made to delimit further the function of the frontal association areas (Brodmann's areas 9, 10, 11 and 12) through experimental analysis of two different delayed response situations in which adaptive behaviour in animals deprived of the frontal cortex can be demonstrated in the one case to be impaired, and in the other, to be maintained. Two monkeys were trained to delay response according to a method which allowed a complete, but unrewarded, run to one of two drawers on the pre-delay (presentation) trial. Following the attainment of a stable level of suprachance performance during 200 test trials, the animals were subjected to simultaneous bilateral frontal lobectomy. Post-operative results indicate, in accordance with the standard delayed response technique (Jacobsen), that performance in the present problem was completely abolished. Successful response was reinstated, however, by actually rewarding the subjects on the pre-delay trial for running to the presented drawer. Results obtained under this altered condition proved comparable in terms of accuracy and length of delay to those yielded by the same animals under preoperative conditions. The possibility of differentiating in terms of adaptation conditioned, respectively, by (1) a single unreinforced (unrewarded and unpunished) presentation, and (2) a single directly reinforced presentation, is considered. A "derived" reinforcing agency of the intact frontal areas is tentatively suggested. (Author's abstr.)

Some Personality Changes in Adolescence as Revealed by the Rorschach Method.

One hundred and fifty-two Rorschach records from 76 children participating in the long-term study of developmental growth at the Brush Foundation were selected for study. The children were tested at 12 and 15 years of age. Patterns which purport to reveal emotional stability, instability, adaptability, egocentricity, impulsiveness, inner living and fantasy life were subjected to statistical analysis to determine age and sex differences. Rorschach "Erlebnistypen" were analysed qualitatively to determine dominant personality trends from 12 to 15 years of age, and constancy or change in personality pattern.

It is concluded that the Rorschach method is highly serviceable in analysing and describing adolescent personality. Despite the small number of cases, age and sex differences are revealed in many patterns. Twelve-year-old children tend to be more extratensive than introversive. They are more impressionable to outside stimuli and more occupied with relationships to the outside world. Boys are, as a rule, more extratensive than girls at this age.

At 15 years of age children tend to be more introversive. They show more inner living and fantasy life and are more concerned with their subjective experiences. They are more emotionally stable and mature at this age. Girls show a greater development of all these tendencies than boys at both ages. However, they also show a surprising degree of excitability and impulsiveness.

The personality patterns studied tend to change from 12 to 15 years of age. The most constant patterns are the introversive ones. The two most characteristic trends noted are the introversial swing and contraction of both sides of the personality.

Differentiating Rorschach patterns are suggested with tentative norms for use in interpreting Rorschach results for similar age and sex groups.

(Author's abstr.)

Sources of Error in Rorschach Test Procedures.

The Rorschach test, as a sound method for studying personality, rests on three foundation stones: (1) Validity in depicting personality as a whole; (2) verifiability of the separate component Rorschach test factors; (3) accurate establishing of the relations between the whole personality and its component processes.

Errors in validating findings in whole personality derive from (*a*) undefined

concepts of the personality—the need for operational definitions of the Rorschach whole personality; (*b*) halo effect from E's observation of S—the blind "diagnosis" can correct this; but (*c*) this involves a uniformity in procedures which does not now obtain.

To verify scientifically the individual Rorschach factors requires consistent classifying of responses according to stable frames of reference. These are at present lacking. Since all Rorschach personality description derives from these factors, their verification by repeating the test is critical for any appraisal of its scientific foundations. The task here is (*a*) to define operationally the criteria whereby we classify each response, e.g. what differentiates a "common" detail (D) from a "rare" one (Dr), or a "good" form (F +) from a "poor" one (F —)? (*b*) to rubric each classification of each response for permanent reference; (*c*) to define operationally the psychological activity to which each Rorschach factor points.

Thirdly, since the psychological operation denoted by each Rorschach factor varies depending on the whole personality background, it is necessary to establish the relation between the whole personality and its separate behaviour manifestations. This requires working out the laws followed by the unit personality. The frames of reference developed for the separate processes cannot be expected to apply to the whole. Suggested leads on the relations involved are found in Gestalt experiments, psychoanalysis and neuropathology. They point to emergence of this supratrait phenomenon, the unit personality as a structure in more dimensions than its component processes, and following laws peculiar to itself.

(Author's abstr.)

PSYCHOL. REV.

VOL. XLVII. JULY, 1940.

REV. NEUROPSIQUIATR.

VOL. III. NO. 1. MARCH, 1940.

Meningo-encephalitis Due to a Neurotropic Virus.

An account of a case of meningo-encephalitis with a marked increase of cerebrospinal fluid with increased intracranial pressure.

Convulsions Induced by Cardiazol in Decerebrate Dogs.

In bulbar animals convulsions could not be elicited ; in mesencephalitic animals the fits resembled those of the intact animal, only differing by their lesser intensity. Diaschisis diminishes the convulsive reaction. The intensity of the fit bears a direct relation to the amount of nervous tissue left intact. There is no evidence of an epileptogenous centre and the epileptic reactions cannot be considered to be special isolated reactions, but rather the simultaneous reactions of the nervous system as a whole.

REV. DI NEUR. E. PSYCHIAT., S. PAULO.

VOL. VI. NO. 1. 1940.

RIV. SPER. FRENIAT.

VOL. LXIII. NO. 3. SEPTEMBER, 1939.

On Disturbances of the Lumbosacral Innervation Due to Spinal Anaesthesia.

After a discussion of the recorded observations on the physiology and pathology of spinal anaesthesia the author gives an account of a patient who suffered from a permanent polyradicular syndrome of the right cauda equina after a novocain spinal anaesthesia induced for surgical purposes. He considers that this effect was due to the existence of septa in the subarachnoid space, preventing free diffusion of the anaesthetic and thus allowing its concentrated action for a considerable time on a few nerve roots.

Extra Medullary Tumours and the Secondary Reaction of the Arachnoid.

Two cases of extramedullary intradural tumours are described—one situated in the cervical region C. IV and V, the other in the region of the conus medullaris. The focal symptoms were not marked, but symptoms attributed by the author to perifocal arachnoiditis were conspicuous in the regions subtended by the spinal cord immediately above and below the tumour.

Trauma and Dementia.

Three cases are described in which the traumatic factor seems to be directly responsible for the occurrence of a progressive dementia. In the first patient an internal haemorrhagic pachymeningitis caused by an injury was the apparent sole cause of a simple dementia. In the second case severe injuries to the head and genitals were followed by symptoms of dementia praecox. The third case was one of sunstroke, which is regarded by the author as a pathogenetic agent in the development of dementia praecox.

Modification of Motor Chronaxie in Insulin Coma.

Motor chronaxic values were determined in ten patients treated by insulin therapy. In the coma produced by insulin there is a disturbance of motor chronaxie values.

VOL. LXIII. NO. 4. DECEMBER, 1930.

Choline Esterase Content of Normal and Pathological Human Brains.

In brains of dements which show signs of organic degeneration there is a marked diminution of choline esterase, especially in the caudate nucleus and the putamen.

On the Curves of the Spinal Cord of Men.

The author has examined the curves existing in the human spinal cord, and attributes their origin to the bands of elastic fibres of the meningeal membranes.

The Manifestations Occurring in Familial Types of Hereditary Diseases of the Nervous System.

The case of two brothers is recorded, one of them afflicted with retinitis pigmentosa and the other with amaurotic idiocy. The author considers that the same disease process is responsible for both cases, and points out the misleading conclusions that may be drawn in such cases if a group of symptoms is accorded the status of a specific disease.

The Shock Treatment of Schizophrenia by Ammonium Chloride.

Following the procedure of Bertolani the authors treated 24 schizophrenics by provoking convulsive attacks by intravenous injection of ammonium chloride. A rapid injection of 5 to 6 c.c. of a 5 per cent. solution of ammonium chloride was followed in a few seconds by a typical epileptic attack. The procedure appears to be without danger. Improvement was noted in 45 per cent. of the cases.

The Variations of the Choline Esterase of the Nervous System in Various Experimental Conditions.

In this state of cerebral excitation with tetanic discharges following the administration of strychnine and tetanus toxin, the choline esterase content of various portions of the central nervous system is increased. Pigeons suffering from beri-beri paralysis have decreased choline esterase.

Lingual Tics in General Paralysis.

A peculiar tic of the tongue with the movements resembling those executed in sucking and swallowing a sticky sweet has been described by Negro ("caramel tic"). It is particularly common as an early sign of general paralysis.

The Influence of Sodium Luminal on the Development of Animals.

Sodium luminal was given to white rats, guinea-pigs and rabbits during their developmental period. Guinea-pigs and rabbits were not affected, but rats showed retardation of development.

VOL. LXIV. NO. 1. MARCH, 1940.

A Clinical Study of Two Cases of Disseminated Encephalomyelitis.

After a brief review of the literature dealing with the differential diagnosis of encephalomyelitis from disseminated sclerosis the author describes two interesting cases, and comes to the conclusion that a clinical differentiation of the two diseases is at present impossible.

The Syndrome of Cotard.

Cotard described a syndrome in cases of melancholia characterized by negativism, ideas of grandeur, damnation and possession with disturbances of perception and hallucinatory reactions. The author describes such a case.

The Choroid Plexus and the Sylvian Aqueduct in a Case of Hydrocephalus Occlusus.

The pathological anatomy of a case of " hydrocephalus occlusus triventricularis " is described. The condition was secondary to a gliomatosis.

A Contribution to the Study of Adiposo-genital Dystrophy.

A case presenting this syndrome is described. It appeared after an infectious illness and recovered after pluriglandular therapy.

Painful Paralysis of the Inferior Brachial Plexus in a Case of Tumour of the Apex of the Lung.

A case of tumour of the apex of the left lung is described which first manifested itself clinically as a painful palsy of the brachial plexus with a Bernard-Horner syndrome.

Deficiency Factors in the Genesis of Primary Degenerations of the Spinal Cord.

Two brothers became ill at the age of 6 with pellagra and disturbances of gait. The elder brother presented a clinical picture of Friedreich's disease, together with pellagrous myelopathy. After a discussion on the aetiology of various types of tract lesion, the author concludes that vitamin deficiency must be considered to be an occasional aetiological factor.

A Case of Progressive Lipodystrophy.

The subject—a woman, aged 22—began at the age of 12 to show a slow and progressive diminution of adipose tissue in the upper part of the body whilst there was a progressive fat accumulation in the thighs and buttocks. X-rays showed a moderate enlargement of the sella turcica.

Whether Convulsive Attacks can be Produced in Epileptics by Preventing Sleep for Various Periods.

Epileptics prevented from sleeping for periods of 72, 96 and 120 hours showed a moderate increase in the number of fits.

SCHWEIZ. ARCH. NEUROL. PSYCHIAT.

VOL. XLV. 1940.

SOVIET. PSICHNEUROL.

VOL. XVI. NO. 1. 1940.

NO. 2.

Z. ANGEW. PSYCHOL.

VOL. LVIII. 1939.

Z. KINDERPSYCHIAT.

VOL. VI. 1940.

Z. PÄDAG. PSYCHOL.

VOL. XLI. 1940.

Z. TIERSPSYCHOL.

VOL. III. 1940.

1. Biochemistry, Pathology, etc.

Electrophoresis of the Products of Acid Hydrolysis of Protein in Nerve Disorders. Mints, P. P., and Mints, I. Ya. [*Sovet. Vrachebnyi Zhur.*, **42**, 277–88 (1938); *Chem. Zentr.*, **2**, 884–5 (1938).]

Nerve disorders were treated with acid hydrolyzates of proteins, which became effective in the region of the vertebral column through cataphoresis. The effect on sleep was very good, especially in the case of neurasthenic patients and those suffering from vegetative neurosis (hemicrania and acrocyanosis).

MARY G. MOORE (Chem. Abstr.).

Thyroid Gland and the Nervous System. Issekutz, Bela. [*Math. naturw. Anz. ungar. Akad. Wiss.*, **58**, 783–92 (1939).]

In decapitated or narcotized animals, thyroxine increases the sensitivity of nerve endings to adrenaline and thus increases the metabolism. The increased

activity of the centres governing metabolism causes an increasing activity in the thyroid gland. This is indicated by the decrease of iodine content of blood, and explains the therapeutic effect of these preparations.

S. S. DE FINALY (Chem. Abstr.).

Lipide Composition of Intracranial Tumours. *Lowell, O. Randall.* [*Am. J. Cancer*, **38**, 92–4 (1940); *cf. C.A.*, **32**, 9248[5].]

The average phospholipide, cerebroside and cholesterol contents are lowest in neuromas, intermediate in meningiomas and highest in gliomas. The lipide contents of neuromas and gliomas are less than those of normal nerve and brain tissue. The lipide content of neuromas is in the range found for benign tumours, while that of meningiomas and gliomas is in the range for malignant tumours. The neutral fat contents of the tumours show no significant differences.

E. R. MAIN (Chem. Abstr.).

Disturbance of the Central Regulating Mechanism of Sodium Chloride Metabolism. *Glatzel, H., and Wolf, H. J.* [*Deut. Arch. klin. Med.*, **183**, 243–63 (1939).]

A case is described of chronic "dermatitis" with periodic attacks of profuse sweating with a burning sensation in the skin, which was red and thickened. Basal metabolic rate was normal, with a lowered specific dynamic protein effect. An increase in the elimination of water by the kidneys (induced by salyrgan) caused a sharp increase in dermatitic symptoms. The ion-concentration ability of the kidneys was only $\frac{1}{5}$ to $\frac{1}{8}$ as great as normal; towards Na and K only $\frac{1}{10}$ to $\frac{1}{20}$. The NaCl and Ca accumulated over a period of days was eliminated in the perspiration within 2 hours. The disorder was attributed to a disturbance of the hypophysis-midbrain system.

P. Y. JACKSON (Chem. Abstr.).

Chemical and Metabolic Studies on Phenylalanine. II. The Phenylalanine Content of the Blood and Spinal Fluid in Phenylpyruvic Oligophrenia. *Jervis, Geo. A., Block, Richard J., Bolling, Diana and Kanze, Edna.* [*J. Biol. Chem.*, **134**, 105–13 (1940); *cf. C.A.*, **33**, 7285, 7287[9].]

Seven male and 9 female patients and 4 normal controls were studied. The ages of the patients varied between 4 and 40 years, and their intelligence quotients were between 5 and 50. The phenylalanine content of the blood varied from 15 to 41 mgm. per 100 c.c. and no phenylpyruvic acid was present. Significant increases followed the injection of proteins, phenylalanine and phenylpyruvic and phenyllactic acids, but no determinable amounts of the latter two substances appeared in the blood. The spinal fluid also contains phenylalanine but no phenylpyruvic acid, and its amount is also increased by ingestion of phenylalanine. Neither compound can be established in appreciable amounts in the blood of normal individuals.

A. P. LOTHROP (Chem. Abstr.).

Chronaxia. *Ando, Kiiti.* [*Nagoya Igakkai Zasshi*, **48**, 981 *et seq.* (1938); *Nagoya J. Med. Sci.*, **13**, *Abstracts* 180–1 (1939) (*in German*); *cf. C.A.*, **33**, 4680[1].]

The chronaxia of the four extremities was determined in healthy men, corpses, beri-beri sufferers and persons with CS_2 poisoning. Beri-beri and CS_2 poisoning distinctly diminished the chronaxia of muscle flexion. The results were not in agreement with the law of Bourguignon. In Pb and CS_2 poisoning, the changes in the chronaxia of the nerves and muscles of the four extremities are probably caused by changes in the mesencephalon.

W. C. TOBIE (Chem. Abstr.).

The Cerebro-spinal Fluid in Alkalosis. *Agar, Herbert, and Macpherson, Ian.* [*Lancet*, **1**, 171–3 (1940).]

The increase in urea and decrease in chloride content of the cerebro-spinal fluid observed in alkalosis appear to be sufficiently characteristic to be of aid in differential diagnosis.

E. R. MAIN (Chem. Abstr.).

Aneurin in Cerebro-spinal Fluid. Saker, A. [*Klin. Wochenschr.*, **19**, 99–102 (1940).]

In contrast to the negative results reported with the thiochrome method, the phycomyces test shows varied amounts of vitamin B_1 (traces to 18·5γ per cent.) to be present in the cerebro-spinal fluid. These values are unrelated to the vitamin content of the blood, pathological picture or the condition of the fluid. Following intravenous injection of 50 mgm. vitamin B_1, aneurin is found in the cerebro-spinal fluid (maximum 31γ per cent.). After intra-spinal injection, the vitamin diffuses only slightly in the upper spinal cord canal, and is very rapidly resorbed in the blood from the lumbar arachnoid space. Intraspinal injection has no practical advantage over the intravenous or subcutaneous route.

J. PINCHACK (Chem. Abstr.).

Psychoses Caused by Estrogenic Hormones and Circulatory Disturbances. Baruk, H., David, Racine and Leuret. [*Presse méd.*, **48**, 281–2 (1940).]

Vasomotor disturbances and psychoses show frequently parallelism pointing to a common source which is probably an over-production of estrogenic hormones. They produce peripheral vasodilatation, flushed face and humming in the ear. A dilatation of the cerebral blood vessels was directly observed in the rabbit.

A. E. MEYER (Chem. Abstr.).

Oxidation Processes in the Central Nervous System during Ontogenesis. I. *Changes in Catalase and Peroxidase Activity.* Rozenfeld, L. E., and Goldman, S. S. [*Biochem. J.* (*Ukraine*), **14**, 125–41 (*in Russian*), 142–3; *in English*, 143–4 (1939).]

In all regions of the rabbit brain the catalase activity decreases with the age of the embryo and shows an abrupt drop 14 to 25 days after birth. The peroxidase activity fluctuates much more, and a certain amount of reciprocal behaviour is noted between the levels of catalase and peroxidase activity.

R. LEVINE (Chem. Abstr.).

Effect of Mechanical Trauma of the Head on the Nitrogen Composition of the Brain. Barmina, O. N. [*Biochem. J.* (*Ukraine*), **14**, 69–82 (*in Russian*; *in English*, 82–3) (1939).]

After mechanical trauma of the head of rabbits by a freely falling weight, the total N content of the brain decreases. Various areas of the brain are affected to a greater or less extent. The rate of proteolysis is increased in the brain cortex, and decreased in the white matter and in the caudate nucleus. Normal chemical composition is restored only after 20–38 days following the initial trauma.

R. LEVINE (Chem. Abstr.).

Glycolysis of Nerve Tissue. IV. *Glycolysis of Nerve Tissue after Freezing in Liquid Air.* Lenti, C., and Fuortes, M. [*Atti accad. sci. Torino, Classe sci. fis., mat. nat.*, **74**, 558–62 (1939).

Nerve tissue after exposure for three hours to liquid air entirely loses its glycolytic activity. Muscle tissue and malt in which glycolysis is preceded by phosphorylization do not lose their glycolytic power in liquid air.

A. W. CONTIERI (Chem. Abstr.).

Glycolysis in Cell-free Extracts of Brain. Geiger, A. [*Biochem. J.*, **34**, 465–82 (1940); *cf. C.A.*, **33**, 8271[9].]

Aqueous extracts of brain tissue were prepared with and without the use of phosphate. The extracts without phosphate rapidly lost their activity at 37° unless they were diluted. The extracts had about four times the glycolytic activity of brain slices. Dialysis against water destroyed the activity, but dialysis against

0·6 per cent. NaCl caused no loss of activity. Mg. in a concentration of 0·013 M was necessary for optimum glycolysis. Hexose diphosphate caused a small increase in the glycolytic rate. Phosphocreatine had to be added to dialysed brain extracts to obtain glycolytic activity. In fresh extracts it was necessary when glucose was the substrate, but not when glycogen was. Glutathione activated brain glycolysis, but its effect was variable. Adenosine triphosphate and cozymase were coenzymes of brain glycolysis. There was also probably a third coenzyme which was not identified. Large amounts of lactic acid were formed from fructose, glucose and mannose. Other sugars gave little or no lactic acid. None was formed from the intermediary phosphorylated products of muscle glycolysis. The presence of inorganic phosphate was necessary for glycolysis in brain extracts. It was esterified during the glycolysis of lactic acid-forming sugars with the formation mainly of a monophosphate along with a pyrophosphate and hexose diphosphate. In the presence of NaF and pyruvic acid, phosphopyruvic acid accumulated. Extracts poisoned with iodoacetate transferred P from adenosine triphosphate to glucose, forming hexose diphosphate. E. W. Scott (Chem. Abstr.).

The Influence of Graded Doses of Vitamin A upon the Pathological Changes in the Central Nervous System of the Rat, with Suggestions for a Prophylactic Assay of the Vitamin. Irving, J. T., and Richards, M. B. [*Biochem. J.*, **34**, 198–201 (1940); *cf. C.A.*, **34**, 1362[5].]

Rats were placed at weaning on a vitamin A-free diet and given graded doses of vitamin A. They were killed after seven weeks and their medullas examined. Degeneration was found in the funiculus praedorsalis in those receiving 1 I.U. or less per day, but not in those getting 1·5 I.U. or more. The main source of error in the curative method, i.e., the pathological differences in the animals used would be avoided by using the above procedure for assay.

E. W. Scott (Chem. Abstr.).

Retention of Nicotinic Acid in the Body Fluids of Pellagra Patients and Healthy Subjects. Kuhnau, Wolfram W. [*Klin. Wochenschr.*, **18**, 1333–4 (1939).]

Normal subjects show 2·5–4·5 mgm. per cent. nicotinic acid in the blood; pellagra patients 0·75–1·8. The latter excrete 0·64–1·05 mgm. per cent. nicotinic acid in the urine, which is practically the normal amount (0·5–3 mgm. per cent.). After ingestion of nicotinic acid both groups excrete essentially the same amount of acid. Unexpectedly high values (1–1·4 mgm. per cent.) were found in the cerebro-spinal fluid of two pellagra patients with neurological symptoms and a low blood value (0·7 mgm. per cent.) in one pellagrin with anaemia and glossitis. These may be of diagnostic importance. J. Pinchack (Chem. Abstr.).

Vitamin B_1 and Acetylcholine Formation in Isolated Brain. Mann, P. J. G., and Quastel, J. H. [*Nature*, **145**, 856–7 (1940); *cf. C.A.*, **33**, 8271[4].]

Addition of vitamin B_1 to isolated polyneuritic pigeon brain increases the rate of synthesis of acetylcholine when the brain is incubated aerobically in a bicarbonate-pyruvate medium containing a relatively high concentration of K ions. No such increase occurs when it is added to normal pigeon brain examined under similar conditions. E. D. Walter (Chem. Abstr.).

Occurrence of Fits of an Epileptic Nature in Rats Maintained for Long Periods on a Diet Reprived of Vitamin B_6. Chick, Harriette, El Sadr, M. M., and Worden, Alastair N. [*Biochem. J.*, **34**, 595–600 (1940).]

Fits were observed in rats maintained for four to five months and over on a purified synthetic diet supplemented with cod-liver oil, pure vitamin B_1, riboflavin and purified yeast filtrate factor. The fits were prevented and cured by the administration of pure vitamin B_6, 10–15μ gm. daily. No fits occurred when purified rice starch was the carbohydrate in the diet, and the diet was cooked with water.

The nature of these fits and the circumstances in which they developed showed a very close resemblance to the epileptic fits previously observed in young pigs. The basal diets and the supplements given were similar in the two cases. Hence lack of vitamin B_6 was probably the cause of the fits in pigs.

The Incidence of Neuropathy in Pellagra. The Effect of Cocarboxylase upon its Neurologic Signs. Lewy, F. H., Spies, T. D., and Aring, C. D. [*Am. J. Med. Sci.*, **199**, 840–9 (1940); *cf. C.A.*, **33**, 7858[4].]

Improvement in neuropathologic symptoms in pellagrins resulted within one to four hours, from 50 mgm. or more of cocarboxylase (phosphorylated thiamine) given intravenously, was maintained one to five days and then disappeared. The clinical effect of cocarboxylase was identical with that previously found for binding substances and arterio-venous O difference paralleled clinical neurologic improvement. Patients who retained most of the injected cocarboxylase improved, in contrast to those who did not retain it. The injection of riboflavin did not affect the neurologic signs. Apparently the neuropathy common among pellagrins is due to lack of thiamine. FERRIN B. MORELAND (Chem. Abstr.).

Relation of Diet to a Type of Leg Weakness in Swine Induced by Nerve Degeneration. Ellis, N. R., and Madsen, L. L. [*Proc. Am. Soc. Animal Production*, **32**, 393–4 (1939).]

The disease is of frequent occurrence among pigs confined in small pens with concrete or board floors and fed on diets, such as used in record-of-performance (R.O.P.) tests, heretofore considered adequate for normal yellow corn trinity protein mixture and mineral mixture with the three parts self-fed, resulted in a wide range in incidence and severity of the lameness and inco-ordination. The disease can be produced at will in the usual case by the feeding of a heat-treated diet supplemented with cod-liver oil. It does not respond readily to curative treatment. The protective action of a number of supplements such as liver, whey and rice bran suggests that a factor or factors of the vitamin B complex other than thiamine, riboflavin and nicotinic acid may be involved.

K. D. JACOB (Chem. Abstr.).

The Nitrogen Metabolism of the Brain. Rubel, V. M. [*Bull. biol. med. exptl. U.R.S.S.*, **8**, 369–72 (1939) (*in English*).]

Emotional excitation in dogs is followed by an increased retention by the brain of NH_3-producing substances as indicated by the differences in the NH_3 values of arterial (inflowing) and sinusal (outflowing) blood. The adenylic acid (I) content of sinusal blood generally tends to follow the decreased NH_3 content, but the evidence that I is the source of NH_3 in the blood is not conclusive. The urea and lipoid amino N values of the blood increase during storage under petrolatum at 37° for 22 hours, so these compounds are apparently not responsible for liberation of NH_3. The addition of acetylcholine and choline to arterial sinusal and venous blood *in vitro* caused a definite increase in the NH_3 value only in arterial blood.

S. A. KARJALA (Chem. Abstr.).

The Cerebellum and Carbohydrate Metabolism. Kaplan, P. M. [*Med. exptl.* (*Ukraine*), No. **4**, 37–44 (1937); *Chem. Zentr.*, **2**, 2290–1 (1938).]

Using eight dogs as experimental animals, the blood sugar was determined after fasting, and again after feeding glucose. These determinations were made before and after removal of the cerebellum. Removal of this organ was without effect on the blood sugar of the fasting animals. On the other hand, the increase in the blood sugar after the feeding of glucose was much higher after the cerebellum had been removed than before the operation. This more pronounced reaction to glucose, however, was not stable; the normal reaction was shown once more after 18–20 days. M. G. MOORE (Chem. Abstr.).

Fructose Tolerance in Various Forms of Psychoses. Yuki, K. [*Fukuoka Acta Med.*, **32**, 42 (1939).]

In schizophrenics the maximum blood-sugar value is higher than in healthy persons, but the curve is otherwise normal. Manic depressives and patients with general paralysis of the insane exhibit a tendency towards a prolongation of the high blood sugar following the test. In tabes dorsalis, morphinism, alcoholism and senile dementia, the blood sugar rises to a very high level, but the curves are otherwise unremarkable. B. C. P. A. (Chem. Abstr.).

Liberation of Acetylcholine from the Perfused Cat Brain. Chute, A. L., Feldberg, W., and Smyth, D. H. [*Quart. J. Exptl. Physiol.*, **30**, 65–72 (1940).]

The almost completely isolated cat brain was perfused with 50 per cent. defibrinated blood. The addition to it of eserine produced increased reflex excitability with spontaneous movements followed by depression, and caused the appearance in the blood of small amounts of acetylcholine which were liberated from the brain. This liberation was temporarily increased by the injection of KCl.

RACHEL BROWN (Chem. Abstr.).

The Mechanism of Sensitization to Acetylcholine by Denervation. Lee, Lao-Ying. [*Chinese J. Physiol.*, **14**, 357–73 (1939).]

The increased sensitivity of skeletal muscle to acetylcholine (I) is correlated with a diminution of K. Diminution of muscle K brought about by other means, such as soaking in K-free Ringer solution, is also accompanied by an increased sensitivity to I. Conversely, when the muscle K is increased, its sensitivity to I is decreased. The normal sensitivity to I of the same muscle or different muscles appears to vary inversely with the K content. The change in sensitivity to I is correlated with changes in sensitivity to nicotine.

WALTER H. SEEGERS (Chem. Abstr.).

The Formation of an Acetylcholine-like Substance in Afferent Nerve Stems. Yachimovich, F. A. [*Bull. biol. med. exptl. U.R.S.S.*, **8**, 403–8 (1939) (*in German*).]

Severance of the N infra-orbitalis in rabbits causes the formation of a vago-mimetic substance similar in behaviour to acetylcholine.

S. A. KARJALA (Chem. Abstr.).

Effect of Acetylcholine on the Adrenaline Output in Cats. Tâneiti, Yosiharu. [*Tohoku J. Exptl. Med.*, **38**, 147–51 (1940).]

Injection of acetylcholine in doses of 0·4 to 1 mgm. per kgm. body-weight into the coeliac artery of anaesthetized cats causes an acceleration of adrenaline output (2 to 8 times normal). Adrenaline concentration was measured on the isolated rabbit intestine. ZELMA BAKER (Chem. Abstr.).

Role of the Sympathetic Nervous System in Blood Regeneration. Somogyi, J. C. [*Magyar Orvosi Arch.*, **40**, 195–203 (1939).]

Ergotamine (0·2 mgm. per kgm. daily) inhibited blood regeneration after haemorrhage in cats. Partial sympathectomy caused a decrease of red corpuscles and haemoglobin, and an increase of leucocytes. Cervical sympathetic stimulation increased the red corpuscles and the haemoglobin, the latter effect disappearing when stimulation followed thyroidectomy. B. C. P. A. (Chem. Abstr.).

Haemato-encephalic Barrier. Stern, L. S. [*Trav. inst. recherches physiol. Moscou*, **2**, 12–26 (1936) (*in Russian*).]

The haemato-encephalic barrier refers to the mechanism which regulates the composition of the cerebro-spinal fluid, and protects the central nervous system from many substances which are not required by, or may be toxic to, the nervous tissue. Morphologically it is represented by the capillary endothelium, especially that of the choroid plexus, as well as by the mesoglia and the microglia, the latter

protecting the nerve cells from substances in the cerebro-spinal fluid. Certain correlations have been observed between local morphological changes and certain crystalloids, while changes in the capillary endothelium of the brain were correlated with an increase in permeability to some colloids. The function of the haemato-encephalic barrier was determined chiefly by the introduction of substances normally absent from the blood or from the cerebro-spinal fluid, or by the determination of permeability to Br. Inability to detect in the cerebro-spinal fluid certain substances introduced into the blood stream does not necessarily indicate impermeability of the haemato-encephalic barrier, since many of these substances may be adsorbed by the nerve cells. Such adsorption explains the inability to detect the cations of basic dyes in the cerebro-spinal fluid. The permeability properties of the endothelium vary in the capillaries of the different organs, as well as in different regions of the same organ. Moreover, various experimental and pathological changes influence the different capillary regions in a different direction. The nature of the haemato-encephalic barrier varies with different species, age and sex, and can be changed by various experimental procedures, such as the introduction into the blood stream of hormones, drugs, toxins, changes in blood constituents (pH, osmotic pressure) and infections. The distribution of normal constituents between the cerebro-spinal fluid and the blood cannot at present be explained by simple physico-chemical laws (such as ultrafiltration, Donnan equilibrium). For most of the normal constituents the permeability co-efficient (concentration in the cerebro-spinal fluid divided by the concentration in the blood plasma) is less than unity, with the exception of Cl for which the permeability coefficient is above 1. There is a correlation between the condition of the haemato-encephalic barrier and the functional changes in the central nervous system. Thus, in most cases an increase in the K/Ca ratio in the cerebro-spinal fluid was accompanied by increased excitability of the CNS, while a decrease in K/Ca corresponded to inhibition and a decreased tonus of the nervous system. That the change in the K/Ca ratio is the primary factor is indicated by the fact that injection of small doses of K into the cerebro-spinal fluid produced a marked increase in excitability, while Ca injection produced inhibition. Also, experimental epilepsy in dogs (produced by electrical stimulation of the brain) was not accompanied by changes in the composition of the cerebro-spinal fluid, except after prolonged repeated stimulation. Narcosis was accompanied by a decrease in K/Ca, while experimental stimulation often corresponded with an increase in K/Ca.

S. A. CORSON (Chem. Abstr.).

The Chemical Basis of Sleep: The Role of the Haemato-encephalic Barrier. Stern, L. A. [*Trav. inst. recherches physiol. Moscou*, **2**, 27–38 (1936) *in Russian*).]

Experiments were performed for a period of 1·5 years on dogs kept without sleep for 8–14 days, and on human subjects kept without sleep for 3–4 days. In all cases prolonged lack of sleep was accompanied by a decrease in the K/Ca ratio (from a value of about 2 to 1 or less) and in the concentration of K in the cerebro-spinal fluid. At the same time there was an increase in the concentration of sugar in the cerebro-spinal fluid and a general increase in the permeability of the haemato-encephalic barrier to a great many substances. In dogs there was an increase in the Ca concentration in the cerebro-spinal fluid (interpreted as an increase in permeability to Ca), while in the human subjects the Ca concentration was decreased. In all cases all the values returned to normal after the animal was permitted to sleep. Similar reversible changes in the haemato-encephalic barrier were observed during ether anaesthesia.

S. A. CORSON (Chem. Abstr.).

The Influence of Histamine and Peptone Shock on the Haemato-encephalic Barrier. Khvoles, G. Ya, Nikol'skaya, M. I., and Govorovich, E. A. [*Trav. inst. recherches physiol. Moscou*, **2**, 39–52 (1936) (*in Russian*).]

Shock was produced in dogs and cats by the injection of histamine (0·5–5·0 mgm./kgm. body weight) or peptone (0·2–0·8 grm./kgm. body weight). The shock lasted

for 10 min. to 4 hours. During the initial excitatory stage of the shock (characterized by increased reflex excitation) there was an increase in the K content of the cerebro-spinal fluid, while the K/Ca ratio was either increased or unchanged. During the longer inhibitory stage of the shock (characterized by decreased reflex excitation) the K, K/Ca ratio and inorganic P of the cerebro-spinal fluid were decreased, while the Ca concentration was increased. In the blood plasma the concentration of K was decreased and that of Ca increased, while the concentration of inorganic P was decreased in the beginning of the shock, and increased at the later stages. A shock of short duration was accompanied by an increase in the concentration of sugar, both in the cerebro-spinal fluid and in the blood plasma, while a shock of longer duration showed a decrease in the sugar concentration. The resistance of the haemato-encephalic barrier was increased in respect to K and P and decreased in relation to sugar, Ca and $Na_4Fe(CN)_6$ (which does not normally appear in the cerebro-spinal fluid). There was no change in the resistance to trypan blue or in the Cl content of the blood plasma or cerebro-spinal fluid. S. A. CORSON (Chem. Abstr.).

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2. Pharmacology, Treatment, etc.

Benzedrine (β-phenylisopropylamine) and Brain Metabolism. *Mann, P. J. G., and Quastel, J. H.* [*Biochem. J.*, **34**, 414–31 (1940); *cf. C.A.*, **34**, 1400[1].]

When brain respiration in a glucose medium was measured in the presence of tyramine (I), β-indolethylamine or isoamylamine, a fall in respiration was noted. This could be neutralized by the addition of benzedrine (II) to the system. Both brain slices and mince were affected. I also caused a fall when glucose was replaced with Na succinate. The fall due to I was traced to the aldehyde formed by oxidation, or a further oxidation product, at least in part. Succinate protected the succinic dehydrogenase from the toxic acid of this oxidation product. II owed its stimulating influence to its ability to compete reversibly with other amines for the amine oxidase of the brain and other organs; thus the rate of formation of the oxidation products affecting the respiration is reduced. *l*-Ephedrine (III), 3, 4-methylenedioxy-(IV) and 3-methoxy-4-hydroxy-phenylisopropylamine (V) possessed the same ability as II (although III and V were much less active) in counteracting the effect of I on respiration. IV was about as active as II. Aldehydes such as isovaleraldehyde and *p*-hydroxybenzaldehyde were inhibitors of brain respiration, but their effects were not counteracted by II. II had no retarding influence on the fall of brain respiration produced by the addition of phenobarbital, chloretone or bulbocapnine. The effects of II, III and derivatives of II in these experiments parallel their effects *in vivo* on the central nervous system.

E. W. SCOTT (Chem. Abstr.).

Experimental Studies on the Toxicity of Benzedrine Sulphate in Various Animals. *Ehrlich, W. E., Lewy, F. H., and Krumbhaar, E. B.* [*Am. J. Med. Sci.*, **198**, 785–803 (1939); *cf. C.A.*, **31**, 6739[5].]

The effects, minimum lethal dose, tolerance and greatest non-toxic dose of benzedrine sulphate were studied in guinea-pigs, rabbits, monkeys, dogs and sheep of varying ages. The minimum lethal doses in mgm./kgm. are: For young guinea-pigs, 40–150; adult, 50–100; young rabbits, 50; adult, 20; young monkeys, 5; adult, 20–25; adult dogs, 20; adult sheep, 15. Continued administration at first decreases tolerance, then increases it. The lowest maximum non-toxic dose obtained was 1–2 mgm./kgm. For humans, doses which do not raise blood pressure or cause loss in weight, anaemia or granulocytosis should be harmless even over long periods. FERRIN B. MORELAND (Chem. Abstr.).

Insulin Sensitivity of Cats with Hypothalamic Lesions and Cats with Cervical Cord Section. Brobeck, John R. [*J. Lab. Clin. Med.*, **25**, 717–25 (1940).]

In normal cats subcutaneous injection of 0·5 unit of insulin per kgm. of body weight produced a hypoglucaemia which was more prolonged, and in some instances more marked, than that following the intravenous injection of the same amount of insulin. In a large group (76) of cats with lesions in various portions of the hypothalamus, normal fasting blood sugars and normal insulin reactions were obtained following the insulin test. Insulin hypersensitivity was observed in four cats with lesions in the medial part of the anterior tuberal portion of the hypothalamus. Spinal cats recovered as well as normal cats on receiving this dose of insulin. HOWARD W. ROBINSON (Chem. Abstr.).

A Note on the Level of Glucose and of Non-fermentable Reducing Substances in Therapeutic Insulin Shock. Forbes, W. H., and Czarski, T. [*J. Lab. Clin. Med.*, **25**, 679–83 (1940).]

Glucose can be determined with a probable error of ± 2 mgm. by subtracting 4 mgm. from the blood sugar, as determined upon the filtrate of unlaked blood by the revised method of Folin and Wu (*C.A.*, **23**, 2998). In therapeutic insulin shock in schizophrenic patients the glucose (fermentable reducing substance) may fall below 10 mgm. per 100 c.c. of blood and remain there for periods up to an hour without any apparent harm to the patient. The non-fermentable reducing substances do not change in amount as the blood sugar falls.
HOWARD W. ROBINSON (Chem. Abstr.).

Decorticate and Decerebrate Preparations Produced by Insulin Shock. Ziskind, Eugene, and Tyler, David B. [*Proc. Soc. Exptl. Biol. Med.*, **43**, 734–5 (1940).]

Cats, fasted 18 hours, were given 15–20 units insulin per kgm. body weight. Persistent brain damage was produced. Some of the treated cats behaved like decorticate or decerebrate preparations. L. E. GILSON (Chem. Abstr.).

Action of Metrazol on Reflexes in the Frog. Kollensperger, Friedrich K. [*Klin. Wochenschr.*, **18**, 1521–4 (1939).]

Oral, intralymphatic or intramuscular administration of 1–5 mgm. metrazole results, after a short latency, in a sudden increase in reflexes, often with rise in tonus. Doses of 10 mgm. produce tonic rigidity of the legs and occasionally strychnine-like convulsions. Repeated small doses have an additive effect which is shown by the sudden recovery of animals paralysed by curare. Metrazole increases the irritability of the peripheral nervous system as well as that of the spinal cellular elements. J. PINCHACK (Chem. Abstr.).

Effect of Metrazole on Cerebral Vessels. Forbes, Henry S., and Nason, Gladys I. [*Proc. Soc. Exptl. Biol. Med.*, **43**, 762–5 (1940).]

In animals metrazole caused cerebral vasodilation. This was unrelated to changes in blood pressure or respiration, and showed no consistent relation to convulsive seizures. L. E. GILSON (Chem. Abstr.).

A Clinical Comparison of Picrotoxin, Metrazole and Coriamyrtin used as Analeptics and as Convulsants. Bleckwenn, W. J., Hodgson, E. R., and Herwick R. P. [*J. Pharmacol.*, **69**, 81–8 (1940).]

Selected human subjects were used. The potency of the compounds decreases in the order coriamyrtin, picrotoxin and metrazol. But from the standpoint of effectiveness and safety, for counteracting barbiturates, they should be rated in the order, picrotoxin, metrazole and coriamyrtin. Metrazole is the best for inducing therapeutic convulsions. L. E. GILSON (Chem. Abstr.).

Convulsions Caused by Pentamethylenetetrazole. Glucaemia in the Treatment with Metrazole and its Combination with Insulin, Glucose and Adrenaline. Robuschi, L., and Simmons, G. [*Sperimentale*, **94**, 196–214 (1940).]

Metrazole produces immediately hyperglucaemia reaching a maximum after 30 minutes. A second injection reproduces shock and hyperglucaemia. Simultaneous injections of insulin do not affect the glucaemia. If repeated injections are so timed as to coincide with the maximal hypoglucaemic effect of the insulin, an increase of the blood sugar is still produced and it may exceed the normal value. Intravenous glucose injections have no noticeable influence. The hyperglucaemic effect of metrazole persists even if the blood sugar is already high as a consequence of preceding application of adrenaline. A. E. MEYER (Chem. Abstr.).

Modifications in Blood Sugar by Metrazole, Insulin-Metrazole, Adrenaline-Metrazole and Glucose-Metrazole. Robuschi, L., and Simmons, G. [*Boll. soc. ital. biol. sper.*, **15**, 418–19 (1940).]

In rabbits, metrazole injections were followed by an immediate hyperglucaemia, reaching a maximum in 30 minutes, and returning to normal in 3–5 hours. Insulin, preceding or with metrazole, did not substantially modify the hyperglucaemia. Metrazole injected after injections of glucose or adrenaline further increased the hyperglucaemia. HELEN LEE GRUEHL (Chem. Abstr.).

Detoxicating Hormone of the Liver (Yakriton). XCI. Effect of Removal of Cerebral Hemispheres in Rabbits with Varying Liver Function. Kuribayashi, Saburo. [*Tohoku J. Exptl. Med.*, **37**, 573–5 (1940).]

Rabbits with low liver ability for NH_3 detoxication develop convulsions in 24 hours after extirpation of cerebral hemispheres. The convulsions are not severe and occur at long intervals in the beginning, but become continuous toward death at 50 hours after the operation. Rabbits with high liver ability for NH_3 detoxication remain free from convulsions and survive for 68 hours.
C. R. ADDINALL (Chem. Abstr.).

XCII. Effect of Yakriton on Epilepsy in Children and Effect of Prominal on its Action. Takamatu, Akira, and Sato, Siu. [*Ibid.*, **37**, 576–88.]

On the basis of the cardiazole test, yakriton has, by itself, a curative effect on some cases of epilepsy. In some cases it exerts a favourable influence in combination with prominal (N-methylethylphenylmalonylurea).
C. R. ADDINALL (Chem. Abstr.).

Electrocortical Studies on Point of Action of Various Hypnotics. Drohocki, Z., and Drohocka, J. [*Klin. Wochenschr.*, **18**, 606–8 (1939); *cf. C.A.*, **33**, 2212[1], 9437[3]; **34**, 161[5].]

Nembutal, chloral hydrate and urethan produce changes in the electrogram in different parts of the brain, including the cortex and thalamus; hypnotics cannot be divided into cerebral and brain-stem groups. B. C. P. A. (Chem. Abstr.).

Effects of Cobra Venom and Other Analgesics on Mental Efficiency. Macht, David I., and Macht, Moses B. [*Arch. intern. pharmacodynamie*, **63**, 179–88 (1939).]

Various analgesics including morphine were compared with cobra venom in their effect on the ability to solve simple problems in mental arithmetic. Tests were given before and after the administration of the drugs. Morphine, codeine, dilaudid and heroine depressed mental performance and cobra venom definitely stimulated it. M. L. C. BERNHEIM (Chem. Abstr.).

Further Observations on the Action of Pyridine-β-Carboxydiethylamide (Coramine) on the Nervous System (Mammalian), with Special Reference to the Vagus. Burton, Andrew F. [*Arch. intern. pharmacodynamie*, **63**, 292–9 (1939); *cf. C.A.*, **33**, 4316⁴.]

In the cat and rabbit, large doses of coramine stimulate and then depress the cardiac vagus, but do not affect the sympathetic nervous system. In the cat the vagal depression is greater than in the rabbit, but the latter is more affected by terminal asphyxia and tremors from paralysis of the peripheral nerves.

M. L. C. BERNHEIM (Chem. Abstr.).

The Detoxication of Local Anaesthetics. I. Measurements of the Anti-convulsive Action of Calcium Salts (and Various Other Substances). Wastl, H. [*Arch. intern. pharmacodynamie*, **63**, 145–78 (1939).]

Procaine-HCl and procaine-HCO_3 were compared by intramuscular injection in guinea-pigs, and the latter was found to give a greater percentage of convulsions, which are longer and more intense. The detoxifying and anticonvulsant effects of many Ca salts and sedatives were studied after procaine-HCl or butyn-SO_4. The best protection against procaine-HCl convulsions was Ca salicylate, then Ca levulinate, but the latter worked best for butyn-SO_4. Ca gluconate and the halides are less effective. In all, 3,800 experiments were performed.

M. L. C. BERNHEIM (Chem. Abstr.).

The Condition of the Cerebro-spinal Fluid during Procaine Block in Septic Processes of Horses. Rasskazovskii, P. A. [*Sovet. Veterinariya, No.* **3**, 42–5 (1939); *Khim. Referat. Zhur. No.* **7**, 38 (1939).]

During procaine block the globulin fraction of the cerebro-spinal fluid increases, while the albumin fraction decreases. The content of sugar in the fluid and in blood increased during septic processes. W. R. HENN (Chem. Abstr.).

Neurohistological Tests on Pigeons Poisoned by Diseptal. Beck, E. [*Klin. Wochenschr.*, **18**, 1416–17 (1939).]

Pigeons poisoned by uliron or diseptal B exhibited no histological changes in the central or peripheral nervous system, or in the muscles, in spite of the clinical symptoms of polyneuritis. J. PINCHACK (Chem. Abstr.).

Cortical Hormone in the Treatment of Bromide Intoxication. Campbell, Coyne H. [*J. Okla. State Med. Assoc.*, **32**, 447–8 (1939).]

Seven patients were studied, having serum Br between 150 and 400 mgm. per cent. In six the daily administration of 6 to 10 gm. of NaCl was supplemented by injection of 2·5 c.c. of eschatin twice daily, and the serum Br reduced to 50–115 mgm. per cent. in one to four days; one patient required a longer time for recovery. The seventh patient with an original serum Br of 400 mgm. per cent. was given 8 to 10 gm. of NaCl daily for 18 days, and then showed a serum Br of 200 mgm. per cent. Empirically, cortical hormones may be helpful in the treatment of toxic psychoses. JAMES C. MUNCH (Chem. Abstr.).

Bromide Intoxication. Preu, Paul Wm. [*Rhode Is. Med. J.*, **22**, 179–82 (1939); *cf. C.A.*, **33**, 2990⁶.]

Bromide intoxication was encountered in 18 of 2,000 admissions to the New Haven Hospital. Treatment consisted of 10 gm. of NaCl in capsules daily, enemas, a high-caloric soft diet and large volumes of fluids. A blood-serum Br level of 250 mgm. per cent. is associated with delirium. Two case histories are presented, each patient showing 300 mgm. per cent. of serum Br. Br accumulates in the tissues, and should be used with care in patients with dehydration and dietary deficiency. JAMES C. MUNCH (Chem. Abstr.).

Side Effects of Barbiturate Sedation. Shelton, Prior. [*J. Missouri State Med. Assoc.*, **36**, 488–90 (1939).]

The distribution of various barbiturates as well as narcotics follows the Meyer-Overton law. Continued administration of barbiturates in sublethal doses to animals or humans leads to the development of a mucinoid material in the brain cells, developing simultaneously with the symptoms of chronic barbiturate poisoning. These changes do not follow a single sublethal dose. Therapeutic doses frequently administered may cause a moderate amount of tissue damage, especially in the higher centres of the central nervous system.

JAMES C. MUNCH (Chem. Abstr.).

The Cerebro-spinal Fluid of Morphinism. Mei, C., Ito, K., and Matuo, S. [*J. Chosen Med. Assoc.*, **30**, 352–62 (*German abstr.*, 24–5) (1940).]

The total protein, PO_4, NaCl, lactic acid and glucose contents are about the same in spinal fluids of normal persons (A), and those of morphine addicts during habitual (B) and abstinent periods (C). As compared to A, however, B give the Pandy reaction, show greater pressures and globulin ; albumin ratios, and slightly higher permeabilities, and have the same pressures and cell counts. C have greater cell counts, and globulin : albumin ratios than A ; and show lower pressures and greater globulin : albumin ratios and permeabilities than B. Cholesterol is absent in B and C.

S. TASHIRO (Chem. Abstr.).

Effects of Anaesthesia on the Blood Supply to the Hypothalamus. Laidlaw, Arthur E., and Kennard, Margaret A. [*Am. J. Physiol.*, **129**, 650–8 (1940).]

Focal changes in the state of the capillaries in the central nervous system after the administration of different anaesthetics can be observed after injection of indian ink and gelatin into the vascular system. After barbiturate anaesthesia many dilated capillaries are seen in the supra-optic and paraventricular nuclei of the hypothalamus ; but after ether relatively few capillaries are open and these appear constricted. In contrast the capillaries of the cortex are more dilated by ether than by the barbiturates. These findings are further evidence for a hypothalamic site of barbiturate action.

E. D. WALTER (Chem. Abstr.).

The Influence of Caffeine on the Autonomic Nervous System. Barry, D. T. [*Arch. intern. pharmacodynamie*, **63**, 129–44 (1939).].

Sensitization of the vagus and the renal splanchnic nerves was demonstrated in the dog after the injection of 20–50 mgm./kgm. caffeine. The rabbit vagus showed much less effect. Paralysis of the nerves occurred with widely different doses of caffeine, varying with the species, the individual and the rate of injection.

M. L. C. BERNHEIM (Chem. Abstr.).

Obituary Notice.

HENRY DEVINE, *O.B.E.*, M.D.Lond.&Brist., F.R.C.P.

HENRY Devine, who died on May 1 at Portsmouth, was one of the outstanding figures in British psychiatry. He was born on May 2, 1879, and educated at the Merchant Venturers' School, Bristol. He studied medicine at University College and the General Hospital, Bristol, qualifying in 1902. He obtained the London M.B. degree, and subsequently the M.D., being awarded the gold medal in mental diseases. After the formation of the University of Bristol in 1909, he became an M.D. of this University also. He became M.R.C.P. in 1906, and was elected F.R.C.P. in 1919.

After a house appointment at Bristol he turned to psychological medicine, which remained the dominating interest of his professional life. He entered the L.C.C. mental hospital service at Cane Hill, and transferred to Long Grove at Epsom when it was opened in 1907. He availed himself there of every opportunity to enlarge his theoretical and practical experience of psychiatry and its sister sciences. He studied experimental psychology under Prof. Spearman at University College, London, and obtained a grant of special leave to attend Kraepelin's clinic at Munich, then the Mecca of psychiatry in Europe. During this period he was awarded the Gaskell Prize of the Medico-Psychological Association. From Long Grove he went as senior medical officer to Wakefield Mental Hospital, a hospital with a long tradition of able men, and then became medical superintendent of the Portsmouth Mental Hospital (now St. James's Hospital). Devine was in command there during the last war, when the hospital was partly converted to military purposes, and for his war services he received the O.B.E. in 1919, and was appointed consulting psychiatrist to the Royal Victoria Hospital at Netley. Finally he became medical superintendent of the Holloway Sanatorium at Virginia Water, a post which he held until his retirement on account of ill-health in 1938.

Devine's professional activities and interests extended over a wide field. He was for many years lecturer in psychology at the Maudsley Hospital, and was appointed examiner by the Royal College of Physicians for the Diploma in Psychological Medicine. He was a past president of the Section of Psychiatry of the Royal Society of Medicine, and played a prominent part in the work of the Child Guidance Council.

Throughout his career he was closely associated with the British Medical Association and its Journal, being for many years a contributor to the latter, and its adviser in psychological medicine. At the Liverpool meeting of the Association in 1912 he was honorary secretary of the Section of Neurology and Psychological Medicine, and when the Association met in 1923 at Portsmouth, the town linked with so much of his work, he naturally presided over the Section. In 1932 he was vice-president of the Section at the Centenary Meeting in London.

He became assistant editor of this Journal in 1916, and was co-editor from 1920 to 1927. As regards his other literary activities, he contributed numerous papers to psychiatric and psychological journals, including the articles on "Psychoses" in the *Encyclopaedia Britannica* and in various systems of medicine.

For a long period he was responsible for the psychiatric sections of the *Medical Annual*, a task which he embraced with enthusiasm because it enabled him to keep abreast of the growing flood of psychiatric literature at home and abroad. This was of great service to him when he produced in 1929 his most ambitious work, *Recent Advances in Psychiatry*. He attempted here to co-ordinate and place in perspective the divergent and largely independent schools of scientific thought in modern psychiatry, and the attempt was eminently successful. A second edition was soon demanded, and the book remains one of the most helpful and illuminating available to the student. Devine was pre-eminently qualified to undertake a work of this kind, because he had always steadfastly avoided attaching himself to any one school of thought, but maintained a balanced and impartial attitude, ready to examine and appraise every alleged advance and to co-ordinate it, if it could be established, in the structure of psychiatry. His interests extended to every avenue which promised aid in the solution of the problems of psychiatry, and neurology, chemistry, psychology and sociology all came within his critical purview. His writings were therefore distinguished, not so much by the initiation of original research, as by his comprehensive grasp of the value of the contributions offered by the various schools of thought which are to-day working in the field of psychiatry, and by a nice and cool judgment in assessing their import and relationships.

Devine's personality was extraordinarily attractive, and he was one of the most lovable of men. To his many friends he was always "Henry," and personal characteristics which might have been defects in another, notably a charming absent-mindedness in the affairs of everyday life, seemed in him to fit with entire congruity into a character which endeared him to all. He had an intense interest in all human affairs, and an unbounded capacity for sympathizing with human difficulties and frailties, which manifested itself both in his relations with patients and in the administration and guidance of the institutions and staffs which were under his care. He was an able administrator, but still more he was a great physician. BERNARD HART.

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(E.) indicates the *Epitome* section; the title of the abstract is followed by the author's name, thus: "Age and human ability. Miles, W. R. (E.)"

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