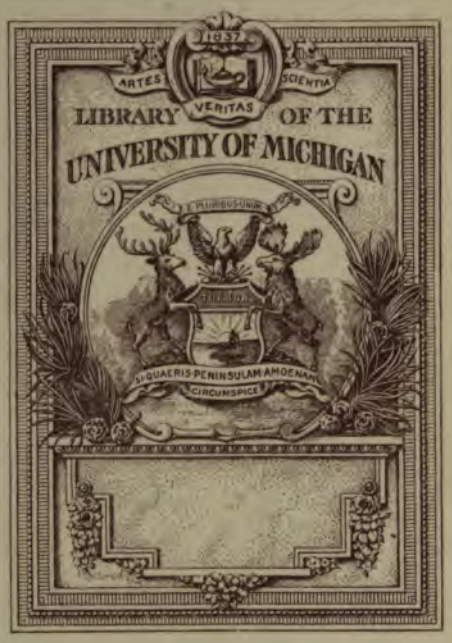

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1868 HOOKER, SIR JOSEPH DALTON, M.D., C.B., G.C.S.I., D.C.L., LL.D., F.R.S., Corresponding Member of the Academy of Sciences of France; The Camp, Sunningdale.

1878 AVEBURY, The Right Hon. LORD, D.C.L., LL.D., F.R.S., High Elms, Farnborough, Kent, R.S.O.

1887 FOSTER, SIR MICHAEL, K.C.B., M.D., LL.D., F.R.S., Professor of Physiology in the University of Cambridge, Nine Wells, Great Shelford, Cambridge.

1887 TURNER, SIR WILLIAM, M.B., D.C.L., LL.D., F.R.S., Principal of the University of Edinburgh; 6, Eton Terrace, Edinburgh.

1896 KELVIN, The Right Hon. LORD, P.C., G.C.V.O., F.R.S., Pres. R.S.E., D.C.L., LL.D., &c., Glasgow.

1905 BARNES, ROBERT, M.D., F.R.C.P., Bernersmede, Eastbourne.

1905 GAIRDNER, SIR WILLIAM, K.C.B., M.D., F.R.S., LL.D., 32, George Square, Edinburgh.

1905 GASKELL, WALTER HOLBROOK, M.D., F.R.S., The Uplands, Great Shelford, Cambridge.

1905 LISTER, The Right Hon. BARON, O.M., F.R.S., D.C.L., LL.D., D.Sc., F.R.C.S., 12, Park Crescent, Portland Place, W.

1905 RAMSAY, SIR WILLIAM, K.C.B., F.R.S., LL.D., D.Sc., F.C.S., 19, Chester Terrace, Regent's Park, N.W.

1905 RAYLEIGH, The Right Hon. BARON, O.M., F.R.S., D.C.L., LL.D., Sc.D., Terling Place, Witham, Essex.

1905 WILKS, SIR SAMUEL, Bart., M.D., F.R.S., LL.D., F.R.C.P., 8, Prince Arthur Road, Hampstead, N.W.

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OF THE

ROYAL MEDICAL AND CHIRURGICAL SOCIETY

OF LONDON

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L.—Hon. Librarian.
S.—Hon. Secretary.
C.—Member of Council.
Sci. Com.—Member of a Scientific Committee.
Ho. Com.—Member of House Committee.
Lib. Com.—Member of Library Committee.
Bldg. Com.—Member of Building Committee.
Dis. Com.—Member of Discussions Committee.
Cent. Com.—Member of Centenary Committee.

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Names printed in this type and underlined are of those Fellows who have paid the Composition Fee in lieu of further annual subscriptions.

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[N.B.—Fellows are reminded that they are, themselves, responsible for the correctness of the descriptions in the following lists, and it is particularly requested that any change of Title, Appointment, or Residence may be communicated to the Secretary before the 1st of July in each year.]

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1898 AARONS, S. JERVOIS, M.D., 14, Stratford place, Oxford street, W.

1885 ABRAHAM, PHINEAS S., M.A., M.D., Dermatologist to the West London Hospital, Assistant Surgeon to Hospital for Diseases of the Skin, Blackfriars; 2, Henrietta street, Cavendish square, W.

1885 ACLAND, THEODORE DYKE, M.D., Physician to St. Thomas's Hospital, and Physician to the Hospital for Consumption and Diseases of the Chest, Brompton; 19, Bryanston square, W. C. 1906—. *Ho. Com.* 1906—. *Referee*, 1905-6.

1897 ADDISON, CHRISTOPHER, M.D., Charing Cross Hospital Medical School, Chandos street, W.

1879 ALLCHIN, WILLIAM HENRY, M.D., F.R.S.Ed., Senior Physician to the Westminster Hospital; 5, Chandos street, Cavendish square, W. C. 1898-9. *Referee*, 1897.

1888 ANDERSON, JOHN, M.D., C.I.E., Physician to the Seamen's Hospital, Greenwich; Lecturer on Tropical Medicine at St. Mary's Hospital Medical School; 9, Harley street, Cavendish square, W.

1891 ANDREWES, FREDERICK WILLIAM, M.D., Highwood, Hampstead lane, Highgate, N.

1904 ARKWRIGHT, JOSEPH ARTHUR, M.D., The Garth, Kenley; and 13, Welbeck street, Cavendish square, W.

1902 ARMOUR, DONALD JOHN, M.B., Assistant Surgeon to the West London Hospital; Senior Assistant Surgeon to the Belgrave Hospital for Children; 89, Harley street, W.

1903 ASCHERSON, WILLIAM LAWRENCE, M.B., B.C., 37, Brunswick gardens, Campden hill, W.

1893 BAILEY, ROBERT COZENS, M.S., 21, Welbeck street, Cavendish square, W.

Elected

1891 BAKER, CHARLES ERNEST, M.B., 5, Gledhow gardens South Kensington, S.W.

1900 BALDWIN, ASLETT, 6, Manchester square, W.

1887 BALL, JAMES BARRY, M.D., Physician to the West London Hospital; 12, Upper Wimpole street, Cavendish square, W.

1885 BALLANCE, CHARLES ALFRED, C.V.O., Pruss. O.C.3, M.S., Assistant Surgeon to St. Thomas's Hospital and to the Hospital for Sick Children, Great Ormond street; Surgeon to the National Hospital for the Paralysed and Epileptic, Queen square; 106, Harley street, Cavendish square, W. *Referee*, 1904—. *Trans.* 6.

1879 BARKER, ARTHUR EDWARD JAMES, Professor of the Principles and Practice of Surgery and Professor of Clinical Surgery at University College, and Surgeon to University College Hospital, London; 87, Harley street, Cavendish square, W. C. 1895-7. *Referee*, 1897—. *Trans.* 7.

1876 **Barlow**, SIR THOMAS, Bart., K.C.V.O., M.D., B.S., *Trustee for Debenture-holders;* Physician to His Majesty's Household; Physician to University College Hospital; 10, Wimpole street, Cavendish square, W. C. 1892. S. 1899-1902. *Referee*, 1896-9. *Trans.* 2.

1902 BARNARD, HAROLD L., M.S., 21, Wimpole street, W.

1893 BARRETT, HOWARD, 49, Gordon square, W.C.

1880 BARROW, A. BOYCE, Surgeon to King's College Hospital; 8, Upper Wimpole street, Cavendish square, W. C. 1903—4.

1896 BARTON, JAMES KINGSTON, 14, Ashburn place, Courtfield road, South Kensington, S,W.

1904 BARWELL, HAROLD SHUTTLEWORTH, M.B., 55, Wimpole street, W.

1859 BARWELL, RICHARD, Consulting Surgeon to the Charing Cross Hospital; 55, Wimpole street, W. C. 1876-77. V.P. 1883-4. *Referee*, 1868-75, 1879-82. *Trans.* 12. *Pro.* 1.

Elected

1868 **Bastian,** HENRY CHARLTON, M.A., M.D., F.R.S., Emeritus Professor of the Principles and Practice of Medicine and of Clinical Medicine in University College, London; Consulting Physician to University College Hospital and Physician to the National Hospital for the Paralysed and Epileptic; 8A, Manchester square, W. C.1885. V.P.1904-5. *Referee*, 1886-96. *Trans.* 3.

1890 BATEMAN, WILLIAM A. F., Bridge House, Richmond, Surrey.

1891 BATTEN, FREDERICK E., M.D., B.C., 33, Harley street, W.

1905 BATTLE, WILLIAM HENRY, 49, Harley street, Cavendish square, W.

1875 BEACH, FLETCHER, M.B., Physician to the West End Hospital for Nervous Diseases, Winchester House, Kingston Hill [79, Wimpole street, W.].

1883 BEALE, EDWIN CLIFFORD, M.A., M.B., Physician to the City of London Hospital for Diseases of the Chest, and Physician to the Great Northern Central Hospital; 23, Upper Berkeley street, W. C. 1906—.

1897 BEDDARD, A. P., M.D., Assistant Physician to Guy's Hospital; 44, Seymour street, W.

1880 BEEVOR, CHARLES EDWARD, M.D., Physician for Out-patients to the National Hospital for the Paralysed and Epileptic, and to the Great Northern Hospital; 135, Harley street, Cavendish square, W. C. 1900-2. *Referee*, 1896-1900, 1906—. *Trans.* 1.

1901 BEEVOR, SIR HUGH REEVE, Bart., M.D., 17, Wimpole street, Cavendish square, W.

1877 BENNETT, SIR WILLIAM HENRY, K.C.V.O., Surgeon to St. George's Hospital; 1, Chesterfield street, Mayfair, W. C. 1893-4. *Referee*, 1892-93, 1899—. *Trans.* 4.

1897 BERKELEY, COMYNS, M.B., B.C., Physician to Out-Patients, Chelsea Hospital for Women; 53, Wimpole street, W.

Elected

1885 BERRY, JAMES, B.S., Surgeon to the Royal Free Hospital, and Lecturer on Surgery at the London School of Medicine for Women; Demonstrator of Practical Surgery, St. Bartholomew's Hospital; 21, Wimpole street, Cavendish square, W.

1893 BIDWELL, LEONARD A., Senior Assistant Surgeon to the West London Hospital; 15, Upper Wimpole street, Cavendish square, W.

1897 BLACKER, G. F., M.D., Obstetric Physician to University College Hospital and to the Great Northern Central Hospital; 45, Wimpole street, Cavendish square, W.

1901 BLAIKIE, J. BRUNTON, M.D., C.M., 80, Brook street, Grosvenor square W.

1883 **Bland-Sutton,** JOHN, Surgeon to the Middlesex Hospital; Surgeon to the Chelsea Hospital for Women; 47, Brook street, Grosvenor square, W. C. 1906—. *Trans.* 6.

1865 **Blandford,** GEORGE FIELDING, M.D., Lecturer on Psychological Medicine at St. George's Hospital; 48, Wimpole street, Cavendish square, W. C. 1883-4. V.P. 1898-1900.

1902 BLUMFELD, JOSEPH, M.D., B.C., 7, Cavendish place, Cavendish square, W.

1891 BOKENHAM, THOMAS JESSOPP, 10, Devonshire street, Portland place, W.

1903 BOLTON, CHARLES, M.D., 16, Devonshire street, W.

1905 BOSANQUET, WILLIAM CECIL, M.A., M.D., 117A, Harley street, W.

1882 **Bowlby,** ANTHONY ALFRED, C.M.G., Surgeon to St. Bartholomew's Hospital; 24, Manchester square, W. C. 1903—4. *Trans.* 8.

1886 BOXALL, ROBERT, M.D., Obstetric Physician to Outpatients, and Lecturer on Midwifery and Diseases of Women, at the Middlesex Hospital; 40, Portland place, W.

Elected

1884 BOYD, STANLEY, B.S., Surgeon to, and Lecturer on Surgery at, the Charing Cross Hospital; Surgeon to the Paddington Green Children's Hospital; Consulting Surgeon to the New Hospital for Women; 134, Harley street, Cavendish square, W. C. 1904-6. *Referee*, 1895—1904. *Trans.* 1.

1890 BRADFORD, JOHN ROSE, M.D., D.Sc., F.R.S., Physician to University College Hospital; 8, Manchester square, W. *Referee*, 1899—. *Trans.* 1.

1904 BRANSON, WILLIAM PHILIP SUTCLIFFE, M.D., 59, Gordon square, W.C. *Trans.* 1.

1901 BREWERTON, ELMORE WRIGHT, 84, Wimpole street, W.

1904 BRIMACOMBE, RICHARD WILLIAM, M.D., Colebrook Lodge, Putney Heath, S.W.

1898 **Broadbent**, J. F. H., M.D., 35, Seymour street, W.

1868 **Broadbent**, SIR WILLIAM HENRY, Bart., K.C.V.O., M.D., F.R.S., LL.D., Physician in Ordinary to H.M. the King; Consulting Physician to St. Mary's Hospital Consulting Physician o the London Fever Hospital; 84, Brook street, Grosvenor square, W. C. 1885. V.P. 1905-6. *Referee*, 1881-4, 1891-7. *Trans.* 5.

1905 BROWN, WILLIAM CARNEGIE, M.D., 32, Harley street, W.

1881 BROWNE, OSWALD AUCHINLECK, M.A., M.D., Physician to the Royal Hospital for Diseases of the Chest and to the Metropolitan Hospital; 7, Upper Wimpole street, W.

1874 BRUCE, JOHN MITCHELL, M.D., Physician to, and Lecturer on Medicine at, the Charing Cross Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 23, Harley street, W. C. 1892, 1897-9. S. 1893-6. *Sci. Com.* 1889-1902. *Ho. Com.* 1898-9. *Referee*, 1886-91. *Lib. Com.* 1888-91. *Trans.* 3.

1898 BRUCE, SAMUEL NOBLE, 15, Queensborough terrace, Hyde Park, W.

1905 BRUCE-PORTER, HARRY EDWIN BRUCE, M.D., 6, Grosvenor street, Grosvenor square, W.

Elected

1871 BRUNTON, SIR THOMAS LAUDER, M.D., D.Sc. LL.D., F.R.S., Consulting Physician to, and late Lecturer on Pharmacology and Therapeutics at, St. Bartholomew's Hospital; 10, Stratford place, Oxford street, W. C. 1888-9. *Referee*, 1880-87. *Lib. Com.* 1882-7. *Trans.* 2.

1860 **Bryant**, THOMAS, M.Ch., Honorary Surgeon-in-Ordinary to H.M. the King, Consulting Surgeon to Guy's Hospital; Member of the Société de Chirurgie, Paris; 42, Norfolk square, W. P. 1898-1900. C. 1873-4. V.P. 1885-6. *Sci. Com.* 1863. *Referee*, 1882-4. *Lib. Com.* 1868-71. *Trans.* 17. *Pro.* 1.

1901 BUCKNALL, THOMAS RUPERT HAMPDEN, M.S., M.D.; 16, Devonshire street, Portland place, W. *Trans.* 1.

1893 BURGHARD, FRÉDÉRIC FRANÇOIS, M.D., M.S., Surgeon to King's College Hospital and Paddington Green Children's Hospital; 86, Harley street, Cavendish square, W.

1903 BURROWS, HAROLD, M.B., B.S., Caragh, Lyford road, Wandsworth common, S.W.

1885 BUTLER-SMYTHE, ALBERT CHARLES, Senior Out-Patient Surgeon, Samaritan Free Hospital for Women and Children, Soho; Senior Surgeon to the Grosvenor Hospital for Women and Children; 76, Brook street, Grosvenor square, W.

1873 **Butlin**, HENRY TRENTHAM, D.C.L., Surgeon to St. Bartholomew's Hospital; 82, Harley street, Cavendish square, W. C. 1887-8. V.P. 1904—6. *Referee*, 1893—1904. *Trans.* 4. *Pro.* 1.

1896 BUTTAR, CHARLES, M.D., 10, Kensington gardens square, Bayswater, W. *Pro.* 1.

1883 BUXTON, DUDLEY WILMOT, M.D., B.S., Administrator, and Teacher of the Use, of Anæsthetics, in University College Hospital; Consulting Anæsthetist to the National Hospital for the Paralysed and Epileptic, Queen square, and Anæsthetist to the London Dental Hospital; 82, Mortimer street, Cavendish square, W.

Elected

1899 BUZZARD, EDWARD FARQUHAR, M.D., 33, Harley street, Cavendish square, W.

1868 **Buzzard**, THOMAS, M.D., Physician to the National Hospital for the Paralysed and Epileptic; 74, Grosvenor street, Grosvenor square, W. C. 1885-6. V.P. 1905—. *Referee*, 1887-1905.

1885 CAHILL, JOHN, M.D., 12, Seville street, Lowndes square, S.W.

1893 CALEY, HENRY ALBERT, M.D., Physician in charge of Out-patients, Lecturer on Materia Medica and Therapeutics, and Dean of the Medical School, St. Mary's Hospital; 24, Upper Berkeley street, Portman square, W.

1887 CALVERT, JAMES, M.D., 113, Harley street, W. *Trans.* 1.

1905 CAMMIDGE, PERCY JOHN, M.B., D.P.H., 2, Beaumont street, Portland place, W. *Trans.* 2.

1897 CANTLIE, JAMES, M.B., 140, Harley street, W.

1901 CARGILL, LIONEL VERNON, Ophthalmic Surgeon to King's College Hospital; Ophthalmic Surgeon to the Seamen's Hospital Society; Surgeon to the Royal Eye Hospital, Southwark; 31, Harley street, Cavendish square, W.

1888 CARLESS, ALBERT, M.S., Professor of Surgery in King's College, London; Surgeon to King's College Hospital; 6, Upper Wimpole street, W.

1896 CARR, J. WALTER, M.D., Physician to the Royal Free Hospital; Physician to the Victoria Hospital for Children; 19, Cavendish place, W. *Trans.* 1.

1903 CARRUTHERS, SAMUEL WILLIAM, M.D., C.M., 44, Central hill, Norwood, S.E.

1888 CAUTLEY, EDMUND, M.D., B.C., 15, Upper Brook street, W. *Trans.* 2.

Elected

1871 **Cayley,** WILLIAM, M.D., Consulting Physician to the Middlesex Hospital, Consulting Physician to the London Fever Hospital, and to the North-Eastern Hospital for Children; 120, Queen's road, Richmond, S.W. C. 1888. *Referee*, 1886-7, 1899-1903. *Lib. Com.* 1886-7. *Trans.* 2.

1879 CHAMPNEYS, FRANCIS HENRY, M.D., Physician-Accoucheur and Lecturer on Obstetric Medicine at St. Bartholomew's Hospital; 42, Upper Brook street, Grosvenor square, W. C. 1898-1900. *Referee*, 1891-8. *Lib. Com.* 1885-98. *Trans.* 8.

1868 **Cheadle,** WALTER BUTLER, M.D., Physician to, and Lecturer on Clinical Medicine at, St. Mary's Hospital; Consulting Physician to the Hospital for Sick Children; 19, Portman street, Portman square, W. *Trustee* 1888-1903. *Marshall Hall Trustee* 1873-1903. S. 1886-8. C. 1890-91. V.P. 1904-5. *Sci. Com.* 1889-95. *Bldg. Com.* 1889-92. *Referee*, 1885. *Trans.* 1.

1879 CHEYNE, WILLIAM WATSON, C.B., M.B., F.R.S., Surgeon to King's College Hospital, and Professor of Clinical Surgery in King's College, London; 75, Harley street, Cavendish square, W. C. 1897-9. *Referee*, 1894-7, 1904—. *Lib. Com.* 1886-8, 1891-6. *Trans.* 1.

1866 **Church,** SIR WILLIAM SELBY, Bart., K.C.B., M.D., *Hon. Treasurer*, President of the Royal College of Physicians of London, Physician to, and Lecturer on Clinical Medicine at, St. Bartholomew's Hospital; 130, Harley street, Cavendish square, W. C. 1885-6. V.P. 1892-4. T. 1894—. *Referee*, 1874-81. *Ho. Com.* 1898—.

1879 CLARK, ANDREW, Surgeon to, and Lecturer on Surgery at, the Middlesex Hospital; 71, Harley street, Cavendish square, W. C. 1906—.

1882 CLARKE, ERNEST, M.D., B.S., Surgeon to the Central London Ophthalmic Hospital; Ophthalmic Surgeon to the Miller Hospital; 3, Chandos street, Cavendish square, W.

Elected

1890 CLARKE, JAMES JACKSON, M.B., Surgeon to the North-West London and City of London Orthopædic Hospitals; 18, Portland place, W.

1881 CLARKE, W. BRUCE, M.B., Assistant Surgeon to, and Lecturer on Anatomy at, St. Bartholomew's Hospital; Surgeon to the West London Hospital; 51, Harley street, Cavendish square, W. C. 1899-1901. *Lib. Com.* 1905—. *Trans.* 1.

1905 CLOGG, HERBERT SHERWELL, M.B., M.S., 117A, Harley street, Cavendish square, W.

1879 **Clutton**, HENRY HUGH, M.B., M.C., Surgeon to St. Thomas's Hospital; 2, Portland place, W. C. 1897-9. *Dis. Com.* 1897-8. *Referee*, 1896-7. *Trans.* 3.

1888 COCK, FREDERICK WILLIAM, M.D., 1, Porchester Houses, Porchester square, W.

1902 COLLIER, JAMES STANSFIELD, M.D., B.Sc., 57A, Wimpole street, W.

1897 COLMAN, W. S., M.D., Assistant Physician to St. Thomas's Hospital; 9, Wimpole street, W.

1865 COOPER, SIR ALFRED, Surgeon in Ordinary to H.R.H. the Duke of Saxe-Coburg-Gotha; Consulting Surgeon to the West London Hospital and to St. Mark's Hospital; 9, Henrietta street, Cavendish square, W.

1860 **Couper**, JOHN, Consulting Surgeon to the Royal London Ophthalmic Hospital and to the London Hospital; 80, Grosvenor street, W. C. 1876. *Referee*, 1882-3.

1877 COUPLAND, SIDNEY, M.D., Commissioner in Lunacy; late Physician to, and Lecturer on Medicine at, the Middlesex Hospital; 16, Queen Anne street, Cavendish square, W. C. 1893-4. *Referee*, 1892-3. *Ho. Com.* 1895-8.

1862 **Cowell**, GEORGE, Consulting Surgeon to the Westminster Hospital and to the Royal Westminster Ophthalmic Hospital; 24, Harrington gardens, South Kensington, S.W. C. 1882-3.

Elected

1897 CRAWFURD, RAYMOND H. PAYNE, M.D., 71, Harley street, W.

1878 CRICHTON-BROWNE, SIR JAMES, M.D., LL.D., F.R.S., Lord Chancellor's Visitor in Lunacy; 61, Carlisle place Mansions, Victoria street, S.W.

1874 Cripps, WILLIAM HARRISON, Surgeon to St. Bartholomew's Hospital; 2, Stratford place, Oxford street, W. C. 1890-91. V.P. 1906—. *Trans.* 1.

1882 CROCKER, HENRY RADCLIFFE, M.D., Physician to the Skin Department, University College Hospital; 121, Harley street, Cavendish square, W. C. 1903-4. *Trans.* 3.

1898 CROMBIE, ALEXANDER, C.B., M.D., 3, Bickenhall Mansions, Gloucester place, W.

1905 CROSS, WILLIAM FOSTER, 80, New Cavendish street, W.

1888 CULLINGWORTH, CHARLES JAMES, M.D., D.C.L., LL.D., Consulting Obstetric Physician to St. Thomas's Hospital; 14, Manchester square, W. *Referee*, 1896—.

1879 CUMBERBATCH, A. ELKIN, M.B., Aural Surgeon to St. Bartholomew's Hospital, and to the National Hospital for the Paralysed and Epileptic; 11, Park crescent, Portland place, W. *Trans.* 1.

1898 CURRIE, A. STARK, M.D., 20, Oxford terrace, Hyde park, W.

1886 DAKIN, WILLIAM RADFORD, M.D., Obstetric Physician to, and Lecturer in Midwifery at, St. George's Hospital, and Physician to the General Lying-in Hospital; 8, Grosvenor street, Grosvenor square, W. C. 1904-5. *Lib. Com.* 1902-4.

1872 DALBY, SIR WILLIAM BARTLETT, M.B., Consulting Aural Surgeon to St. George's Hospital; 18, Savile row, W. C. 1896-7. V.P. 1901-2. *Trans.* 4.

Elected

1891 DALTON, NORMAN, M.D., Physician to King's College Hospital; Professor of Pathological Anatomy in King's College, London; 4, Mansfield street, Cavendish square, W.

1896 DAUBER, JOHN HENRY, M.A., M.B., B.Ch., Gynæcologist to the Hospital for Women, Soho square; 39, Hertford street, Mayfair, W.

1889 DEAN, HENRY PERCY, M.S., Surgeon to the London Hospital; 69, Harley street, Cavendish square, W.

1878 DENT, CLINTON THOMAS, Surgeon to, and Lecturer on Surgery at, St. George's Hospital; 61, Brook street, W. C. 1890, 1905—. S. 1901-4. *Bldg. Com.* 1890-2. *Cent. Com.* 1904-5. *Referee*, 1892—1901. *Trans.* 7.

1891 DE SANTI, PHILIP ROBERT WILLIAM, Assistant Surgeon and Aural Surgeon to the Westminster Hospital; 15, Stratford place, W. *Trans.* 1.

1894 DICKINSON, THOMAS VINCENT, M.D., Physician to the Italian Hospital, Queen square; 33, Sloane street, S.W.

1859 Dickinson, WILLIAM HOWSHIP, M.D., Consulting Physician to St. George's Hospital, and Consulting Physician to the Hospital for Sick Children; Honorary Fellow of Caius College, Cambridge; 10, Stanhope place, Marble arch, W. P. 1896-8. C. 1874-5. V.P. 1887. *Referee*, 1869-73, 1882-6. *Sci. Com.* 1867, 1879, 1889-96. *Trans.* 16.

1889 DODD, HENRY WORK, Surgeon to the Royal Westminster Ophthalmic Hospital; Ophthalmic Surgeon to the Royal Free Hospital and to the West-End Hospital for Nervous Diseases; 136, Harley street, Cavendish square, W.

1888 DONELAN, JAMES, M.B., M.C., Chevalier, Crown of Italy, Physician to the Italian Hospital, Queen square; 6, Manchester square, W.

Elected

1877 DORAN, ALBAN HENRY GRIFFITHS, Surgeon to the Samaritan Free Hospital; 9, Granville place, Portman square, W. C. 1893-4. *Lib. Com.* 1891-3, 1899—. *Referee*, 1898—. *Trans.* 4.

1891 DOVE, PERCY W., M.B., 84, Crouch hill, N.

1896 DOWNES, JOSEPH LOCKHART, M.B., C.M., 269, Romford road, E.

1893 DRYSDALE, JOHN H., M.D., 11, Devonshire place, W. *Trans.* 1.

1865 **Duckworth**, SIR DYCE, M.D., LL.D., Physician to, and Lecturer on Clinical Medicine at, St. Bartholomew's Hospital; 28, Grosvenor place, S.W. C. 1883-4. V.P. 1902-4. *Referee*, 1885-97. *Trans.* 2.

1903 DUDGEON, LEONARD, 6, Powis gardens, Bayswater, W.

1880 DUNBAR, JAMES JOHN MACWHIRTER, M.D., Hedingham House, Clapham Common, S.W.

1887 DUNN, HUGH PERCY, Ophthalmic Surgeon to the West London Hospital; 54, Wimpole street, Cavendish square, W.

1898 DUNN, L. A., M.S., 51, Devonshire street, Portland place, W.

1874 **Durham**, FREDERIC, M.B., Consulting Surgeon to the North-West London Hospital; 52, Brook street, Grosvenor square, W.

1905 EASON, HERBERT LIGHTFOOT, M.D., M.S., The College, Guy's Hospital, S.E.

1868 **Eastes**, GEORGE, M.B.Lond., 35, Gloucester terrace, Hyde Park, W. C. 1892-3.

1893 ECCLES, WILLIAM MCADAM, M.S., Assistant Surgeon, St. Bartholomew's Hospital, to the West London Hospital, and to the City of London Truss Society; 124, Harley street, W.

1891 EDDOWES, ALFRED, M.D., 28, Wimpole street, W.

Elected

1883 EDMUNDS, WALTER, M.C., 2, Devonshire place, Portland place, W. *Trans.* 3.

1884 EDWARDS, FREDERICK SWINFORD, Surgeon to the West London Hospital, and to St. Peter's Hospital; Senior Assistant Surgeon to St. Mark's Hospital; 55, Harley street, Cavendish square, W.

1902 ENGLISH, THOMAS CRISP, B.S., Assistant Surgeon to St. George's Hospital and to the Grosvenor Hospital for Women and Children; 47, Upper Brook street, W. *Trans.* 1.

1902 EVANS, ARTHUR, M.S., Assistant Surgeon to, and Lecturer on Surgical Anatomy at, Westminster Hospital, Surgeon to the Seamen's Hospital, Royal Albert Dock; 84, Harley street, W.

1904 EVANS, JOHN HOWELL, 63, Grosvenor street, W.

1898 EVANS, WILLMOTT H., M.D., B.S., B.Sc., Assistant Surgeon and Surgeon in charge of Skin Department, Royal Free Hospital; 2, Upper Wimpole street, W.

1879 EVE, FREDERIC S., Surgeon to the London Hospital; Surgeon to the Evelina Hospital for Sick Children; 61, Harley street, Cavendish square, W. C. 1897-9. *Referee*, 1902—. *Trans.* 4.

1877 Ewart, WILLIAM, M.D., Physician to St. George's Hospital and to the Belgrave Hospital for Children; 33, Curzon street, Mayfair, W. C. 1895-7. *Lib. Com.* 1897—. *Sci. Com.* 1889-1902. *Trans.* 3. *Pro.* 1.

1900 FAIRBAIRN, JOHN SHIELDS, M.B., Assistant Obstetric Physician to St. Thomas's Hospital; 60, Wimpole street, W.

1905 FAULDER, THOMAS JEFFERSON, 50, Welbeck street, Cavendish square, W.

1905 FAWCETT, JOHN, M.D., 66, Wimpole street, W.

1898 FENWICK, E. HURRY, Surgeon to the London Hospital and to St. Peter's Hospital; 14, Savile row, W.

Elected

1880 FERRIER, DAVID, M.D., LL.D., F.R.S., Professor of Neuropathology in King's College, London, and Physician to King's College Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 34, Cavendish square, W. *Referee*, 1891-6. C. 1896-8. *Dis. Com.* 1896—. *Trans.* 2.

1900 FLEMMING, PERCY, M.D., B.S., Professor of Ophthalmic Medicine and Surgery in University College, London; Ophthalmic Surgeon to University College Hospital; Assistant Surgeon to the Royal London Ophthalmic Hospital, City road; 31, Wimpole street, W.

1891 FLETCHER, HERBERT MORLEY, M.D., Assistant Physician to St. Bartholomew's Hospital; Physician to the East London Hospital for Children; 98, Harley street, Cavendish square, W.

1892 FORSBROOK, WILLIAM HENRY RUSSELL, M.D., 40, Lower Belgrave street, Eaton square, S.W.

1896 FOULERTON, ALEXANDER GRANT RUSSELL, Middlesex Hospital, W., and Rhynie, Haywards Heath, Sussex. *Trans.* 1.

1883 FOWLER, JAMES KINGSTON, M.D., Physician to, and Lecturer on Medicine at, the Middlesex Hospital; Physician to the Hospital for Consumption, Brompton, 35, Clarges street, Piccadilly, W. C. 1902-3. *Trans.* 1.

1880 FOX, THOMAS COLCOTT, B.A., M.B., Physician for Diseases of the Skin to the Westminster Hospital, and Physician to the Skin Department of the Paddington Green Hospital for Children; 14, Harley street, Cavendish square, W. C. 1904-5. *Trans.* 1.

1871 FRANK, PHILIP, M.D., 3, Elvaston place, South Kensington, S.W.

1902 FRENCH, HERBERT, M.D., 26, St. Thomas's street, S.E. *Trans.* 2.

1896 FREYER, P. J., M.D., M.Ch., Surgeon to St. Peter's Hospital; 27, Harley street, Cavendish square, W. *Trans.* 1.

Elected

1898 FRIPP, SIR ALFRED DOWNING, C.B., M.V.O., M.S., Honorary Surgeon-in-Ordinary to H.M. the King; Kt. of Grace of St. John; Assistant Surgeon to Guy's Hospital; 19, Portland place, W.

1898 FROST, WILLIAM ADAMS, Ophthalmic Surgeon to St. George's Hospital, and Surgeon to Royal Westminster Ophthalmic Hospital; 30, Cavendish square, W.

1883 FULLER, HENRY ROXBURGH, M.D., 45, Curzon street, Mayfair, W. C. 1906—.

1894 FURNIVALL, PERCY, Assistant Surgeon, London Hospital; Assistant Surgeon, St. Mark's Hospital; 28, Weymouth street, Portland place, W.

1899 FÜRTH, KARL, M.D., Physician to the German Hospital, 39, Harley street, W.

1874 **Galabin**, ALFRED LEWIS, M.D., Obstetric Physician to, and Lecturer on Midwifery and the Diseases of Women at, Guy's Hospital; 49, Wimpole st., Cavendish square, W. C. 1892. *Referee*, 1882-91, 1896—. *Lib. Com.* 1883-4. *Trans.* 2.

1895 GALLOWAY, JAMES, M.D., Physician, Skin Department, and Joint Lecturer on Practical Medicine, Charing Cross Hospital; 54, Harley street, Cavendish square, W.

1854 **Garrod**, SIR ALFRED BARING, M.D., F.R.S., Physician Extraordinary to Her late Majesty Queen Victoria; Consulting Physician to King's College Hospital; 10, Harley street, Cavendish square, W. C. 1867. V.P. 1880-81. *Referee*, 1855-65. *Trans.* 9.

1886 GARROD, ARCHIBALD EDWARD, M.D., Assistant Physician to St. Bartholomew's Hospital; Physician to the Hospital for Sick Children, Great Ormond street; 9, Chandos street, Cavendish square, W. C. 1902-4. *Sci. Com.* 1889-1902. *Lib. Com.* 1896-1902, 1904—. *Referee*, 1906—. *Trans.* 8.

Elected

1905 GASK, GEORGE ERNEST, The Warden's House, St. Bartholomew's Hospital, E.C.

1887 GAY, JOHN, 119, Upper Richmond road, Putney, S.W.

1866 **Gee**, SAMUEL JONES, M.D., *Chairman of Trustees for Debenture-holders;* Honorary Physician to H.R.H. the Prince of Wales; Physician to St. Bartholomew's Hospital; 31, Upper Brook street, Grosvenor square, W. C. 1883-4. L. (June) 1887-99. V.P. 1899-1900. *Sci. Com.* 1879. *Bldg. Com.* 1889-92. *Referee*, 1885-7, 1900—. *Lib. Com.* 1871-6. *Ho. Com.* 1898-1900. *Trans.* 1.

1898 GIBBES, CUTHBERT CHAPMAN, M.D., 89, Harley street, W.

1880 GIBBONS, ROBERT ALEXANDER, M.D., Physician to the Grosvenor Hospital for Women and Children; 29, Cadogan place, S.W. C. 1896-7. *Trans.* 1.

1893 GILES, ARTHUR EDWARD, M.D., B.Sc., Assistant Surgeon, Chelsea Hospital for Women; 10, Upper Wimpole street, W.

1894 GILL, RICHARD, 72, Wimpole street, W.

1906 GOADBY, KENNETH W., 21, New Cavendish street, Portland place, W.

1877 GODLEE, RICKMAN JOHN, M.S., *Hon. Librarian;* Honorary Surgeon-in-Ordinary to H.M. the King; Surgeon to University College Hospital, and Professor of Clinical Surgery in University College, London; Surgeon to the Hospital for Consumption, Brompton; 19, Wimpole street, Cavendish square, W. S. 1892-4. L. 1895—. *Referee*, 1886-91. *Ho. Com.* 1898—. *Cent. Com.* 1905. *Trans.* 11.

1870 **Godson**, CLEMENT, M.D., Consulting Physician to the City of London Lying-in Hospital; 82, Brook street, Grosvenor square, W.

Elected

1886 GOLDING-BIRD, CUTHBERT HILTON, M.B., Surgeon to, and Lecturer on Clinical Surgery at, Guy's Hospital; 12, Queen Anne street, Cavendish square, W. *Trans.* 1.

1897 GOODBODY, F. W., M.D., 6, Chandos street, Cavendish square, W. *Trans.* 1.

1896 GOODALL, EDWARD WILBERFORCE, M.D., B.S., Eastern Hospital, Homerton, N.E.

1883 GOODHART, JAMES FREDERIC, M.D., Physician to Guy's Hospital; Consulting Physician to the Evelina Hospital for Sick Children; 25, Portland place, W. C. 1903–4. *Referee*, 1900-3. *Lib. Com.* 1893-6.

1889 GOODSALL, DAVID HENRY, Surgeon to the Metropolitan Hospital; Surgeon to St. Mark's Hospital; 17, Devonshire place, Upper Wimpole street, W.

1895 GOSSAGE, ALFRED MILNE, M.B., 54, Upper Berkeley street, W.

1877 GOULD, ALFRED PEARCE, M.S., *Hon. Treasurer*, Surgeon to, and Lecturer on Surgical Pathology at, the Middlesex Hospital; 10, Queen Anne street, Cavendish square, W. C. 1892-3. S. 1898–1901. V.P. 1904–6. T. 1906—. *Referee*, 1895-8. *Ho. Com.* 1892-8, 1904–6. *Lib. Com.* 1891. *Cent. Com.* 1904-5. *Trans.* 3.

1891 GOW, WILLIAM J., M.D., Assistant Obstetric Physician to St. Mary's Hospital; Obstetric Physician to the Royal Hospital for Women and Children; Physician to Out-Patients, Queen Charlotte's Lying-in Hospital; 27, Weymouth street, Portland place, W.

1873 Gowers, SIR WILLIAM RICHARD, M.D., F.R.S., Consulting Physician to University College Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 50, Queen Anne street, Cavendish square, W. C. 1891. *Referee*, 1888-90. *Lib. Com.* 1884-6. *Trans.* 7.

1892 GRANT, J. DUNDAS, M.A., M.D., 18, Cavendish square, W.

Elected

1868 **Green**, T. HENRY, M.D., Physician to the Charing Cross Hospital, and to the Hospital for Consumption, Brompton; 74, Wimpole street, Cavendish square, W. C. 1886. *Referee*, 1882-5.

1885 GRIFFITH, WALTER SPENCER ANDERSON, M.D., Assistant Physician-Accoucheur, St. Bartholomew's Hospital; Physician to Queen Charlotte's Lying-in Hospital; 96, Harley street, Cavendish square, W. *Referee*, 1902—.

1903 GRÜNBAUM, OTTO F. F., M.B., B.C., 34, Wimpole street, Cavendish square, W.

1883 GUNN, ROBERT MARCUS, M.B., Surgeon to the Royal London Ophthalmic Hospital, Moorfields; Ophthalmic Surgeon to the National Hospital for the Paralysed and Epileptic; 54, Queen Anne street, Cavendish square, W. C. 1903-4.

1890 GUTHRIE, LEONARD GEORGE, M.D., B.Ch., Physician to the Regent's Park Hospital for Epilepsy and Paralysis; Assistant Physician to the North-West London Hospital; Assistant Physician to the Children's Hospital, Paddington Green; 15, Upper Berkeley street, Portman square, W.

1886 HABERSHON, SAMUEL HERBERT, M.D., Assistant Physician to the Hospital for Consumption, Brompton; 88, Harley street, Cavendish square, W.

1885 HAIG, ALEXANDER, M.D., Physician to the Metropolitan Hospital, and to the Royal Hospital for Children and Women; 7, Brook street, Grosvenor square, W. *Trans.* 7.

1890 HALE, CHARLES DOUGLAS BOWDICH, M.D., 3, Sussex place, Hyde Park, W.

1881 **Hall**, FRANCIS DE HAVILLAND, M.D., Physician to the Westminster Hospital; 47, Wimpole street, Cavendish square, W. C. 1901-3. *Referee*, 1893-7.

Elected

1891 HAMER, WILLIAM HEATON, M.D., 55, Dartmouth park hill, Highgate, N.

1889 HANDFIELD-JONES, MONTAGU, M.D., Obstetric Physician to, and Lecturer on Midwifery and Diseases of Women at, St. Mary's Hospital; Physician to the British Lying-in Hospital; 35, Cavendish square, W.

1905 HANDLEY, WILLIAM SAMPSON, M.S., Assistant to the Middlesex Hospital, late Surgeon to Outpatients, Samaritan Free Hospital, 77, Wimpole street, Cavendish square, W.

1893 **Harley,** VAUGHAN, M.D., 25, Harley street, Cavendish square, W.

1901 HARMER, WILLIAM DOUGLAS, M.B., 45, Weymouth street, Portland place, W.

1892 HAROLD, JOHN, M.B., 91, Harley street, Cavendish square, W.

1870 HARRISON, REGINALD, Surgeon to St. Peter's Hospital; 6, Lower Berkeley street, Portman square, W. C. 1894-5. V.P. 1898-1900. *Trans.* 4.

1904 HARRISON, CHARLES JOSEPH, M.D., B.S., 6, Swan Walk, Chelsea, S.W.

1901 HARTIGAN, T. J. P., 94, Harley street, W.

1896 HARTLEY, PERCIVAL HORTON-SMITH, M.V.O., M.D., 19, Devonshire street, Portland place, W. *Sci. Com.* 1897-1902. *Trans.* 1.

1870 **Haward,** J. WARRINGTON, *President;* Consulting Surgeon to, and Lecturer on Clinical Surgery at, St. George's Hospital; 57, Green street, Grosvenor Square, W. C. 1885. S. 1888-91. V.P. 1894-5. T. (June) 1895-1906. P. 1906—. *Lib. Com.* 1881-4. *Sci. Com.* 1889-91. *Bldg. Com.* (*Sec.*) 1889-92. *Ho. Com.* 1892—. *Trans.* 3.

Elected

1891 HAWKINS, HERBERT PENNELL, M.D., B.Ch., Physician to St. Thomas's Hospital; 56, Portland place, W.

1875 HAYES, THOMAS CRAWFORD, M.D., Physician-Accoucheur and Physician for Diseases of Women and Children to King's College Hospital, and Professor of Midwifery in King's College; Physician for Diseases of Women to the Royal Free Hospital; 17, Clarges street, Piccadilly, W.

1905 HEAD, HENRY, M.D., F.R.S., 143, Harley street, Cavendish square, W.

1895 HENDERSON, EDWARD ERSKINE, B.A., M.B., B.C., 20, Queen Anne street, Cavendish square, W.

1877 HERMAN, GEORGE ERNEST, M.B., Consulting Obstetric Physician to the London Hospital; 20, Harley street, Cavendish square, W. C. 1900-2. *Referee*, 1892-1900. *Lib. Com.* 1898-1900. *Trans.* 1.

1900 HERN, WILLIAM, 7, Stratford place, W.

1877 HERON, GEORGE ALLAN, M.D., Physician to the City of London Hospital for Diseases of the Chest, Victoria Park; 57, Harley street, Cavendish square, W. C. 1904–6. *Ho. Com.* 1904–6.

1891 HERRING, HERBERT T., M.B., B.S., 50, Harley street, Cavendish square, W.

1883 HERRINGHAM, WILMOT PARKER, M.D., Assistant Physician, St. Bartholomew's Hospital; 40, Wimpole street, Cavendish square, W. C. 1903—4. *Lib. Com.* 1902-3, 1904—. *Ho. Com.* 1903—4. *Trans.* 3.

1893 HERSCHELL, GEORGE, M.D., 36, Harley street, Cavendish square, W.

1887 HEWITT, FREDERIC WILLIAM, M.V.O., M.D., Honorary Anæsthetist to H.M. the King; Anæsthetist to, and Instructor in Anæsthetics at, the London Hospital; Anæsthetist at the Dental Hospital of London; 14, Queen Anne street, Cavendish square, W. *Trans.* 3.

Elected

1890 HILL, G. WILLIAM, M.D., B.Sc., 26, Weymouth street, Portland place, W.

1906 HINE, THOMAS GUY MACAULAY, M.B., B.C., St. Bartholomew's Hospital, E.C.

1904 HOBSON, H. OVERTON, M.D., 32, Upper Berkeley street, W.; and Helouan, Egypt.

1856 Holmes, TIMOTHY, M.C., M.A., Consulting Surgeon to St. George's Hospital; Corresponding Member of the Société de Chirurgie, Paris; 6, Sussex place, Hyde Park, W. C. 1869-70. L. 1873-7. S. 1878-80. V.P. 1881-2. T. 1885-7. P. 1890-92. *Bldg.Com.* (*Chairman*) 1889-92. *Referee*, 1866-8, 1872, 1883-4. *Sci. Com.* 1867. *Lib. Com.* 1863-5, 1892-5. *Ho. Com.* 1892-8. *Trans.* 8.

1878 HOOD, DONALD WILLIAM CHARLES, C.V.O., M.D., Senior Physician to the West London Hospital; Examining Physician for King's Messengers, Foreign Office; 43, Green street, Park lane, W. C. 1904-6.

1898 HORDER, THOMAS J., M.D., 141, Harley street, W. *Trans.* 1.

1883 HORSLEY, SIR VICTOR ALEXANDER HADEN, F.R.S., Surgeon to University College Hospital, Surgeon to the National Hospital for the Paralysed and Epileptic; 25, Cavendish square, W. *Referee*, 1897—. *Trans.* 1.

1892 HOWARD, R. J. BLISS, M.D., 31, Queen Anne street, Cavendish square, W.

1906 HUGHES, GERALD S., Bolingbroke Hospital, Wandsworth common, S.W.

1902 HULBERT, ERNEST BEDDOE, M.D., 77, Welbeck street, Cavendish square, W.

1889 HUNTER, WILLIAM, M.D., Senior Assistant Physician to the London Fever Hospital; Curator and Pathologist, Charing Cross Hospital; 103, Harley street, W.

Elected

1856 **Hutchinson,** JONATHAN, F.R.S., Consulting Surgeon to, and Emeritus Professor of Surgery at, the London Hospital; Consulting Surgeon to the Royal London Ophthalmic Hospital, Moorfields, and Senior Surgeon to the Hospital for Diseases of the Skin; 15, Cavendish square, W. C. 1870. V.P. 1882. P. 1894-6. *Referee*, 1876-81, 1883-94. *Lib. Com.* 1864-5. *Trans.* 15. *Pro.* 2.

1888 HUTCHINSON, JONATHAN, Jun., Surgeon to the London Hospital; 1, Park crescent, W. *Trans.* 3.

1897 HUTCHISON, ROBERT, M.D., 22, Queen Anne street, Cavendish square, W.

1871 JACKSON, J. HUGHLINGS, M.D., LL.D., F.R.S., Consulting Physician to the London Hospital; Physician to the National Hospital for the Paralysed and Epileptic; 3, Manchester square, W. C. 1889.

1883 JESSOP, WALTER H. H., M.B., Ophthalmic Surgeon to St. Bartholomew's Hospital; 73, Harley street, W. C. 1906—. *Referee*, 1901-6.

1881 JOHNSON, GEORGE LINDSAY, M.D., Cortina, Netherhall gardens, South Hampstead, N.W., and 55, Queen Anne street, W.

1889 JOHNSON, RAYMOND, M.B., B.S., Assistant Surgeon to University College Hospital; Surgeon to the Victoria Hospital for Children; 11, Wimpole street, Cavendish square, W. *Trans.* 1.

1884 JOHNSTON, JAMES, M.D., 53, Prince's square, Bayswater, W.

1899 **Jones,** GEORGE, M.B., 8, Church terrace, Lee, S.E.

1887 JONES, HENRY LEWIS, M.D., Medical Officer in charge of Electrical Department at St. Bartholomew's Hospital; 143, Harley street, Cavendish square, W. *Referee*, 1906—.

1896 JONES, L. VERNON, B.A., M.D., B.Ch., 7, Arlington street, St. James's, S.W.

Elected

1881 JULER, HENRY EDWARD, Ophthalmic Surgeon to St. Mary's Hospital; Surgeon to the Royal Westminster Ophthalmic Hospital; Consulting Ophthalmic Surgeon to the London Lock Hospital; 23, Cavendish square, W. C. 1901-3. *Ho. Com.* 1902-3.

1898 KEEP, A. CORRIE, M.D., C.M., Surgeon to Out-patients Samaritan Free Hospital for Women and Children; 14, Gloucester place, Portman square, W.

1882 KEETLEY, CHARLES R., B., Senior Surgeon to the West London Hospital; 56, Grosvenor street, Grosvenor square, W. C. 1901-3. *Lib. Com.* 1903—. *Trans.* 1.

1898 KELLOCK, THOMAS HERBERT, M.D., B.C., Assistant Surgeon to Middlesex Hospital and to the Hospital for Sick Children; 8, Queen Anne street, Cavendish square, W.

1901 KELYNACK, T. N., M.D., 120, Harley street, W.

1902 KERR, JAMES, M.D., D.P.H., 3, Hanger lane, Ealing, W.

1857 Kiallmark, HENRY WALTER, 5, Pembridge gardens, W. C. 1890–91.

1881 KIDD, PERCY, M.D., Physician to the Hospital for Consumption, Brompton; Physician to the London Hospital; 60, Brook street, Grosvenor square, W. C. 1900-2. *Referee*, 1905—. *Trans.* 4.

1902 KING, DAVID BARTY, M.A., M.D., Ch.B., 13, Queen street, Mayfair, W.

1900 LAKE, RICHARD, Surgeon Laryngologist, Mount Vernon Hospital for Consumption; Surgeon, Royal Ear Hospital; 60, Harley street, W. *Trans.* 1.

1896 LANE, JAMES ERNEST, Surgeon to Out-patients, St. Mary's Hospital; 46, Queen Anne Street, Cavendish square, W.

1884 LANE, WILLIAM ARBUTHNOT, M.S., Surgeon to Guy's Hospital and to the Hospital for Sick Children, 21, Cavendish square, W. C. 1904–5. *Trans.* 4.

Elected

1882 Lang, William, Ophthalmic Surgeon to, and Lecturer on Ophthalmic Surgery at, the Middlesex Hospital; Surgeon to the Royal London Ophthalmic Hospital, Moorfields; 22, Cavendish square, W. C. 1904–5.

1894 Langdon-Down, Reginald Langdon, M.B., B.C., 47, Welbeck street, W.

1865 Langton, John, Surgeon to, and Lecturer on Clinical Surgery at, St. Bartholomew's Hospital; Surgeon to the City of London Truss Society; 20, Bentinck street, Manchester square, W. C. 1881–2. V.P. 1895-7, *Referee*, 1885-95. *Lib. Com.* 1879-80, 1888-95, *Trans.* 2.

1898 Latham, A. C., M.D., 44, Brook street, Grosvenor square, W.

1890 Law, Edward, M.D., C.M., 8, Wimpole street, Cavendish square, W.

1898 Lawford, J. B., Ophthalmic Surgeon and Lecturer on Ophthalmology, St. Thomas's Hospital; Surgeon to Royal London Ophthalmic Hospital; 99, Harley street, W. *Referee*, 1906—.

1888 Lawrence, Laurie Asher, 9, Upper Wimpole street, W.

1890 Lawrie, Edward, M.B., Surgeon Lieutenant-Colonel, Indian Medical Department; late Residency Surgeon, Hyderabad, Deccan; Harley Lodge, 115A, Harley street, W.

1893 Lawson, Arnold, Ophthalmic Surgeon to the Children's Hospital, Paddington Green; 12, Harley street, Cavendish square, W.

1900 Leaf, Cecil Huntington, M.A., M.B.; 75, Wimpole street, Cavendish square, W.

1896 Lee, William Edward, M.D., 36, Finsbury pavement, E.C.

Elected

1895 LEES, DAVID BRIDGE, M.D., Physician to, and Lecturer on Medicine at, St. Mary's Hospital, and Physician to the Hospital for Sick Children; 22, Weymouth street, Portland place, W. *Trans.* 2.

1899 LEGGE, THOMAS MORISON, M.D., 18, Cheyne row, Chelsea, S.W.

1895 LESLIE, ROBERT MURRAY, M.D., Assistant Physician to Royal Hospital for Diseases of the Chest; 26, Harley street, Cavendish square, W.

1886 LEWERS, ARTHUR HAMILTON NICHOLSON, M.D., Obstetric Physician to the London Hospital; 72, Harley street, Cavendish square, W. *Trans.* 1.

1891 LITTLE, ERNEST MUIRHEAD, Surgeon to the National Orthopædic Hospital; 5, Duchess street, Portland place, W.

1889 LITTLE, JOHN FLETCHER, M.B., 125, Harley street, Cavendish square, W.

1881 LOCKWOOD, CHARLES BARRETT, Surgeon to the Great Northern Central Hospital; Assistant Surgeon to, and Lecturer on Surgical and Descriptive Anatomy at, St. Bartholomew's Hospital; 19, Upper Berkeley street, Portman square, W. C. 1901-3. *Trans.* 5.

1897 LOW, HAROLD, 10, Evelyn gardens, S.W.

1881 LUCAS, RICHARD CLEMENT, B.S., M.B., Surgeon to, and Lecturer on Surgery, late Lecturer on Anatomy at, Guy's Hospital; Consulting Surgeon to the Evelina Hospital for Sick Children; 50, Wimpole street, Cavendish square, W. C. 1900-2. *Ho. Com.* 1901-2. *Trans.* 3.

1888 LUFF, ARTHUR PEARSON, M.D., B.Sc., Physician to Outpatients and Lecturer on Medical Jurisprudence at St. Mary's Hospital; 9, Queen Anne street, Cavendish square, W. *Referee,* 1903—. *Trans.* 1.

1887 LUSH, PERCY J. F., M.B., 4, Maresfield gardens, Hampstead, N.W.

Elected

1898 LYSTER, C. R. C., 70, Wimpole street, Cavendish square, W.

1905 MCCANN, FREDERICK JOHN, M.D., 5, Curzon street, Mayfair, W.

1873 **MacCarthy**, JEREMIAH, M.A., Consulting Surgeon to the London Hospital, late Lecturer on Surgery at the London Hospital Medical College; 1, Cambridge place, Victoria road, Kensington, W. C. 1886-7. *Lib. Com.* 1882-5. *Referee*, 1890–1905.

1899 MACDONALD, GREVILLE, M.D., 85, Harley street, W.

1898 MCFADYEAN, SIR JOHN, The Royal Veterinary College, Camden Town, N.W.

1894 MACFADYEN, ALLAN, M.D., C.M., Lister Institute of Preventive Medicine, Chelsea bridge, S.W. *Referee*, 1905—.

1880 MCHARDY, MALCOLM MACDONALD, Ophthalmic Surgeon to King's College Hospital, and Professor of Ophthalmic Surgery in King's College, London; Senior Surgeon to the Royal Eye Hospital, Southwark; 5, Savile row, W.

1902 MACKENZIE, HECTOR WILLIAM GAVIN, M.A., M.D., 34, Upper Brook street, W.

1881 MACKENZIE, SIR STEPHEN, M.D., Physician to the London Hospital; Physician to the Royal London Ophthalmic Hospital; 18, Cavendish square, W. C. 1899-1900. *Referee*, 1890-9. *Trans.* 1.

1881 MACREADY, JONATHAN FORSTER CHRISTIAN HORACE, Surgeon to the Great Northern Hospital; 42, Devonshire street, W.

1880 MADDICK, EDMUND DISTIN, 31, Cavendish square, W.

1886 MAGUIRE, ROBERT, M.D., Physician to Out-patients and Joint Lecturer on Pathology at St. Mary's Hospital; Physician to the Hospital for Consumption, Brompton; 4, Seymour street, Portman square, W. *Sci. Com.* 1889-1902.

Elected

1880 MAKINS, GEORGE HENRY, C.B., Surgeon to St. Thomas's Hospital; Consulting Surgeon to the Evelina Hospital for Children; 47, Charles street, Berkeley square, W. C. 1899-1900. *Referee*, 1898-9, 1902—. *Trans.* 2.

1885 MALCOLM, JOHN DAVID, M.B., C.M., Surgeon to the Samaritan Free Hospital; 13, Portman street, Portman square, W. *Trans.* 4.

1890 MANSON, SIR PATRICK, K.C.M.G., M.D., C.M., LL.D., F.R.S., Physician to the Seamen's Hospital, Albert Docks; Lecturer on Tropical Medicine at St. George's Hospital; 21, Queen Anne street, Cavendish square, W. *Referee*, 1904—.

1867 MARSH, F. HOWARD, Professor of Surgery, University of Cambridge, late Surgeon to, and Lecturer on Surgery at, St. Bartholomew's Hospital; 14, Hertford street, Mayfair, W. C. 1882-3, 1889. S. 1885-7. V.P. 1891-3. *Lib. Com.* 1880-1. *Trans.* 4.

1891 MARTIN, HENRY CHARRINGTON, M.D., 27, Oxford square, W.

1884 MARTIN, SIDNEY HARRIS COX, M.D., F.R.S., Assistant Physician to University College Hospital, and to the Hospital for Consumption, Brompton; Professor of Pathology, University College, London; 10, Mansfield street, Portland place, W. C. 1906—. *Referee*, 1904-6.

1892 MASTERS, JOHN ALFRED, M.D., 94, Knightsbridge, S.W.

1891 MAY, WILLIAM PAGE, M.D., B.Sc., 9, Manchester square, W.

1880 MEREDITH, WILLIAM APPLETON, M.B., C.M., Surgeon to the Samaritan Free Hospital for Women and Children; 21, Manchester square, W. C. 1897-9. *Ho. Com.* 1898-9. *Trans.* 1.

1894 MICHELS, ERNST, M.D., Surgeon to the German Hospital; 48, Finsbury square, E.C. *Trans.* 3.

Elected

1891 MOLINE, PAUL, M.B., 42, Walton street, Chelsea, S.W.

1873 **Moore**, NORMAN, M.D., *Hon. Librarian*, Physician and Lecturer on Medicine to St. Bartholomew's Hospital; 94, Gloucester place, Portman square, W. C. 1891-2. L. 1899—. S. 1896-9. *Referee*, 1886-90. *Ho. Com.* 1898—. *Sci. Com.* 1889-1902. *Cent. Com.* 1904–5.

1878 MORGAN, JOHN HAMMOND, C.V.O., M.A., Surgeon to the Charing Cross Hospital, and to the Hospital for Sick Children, Great Ormond street; 68, Grosvenor street, W. C. 1895-7. *Dis. Com.* 1896-7. *Referee*, 1901—. *Trans.* 2.

1894 MORISON, ALEXANDER, M.D., 14, Upper Berkeley street, W.

1874 **Morris**, HENRY, M.A., Surgeon to the Middlesex Hospital; 8, Cavendish square, W. C. 1888-9. V.P. 1900-2. *Referee*, 1882-7. *Lib. Com.* 1895-6. *Trans.* 10.

1879 MORRIS, MALCOLM ALEXANDER, Consulting Surgeon to the Skin Department of, and late Lecturer on Dermatology at, St. Mary's Hospital; 8, Harley street, Cavendish square, W. *Sci. Com.* 1889-1902. *Trans.* 1.

1898 MORRISON, JAMES, M.D., 11, Brook street, Grosvenor square, W.

1885 MOTT, FREDERICK WALKER, M.D., F.R.S., Assistant Physician, Charing Cross Hospital; Pathologist to the London County Council; 25, Nottingham place, W. *Referee*, 1900—. *Sci. Com.* 1899—. *Trans.* 1.

1905 MUECKE, FRANCIS FREDERICK, M.B., B.S., 63, Wellington road, St. John's Wood, N.W.

1902 MUMMERY, JOHN PERCY LOCKHART, B.A., 10, Cavendish place, W.

Elected

1888 **Murray**, HUBERT MONTAGUE, M.D., Physician to, and Joint Lecturer on Medicine at, the Charing Cross Hospital; Physician to the Victoria Hospital for Children; 25, Manchester square, W.

1898 MURRAY, JOHN, Assistant Surgeon to the Middlesex Hospital and to the Paddington Green Children's Hospital; 110, Harley street, W.

1880 MURRELL, WILLIAM, M.D., Physician to, Lecturer on Clinical Medicine, and Joint Lecturer on Medicine at the Westminster Hospital; 17, Welbeck street, Cavendish square, W. *Sci. Com.* 1889-1902. *Trans.* 1.

1863 **Myers**, ARTHUR BOWEN RICHARDS, late Brigade-Surgeon, Brigade of Guards; 43, Gloucester street, Warwick square, S.W. C. 1878-9. *Lib. Com.* 1877.

1904 NESS, THOMAS MATHESON, M.B., 80, Brook street, W.

1906 NITCH, CYRIL ALFRED RANKIN, M.S., St. Thomas's Hospital, Albert Embankment, S.E.

1864 **Nunn**, THOMAS WILLIAM, Consulting Surgeon to the Middlesex Hospital; 27, York terrace, York gate, N.W.

1880 OGILVIE, GEORGE, M.B., B.Sc., Senior Physician to the French Hospital, and to the Hospital for Epilepsy and Paralysis, Maida Vale; 22, Welbeck street, Cavendish square, W. C. 1906—. *Trans.* 1.

1891 OGLE, CYRIL, M.A., M.D., Assistant Physician to St. George's Hospital; 96, Gloucester place, Portman square, W.

1860 OGLE, WILLIAM, M.D., late Superintendent of Statistics in the Registrar-General's Department, Somerset House; 10, Gordon street, Gordon square, W.C. *Marshall Hall Trustee*, 1873-1903. S. 1868-70. C. 1876-7. V.P. 1887. *Lib. Com.* 1871-5. *Trans.* 5.

1892 OPENSHAW, T. HORROCKS, C.M.G., M.B., M.S., Surgeon to, and Lecturer on Anatomy at, the London Hospital; 16, Wimpole street, Cavendish square, W.

Elected

1877 ORMEROD, JOSEPH ARDERNE, M.D., Assistant Physician to St. Bartholomew's Hospital; Physician to the National Hospital for the Paralysed and Epileptic, Queen square; 25, Upper Wimpole street, W. C. 1897. *Lib. Com.* 1896-7. *Trans.* 1.

1905 ORMOND, A. W., 37, Queen Anne street, Cavendish square, W. *Trans.* 1.

1879 OWEN, EDMUND, M.B., Consulting Surgeon to St. Mary's Hospital; Consulting Surgeon to the Hospital for Sick Children, Great Ormond street; Surgeon-in-chief to the French Hospital; 64, Great Cumberland place, Hyde park, W. C. 1896-7. *Trans.* 4.

1892 PAGE, H. MARMADUKE, 14, Grenville place, South Kensington, S.W.

1874 PAGE, HERBERT WILLIAM, M.A., M.C., Surgeon to, and Joint Lecturer on Surgery at, St. Mary's Hospital; 146, Harley street, Cavendish square, W. C. 1890-91. V.P. 1906—. *Referee*, 1884-9. *Lib. Com.* 1886-8. *Ho. Com.* 1906—. *Trans.* 4.

1886 PAGET, STEPHEN, *Hon. Secretary*, Surgeon to the West London Hospital; Surgeon to the Throat and Ear Department of the Middlesex Hospital; 70, Harley street, W. S. 1904—. *Lib. Com.* 1902—4.

1905 PARDOE, JOHN GEORGE, M.B., 77, Wimpole street, W. *Trans.* 1.

1895 PARKER, CHARLES ARTHUR, 141, Harley street, Cavendish square, W.

1904 PARKINSON, THOMAS WRIGHT, M.D., 77, Sloane street, S.W.

1889 PARSONS, J. INGLIS, M.D., Physician to the Chelsea Hospital for Women; 3, Queen street, Mayfair, W.

1883 PASTEUR, WILLIAM, M.D., Physician to the Middlesex Hospital; Consulting Physician to the North-Eastern Hospital for Children; 4, Chandos street, Cavendish square, W. C. 1906—.

Elected

1901 PATERSON, HERBERT JOHN, M.A., M.B., B.C., Assistant Surgeon to the London Temperance Hospital, 9, Upper Wimpole street, W.

1891 PATERSON, WILLIAM BROMFIELD, 7A, Manchester square, W.

1891 PATON, EDWARD PERCY, M.D., M.S., 53, Queen Anne street, Cavendish square, W.

1865 **Pavy**, FREDERICK WILLIAM, M.D., LL.D., F.R.S., Consulting Physician to Guy's Hospital; 35, Grosvenor street, W. P. 1900-2. C. 1883-4. V.P. 1893-4. *Referee*, 1871-82. *Trans.* 1.

1869 PAYNE, JOSEPH FRANK, M.D., Physician to, and Lecturer on Medicine at, St. Thomas's Hospital; 78, Wimpole street, Cavendish square, W. C. 1887. V.P. 1906—. *Referee*, 1890-1906. *Sci. Com.* 1879. *Lib. Com.* 1878-85, 1889-1906.

1894 PEGLER, L. HEMINGTON, M.D., 58, Harley street, W.

1898 PENDLEBURY, HERBERT STRINGFELLOW, M.B., B.C., 44, Brook street, Grosvenor square, W.

1887 PENROSE, FRANCIS GEORGE, M.D., Physician to St. George's Hospital and to the Hospital for Sick Children, Great Ormond street; 84, Wimpole street, Cavendish square, W. *Sci. Com.* 1889-1902.

1890 PERRY, SIR EDWIN COOPER, M.D., Physician to Guy's Hospital; The Superintendent's House, Guy's Hospital, S.E.

1895 PHEAR, ARTHUR G., M.D., Assistant Physician and Pathologist to the Metropolitan Hospital; 47, Weymouth street, Portland place, W. *Trans.* 2.

1884 PHILLIPS, GEORGE RICHARD TURNER, J.P., 28, Palace Court, Bayswater hill, W.

1889 PHILLIPS, SIDNEY, M.D., Physician and Lecturer on Medicine at St. Mary's Hospital; Senior Physician to the London Fever Hospital, and to the Lock Hospital; 3, Upper Brook street, Grosvenor square, W. *Trans.* 1.

Elected

1884 PITT, GEORGE NEWTON, M.D., Physician to, and Pathologist at, Guy's Hospital; 15, Portland place, W. S. 1902-6. *Lib. Com.* 1906—. *Referee*, 1897-1902. *Trans.* 2.

1889 PITTS, BERNARD, M.A., M.C., Surgeon to St. Thomas's Hospital and Lecturer on Surgery; Surgeon to the Hospital for Sick Children, Great Ormond street; 109, Harley street, Cavendish square, W. *Referee*, 1897—.

1901 PLIMMER, HENRY GEORGE, 3, Hall road, St. John's Wood, N.W.

1885 POLAND, JOHN, Surgeon to the City Orthopædic Hospital and Miller Hospital, Greenwich; 2, Mansfield street, Cavendish square, W.

1884 POLLARD, BILTON, B.S., Surgeon to University College Hospital; Consulting Surgeon to the North-Eastern Hospital for Children; 24, Harley street, Cavendish square, W. *Trans.* 1.

1865 **Pollock,** JAMES EDWARD, M.D., Consulting Physician to the Hospital for Consumption, Brompton; 37, Collingham place, S.W. C. 1882-3. V.P. 1896-7. *Referee*, 1872-81.

1894 POLLOCK, WILLIAM RIVERS, M.B., B.C., Assistant Obstetric Physician to the Westminster Hospital; 56, Park street, Grosvenor square, W.

1867 **Powell,** SIR RICHARD DOUGLAS, Bart., K.C.V.O., M.D. Physician Extraordinary to H.M. the King; Consulting Physician to, and late Lecturer on Medicine at, the Middlesex Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 62, Wimpole street, Cavendish square, W. P. 1904-6. S. (Oct.) 1883-5. C. 1887-8. V.P. 1902-4. *Referee*, 1879-83, 1886. *Trans.* 3.

Elected

1887 POWER, D'ARCY, M.A., M.B., Surgeon at St. Bartholomew's Hospital; Surgeon to the Victoria Hospital for Children, Chelsea; 10A, Chandos street, Cavendish Square, W. *Lib. Com.* 1896—. *Trans.* 3.

1905 PRICE, FREDERICK WILLIAM, M.B., 77, Wimpole street, W.

1900 PRICE-JONES, CECIL, M.B., Assistant to the Lecturer in Bacteriology, Guy's Hospital, Pathologist to the East London Hospital for Children, Shadwell; Guy's Hospital, S.E., and Beachcote, The Bungalows, Walmer Beach.

1883 PRINGLE, JOHN JAMES, M.B., C.M., Physician in Charge of Skin Department at the Middlesex Hospital; 23, Lower Seymour street, Portman square, W. *Trans.* 2.

1874 **Purves**, WILLIAM LAIDLAW, Aural Surgeon to Guy's Hospital; 20, Stratford place, Oxford street, W. *Trans.* 2.

1877 PYE-SMITH, PHILIP HENRY, M.D., F.R.S., Physician to and Lecturer on Medicine at, Guy's Hospital; 48, Brook street, Grosvenor square, W. C. 1893-4. *Lib. Com.* 1887-93, 1899—. *Referee*, 1897—. *Trans.* 1.

1898 RAMSAY, HERBERT MURRAY, 35A, Hertford street, W.

1893 RANKIN, GUTHRIE, M.D., 4, Chesham street, Belgrave square, S.W. *Trans.* 2.

1899 RAWLING, LOUIS BATHE, M.B., B.C., 16, Montagu street, Portman square, W.

1892 RAYNER, HENRY, M.D., Lecturer on Psychological Medicine to St. Thomas's Hospital; 16, Queen Anne street, Cavendish square, W.

1869 **Read**, THOMAS LAURENCE, 11, Petersham terrace, Queen's gate, S.W. C. 1901-3. *Ho. Com.* 1902-3.

1882 REID, SIR JAMES, Bart., G.C.V.O., K.C.B., M.D., Physician-in-Ordinary to H.M. the King; 72, Grosvenor street, Grosvenor square, W. C. 1904-6. *Cent. Com.* 1904–5.

Elected

1903 RICH, EVELYN ARTHUR, 12, Wilton street, Grosvenor place, S.W.

1887 RICHARDSON, GILBERT, M.A., M.D., 19, Putney hill, S.W.

1863 **Ringer**, SYDNEY, M.D., F.R.S., Holme Professor of Clinical Medicine in University College, London, and Physician to University College Hospital; 15, Cavendish place, Cavendish square, W. C. 1881-2. V.P. 1900-2. *Referee*, 1873-80, 1889-97. *Trans.* 6.

1900 RIVIERE, CLIVE, M.D., 19, Devonshire street, Portland place, W. *Trans.* 1.

1896 ROBERTS, CHARLES HUBERT, M.D., Physician to Out-Patients, Samaritan Hospital for Women; Physician to Out-patients, Queen Charlotte's Lying-in Hospital, London; 21, Welbeck street, W.

1893 ROBERTS, D. WATKIN, M.D., 56, Manchester street, Manchester square, W.

1878 ROBERTS, FREDERICK THOMAS, M.D., Professor of Medicine, and of Clinical Medicine, in University College, London; Physician to University College Hospital; Consulting Physician to the Hospital for Consumption, Brompton; 102, Harley street, Cavendish square, W. C. 1894-5. *Referee*, 1899—. *Sci. Com.* 1889-1902.

1898 ROBERTSON, F. W., M.D., "Ravenstone," 37, Lingfield road, Wimbledon, Surrey.

1901 ROBINSON, GEORGE HENKELL DRUMMOND, M.D., 17, Seymour street, Portman square, W.

1896 ROBINSON, HENRY BETHAM, M.S., Assistant Surgeon to, and Surgeon in Charge of the Throat Department, St. Thomas's Hospital; Assistant Surgeon to the East London Hospital for Children, Shadwell; 1, Upper Wimpole street, W. *Trans.* 1.

Elected

1889 ROBSON, ARTHUR WILLIAM MAYO, Hunterian Professor of Surgery, Royal College of Surgeons; Consulting Surgeon, Leeds General Infirmary; Emeritus Professor of Surgery in the Yorkshire College; 8, Park crescent, London, W. *Trans.* 10. *Pro.* 1.

1890 ROLLESTON, HUMPHRY DAVY, M.D., Physician to St. George's Hospital, and to the Victoria Hospital for Children; 55, Upper Brook street, Grosvenor square, W. *Referee*, 1906—. *Trans.* 1.

1906 ROLLESTON, J. D., M.D., Grove Hospital, Tooting, S.W.

1857 **Rose**, HENRY COOPER, M.D., 16, Warwick road, Maida Vale, W. C. 1886-7. *Trans.* 1.

1888 ROUGHTON, EDMUND WILKINSON, B.S., M.D., Surgeon and Surgical Tutor to the Royal Free Hospital; 38, Queen Anne street, W. *Trans.* 1.

1882 ROUTH, AMAND JULES MCCONNEL, M.D., B.S., Obstetric Physician to, and Lecturer on Midwifery at, the Charing Cross Hospital; Consulting Physician to the Samaritan Free Hospital for Women and Children; 14A, Manchester square, W. C. 1902-4. *Lib. Com.* 1900-2. *Referee*, 1900-2.

1849 **Routh**, CHARLES HENRY FELIX, M.D., Consulting Physician to the Samaritan Free Hospital for Women and Children; 52, Montagu square, W. *Lib. Com.* 1854-5. *Trans.* 1.

1891 RUSSELL, J. S. RISIEN, M.D., Assistant Physician to University College Hospital, and Pathologist to the National Hospital for the Paralysed and Epileptic, Queen square; 44, Wimpole street, Cavendish square, W. *Trans.* 1.

1900 RYALL, CHARLES, 62, Harley street, Cavendish square, W.

1903 RYAN, JOHN RUSSELL, B.A., M.D., B.Ch., B.A.O., 5, Bennett street, St. James's, S.W.

Elected

1886 SAINSBURY, HARRINGTON, M.D., Physician to the Royal Free Hospital; Physician to the City of London Hospital for Diseases of the Chest; 52, Wimpole street, Cavendish square, W. *Trans.* 1.

1902 SAMBON, LOUIS W., M.D., London School of Tropical Medicine, Greenwich, S.E.

1903 SANDWITH, FLEMING MANT, M.D., Knight of Grace of the Order of St. John; Lecturer at the London School of Tropical Medicine; 31, Cavendish square, W. (April—Dec.) Cairo (Jan.—March).

1869 **Sansom**, ARTHUR ERNEST, M.D., Physician to the London Hospital; Consulting Physician, North-Eastern Hospital for Children; 83, Harley street, Cavendish square, W. C. 1887-8. *Referee*, 1889–1905. *Trans.* 3.

1902 SAUNDERS, EDWARD ARTHUR, M.A., M.B., B.Ch., D.Ph., Assistant Physician and Physician to the Department for the Medical Diseases of Children, West London Hospital; 49, Harley street, Cavendish square, W.

1879 SAVAGE, GEORGE HENRY, M.D., Lecturer on Mental Diseases at Guy's Hospital; 26, Devonshire place, W. C. 1898-9.

1905 SCHARLIEB, HERBERT J., C.M.G., M.D., B.S., 149, Harley street, W.

1892 SCHORSTEIN, GUSTAVE M.A., M.B., B.Ch., D.P.H., Assistant Physician to the London Hospital, and to the Hospital for Consumption, Brompton; 11, Portland place, W.

1899 SCOTT, LINDLEY MARCROFT, M.D., 98, Sloane street, S.W.

1905 SCOTT, SYDNEY RICHARD, 44, Welbeck street, Cavendish square, W.

1863 **Sedgwick**, WILLIAM, 72, King Edward's gardens, Acton hill, Acton, W. C. 1884-5. *Trans.* 3.

Elected

1892 SEGUNDO, CHARLES SEMPILL DE, M.B., B.S., 6, Brook street, Hanover square, W.

1892 SELWYN-HARVEY, JOHN STEPHENSON, M.D., 1, Astwood road, Cromwell road, S.W.

1877 SEMON, SIR FELIX, K.C.V.O., M.D., Physician Extraordinary to H.M. the King; Physician for Diseases of the Throat to the National Hospital for Epilepsy and Paralysis, Queen square; 39, Wimpole street, Cavendish square, W. C. 1895-7. *Lib. Com.* 1894-5. *Trans.* 3.

1900 SEQUEIRA, JAMES HARRY, M.D., Physician to the Skin Department and Lecturer on Dermatology at the London Hospital, 63, Harley street, W.

1894 SEWILL, JOSEPH SEFTON, 9A, Cavendish square, W.

1882 SHARKEY, SEYMOUR JOHN, M.D., Physician to, and Joint Lecturer on Medicine at, St. Thomas's Hospital; 22, Harley street, Cavendish square, W. C. 1899-1900. *Referee*, 1897-9, 1902—. *Trans.* 2.

1900 SHAW, HAROLD BATTY, M.D., 7, Devonshire street, Portland place, W.

1886 SHAW, LAURISTON ELGIE, M.D., Physician to Guy's Hospital; 64, Harley street, Cavendish square, W. *Referee*, 1903—.

1903 SHERREN, JAMES, 40, Devonshire street, W.

1896 SHORE, THOMAS WILLIAM, M.D., Woodlawn, 6, Kingswood road, Upper Norwood, S.E.

1899 SHUTTLEWORTH, GEORGE EDWARD, M.D., Ancaster House, Richmond Hill, Surrey, and 27, New Cavendish street, W.

1899 SIMPSON, WILLIAM JOHN RITCHIE, M.D., 13, Queen Anne street, Cavendish square, W.

Elected

1894 SLATER, CHARLES, M.B., 81, St. Ermin's mansions, Westminster, S.W.

1890 SMALE, MORTON, Surgeon Dentist to St. Mary's Hospital; 22A, Cavendish square, W.

1881 SMITH, EUSTACE, M.D., Physician to H.M. the King of the Belgians; Physician to the East London Children's Hospital, and to the Victoria Park Hospital for Diseases of the Chest; 15, Queen Anne street, Cavendish square, W. C. 1899-1900.

1866 SMITH, HEYWOOD, M.A., M.D., 25, Welbeck street, Cavendish square, W.

1889 SMITH, ROBERT PERCY, M.D., B.S., Lecturer on Psychological Medicine, Charing Cross Hospital; 36, Queen Anne street, W.

1863 Smith, SIR THOMAS, Bart., K.C.V.O., Honorary Sergeant-Surgeon to H.M. the King; Consulting Surgeon to St. Bartholomew's Hospital; 5, Stratford place, Oxford street, W. *Marshall Hall Trustee*, 1877—1903. S. 1870-2. C. 1875-6. V.P. 1887-8. *Referee*, 1873-4, 1880-6. *Sci. Com.* 1867. *Trans.* 4.

1874 *Smith*, WILLIAM ROBERT, M.D., D.Sc., F.R.S.Edin., Barrister-at-Law, Professor of Forensic Medicine, and Director of the Laboratories of State Medicine in King's College, London; 74, Great Russell street, W.C. *Trans.* 1.

1889 SPENCER, HERBERT R., M.D., B.S., Professor of Midwifery in University College; Obstetric Physician to University College Hospital; 104, Harley street, W. *Referee*, 1894—.

1887 SPENCER, WALTER GEORGE, M.B., M.S., Surgeon to, and Lecturer on Physiology at, the Westminster Hospital; 35, Brook street, Grosvenor square, W. *Trans.* 2. *Referee*, 1905—. *Lib. Com.* 1904—.

Elected

1888 SPICER, ROBERT HENRY SCANES, M.D., Surgeon to the Department for Diseases of the Throat, St. Mary's Hospital; 28, Welbeck street, Cavendish square, W.

1890 SPICER, WILLIAM THOMAS HOLMES, M.B., Ophthalmic Surgeon to St. Bartholomew's Hospital; Surgeon to the Royal London Ophthalmic Hospital (City road, late Moorfields); Consulting Ophthalmic Surgeon to the Metropolitan Hospital; 5, Wimpole street, Cavendish square, W.

1903 SPRIGGS, EDMUND IVENS, M.D., Assistant Physician to, and Lecturer on Pathological Chemistry at, St. George's Hospital, and Assistant Physician to the Victoria Hospital for Children, 48, Bryanston street, Portman square, W.

1885 SQUIRE, JOHN EDWARD, C.B., M.D., Physician to the Mount Vernon Hospital for Consumption; 5, Harley street, Cavendish square, W. *Trans.* 2.

1897 STAINER, EDWARD, M.A., M.B., 60, Wimpole street, W.

1899 STEWART, PURVES, M.D., 7, Harley street, W. *Trans.* 1.

1856 **Stocker**, ALONZO HENRY, M.D., Peckham House, Peckham, S.E.

1884 STONHAM, CHARLES, C.M.G., Surgeon to, and Lecturer on Surgery and Teacher of Operative Surgery at, the Westminster Hospital; Surgeon to the Poplar Hospital for Accidents; 4, Harley street, Cavendish square, W. C. 1904-6.

1896 SUTHERLAND, GEORGE ALEXANDER, M.D., Physician to Paddington Green Children's Hospital; Assistant Physician to the North-West London Hospital; 73, Wimpole street, Cavendish square, W.

1896 SWAN, CHARLES ROBERT JOHN ATKIN, M.B., B.Ch., 3, Chester place, Hyde Park square, W.

Elected

1890 SYERS, HENRY WALTER, M.D., 75, Wimpole street, W.

1886 SYMONDS, CHARTERS JAMES, M.S., M.D., Surgeon to, and Surgeon in charge of the Throat Department at, Guy's Hospital; 58, Portland place, W. *Referee*, 1904—.

1875 TAY, WARREN, Senior Surgeon to the London Hospital, to the Royal London Ophthalmic Hospital, and to the Hospital for Diseases of the Skin, Blackfriars; Consulting Surgeon to the North-Eastern Hospital for Children; 4, Finsbury square, E.C.

1873 **Taylor**, FREDERICK, M.D., Physician to, and Lecturer on Medicine at, Guy's Hospital; Consulting Physician to the Evelina Hospital for Sick Children; 20, Wimpole street, Cavendish square, W. *Trustee*, 1893-1903. S. 1889-93. C. 1894-6. *Sci. Com.* 1889-1902. *Referee*, 1887-8, 1899—. *Trans.* 4.

1893 TAYLOR, JAMES, M.D., Assistant Physician to the National Hospital for the Paralysed and Epileptic; Physician to the North-Eastern Hospital for Children, and to the National Orthopædic Hospital; 49, Welbeck street, Cavendish square, W. *Trans.* 1.

1890 TAYLOR, SEYMOUR, M.D., Assistant Physician, West London Hospital; 16, Seymour street, Portman square, W.

1905 THOMPSON, ARTHUR RALPH, Superintendent's Office, Guy's Hospital, S.E.

1900 THOMPSON, CHARLES HERBERT, M.D., 133, Harley street, Cavendish square, W.

1862 **Thompson**, EDMUND SYMES, M.D., Consulting Physician to the Hospital for Consumption, Brompton; Gresham Professor of Medicine; 33, Cavendish square, W. S. 1871-4. C. 1878-9. *Sci. Com.* 1889-1902. *Referee*, 1876-7. *Trans.* 1.

Elected

1904 THOMPSON, HENRY EDMUND SYMES, M.D., Assistant Physician, Royal Hospital for Diseases of the Chest; 33, Cavendish square, W. *Trans.* 1.

1862 Thompson, REGINALD EDWARD, M.D., 13, Cheyne gardens, Chelsea, S.W. C. 1879. S. 1880-82. V.P. 1883-4. *Referee*, 1873-8. *Sci. Com.* 1867. *Trans.* 2.

1899 THOMSON, HERBERT CAMPBELL, M.D., Assistant Physician to the Middlesex Hospital and Physician to the Hospital for Epilepsy and Paralysis, Maida Vale; 34, Queen Anne street, W. *Trans.* 3.

1892 THOMSON, STCLAIR, M.D., Physician for Diseases of the Throat in King's College Hospital; 28, Queen Anne street, Cavendish square, W. *Trans.* 2.

1892 THORNE, WILLIAM BEZLY, M.D., 2, Harley street, W.

1899 THURSFIELD, JAMES HUGH, M.D., 84, Wimpole street, W. *Trans.* 2.

1889 TIRARD, NESTOR ISIDORE CHARLES, M.D., Professor of the Principles and Practice of Medicine, King's College; Physician to King's College Hospital, and Physician to the Evelina Hospital for Sick Children; 74, Harley street, Cavendish square, W.

1872 TOMES, CHARLES SISSMORE, M.A., F.R.S., 9, Park crescent, Portland place, W. C. 1887. V.P. 1897-99. *Lib. Com.* 1879.

1882 TOOTH, HOWARD HENRY, C.M.G., M.D., *Hon. Secretary*, Physician to the National Hospital for the Paralysed and Epileptic, Queen square; Assistant Physician to St. Bartholomew's Hospital; 34, Harley street, Cavendish square, W. S. 1906—. C. 1905-6. *Referee*, 1902-5. *Sci. Com.* 1896-1902.

Elected

1879 **Treves,** SIR FREDERICK, Bart., G.C.V.O., C.B., LL.D., Sergeant-Surgeon in Ordinary to H.M. the King; Surgeon in Ordinary to H.R.H. the Prince of Wales; Kt. of Grace of St. John; Consulting Surgeon to the London Hospital; 6, Wimpole street, Cavendish square, W. C. 1895-6. *Referee*, 1890-95. *Sci. Com.* 1889-95. *Trans.* 7.

1902 TREVOR, ROBERT SALUSBURY, M.B., B.C., 21, FitzGeorge avenue, West Kensington, W.

1897 TUNNICLIFFE, FRANCIS WHITTAKER, M.D., 129, Harley street, W.

1889 TURNBULL, GEORGE LINDSAY, M.D., 47, Ladbroke square, W.

1882 TURNER, GEORGE ROBERTSON, Surgeon to, and Joint Lecturer on Surgery at, St. George's Hospital; 41, Half Moon street, Piccadilly, W. C. 1903-4. *Trans.* 1.

1898 TURNER, WILLIAM, M.B., M.S., Assistant Surgeon, Westminster Hospital; 17, Harley street, Cavendish square, W.

1896 TURNER, WILLIAM ALDREN, M.D., Assistant Physician to King's College Hospital and to the National Hospital for the Paralysed and Epileptic, Queen Square; 18, Harley street, W. *Trans.* 3.

1896 TURNEY, HORACE GEORGE, M.D., Joint Lecturer on Pathology and Assistant Physician to St. Thomas's Hospital; 68, Portland place, W. *Trans.* 1.

1892 TWEEDY, JOHN, Professor of Ophthalmic Medicine and Surgery in University College, Ophthalmic Surgeon to University College Hospital, and Surgeon to the Royal London Ophthalmic Hospital; 100, Harley street, Cavendish square, W.

1876 VENN, ALBERT JOHN, M.D., 3, Hanover court, Hanover square, W.

Elected

1870 VENNING, SIR EDGCOMBE, 30, Cadogan place, S.W. C. 1898-1900. V.P. 1902—4. *Ho. Com.* 1903—4.

1902 VINCENT, RALPH, M.D., B.S., 1, Harley street, W.

1891 VOELCKER, ARTHUR FRANCIS, M.D., B.S., Assistant Physician to, and Lecturer on Pathology at, the Middlesex Hospital; Assistant Physician, Hospital for Sick Children, Great Ormond street; 101, Harley street, W.

1896 WAGGETT, ERNEST, M.B., B.C., Surgeon, London Throat Hospital; Surgeon to Out Patients, Throat and Ear Department, Great Northern Central Hospital; 45, Upper Brook street, W.

1884 WAKLEY, THOMAS, jun., 16, Hyde Park Gate, S.W. C. 1905-6.

1896 WALDO, FREDERICK JOSEPH, M.D., City Coroner, 40, Lansdowne road, Holland park, W.

1900 WALKER, H. ROE, 8, Harley street, Cavendish square, W.

1900 WALKER, JOHN WILLIAM THOMSON, M.B., Assistant Surgeon to the North-West London Hospital, and to St. Peter's Hospital; 30, Queen Anne street, W. *Trans.* 1.

1883 WALLER, AUGUSTUS, M.D., F.R.S., Lecturer on Physiology, St. Mary's Hospital; Weston Lodge, 32, Grove End road, St. John's Wood, N.W. *Referee* 1895—. *Trans.* 1.

1888 WALLIS, FREDERICK CHARLES, M.B., B.C., Assistant Surgeon to the Charing Cross Hospital; 107, Harley street, Cavendish square, W.

1896 WALSHAM, HUGH, M.A., M.D., Assistant Physician to the City of London Hospital for Diseases of the Chest; Assistant Medical Officer in Electrical Department, St. Bartholomew's Hospital; 114, Harley street, Cavendish square, W.

1886 WARD, ALLAN OGIER, M.D., 73, Cheapside, E.C.

Elected

1894 WARD-HUMPHREYS, GEORGE HERBERT, 26, Charles street, St. James's, S.W.

1891 WARING, H. J., M.B., M.S., B.Sc., Assistant Surgeon and Demonstrator of Operative Surgery, St. Bartholomew's Hospital; Surgeon, Metropolitan Hospital; 37, Wimpole street, W.

1877 **Warner**, FRANCIS, M.D., Physician to, and Lecturer on Materia Medica and Therapeutics at, the London Hospital; 5, Prince of Wales terrace, Kensington Palace, W. *Referee*, 1905. C. 1899-1901. *Trans.* 3.

1894 WATERHOUSE, HERBERT FURNIVALL, C.M., Senior Assistant Surgeon and Lecturer on Anatomy, Charing Cross Hospital; Surgeon, Victoria Hospital for Children; 81, Wimpole street, W. *Referee*, 1905—.

1903 WATSON, CHARLES GORDON, 44, Welbeck street, Cavendish square, W.

1861 **Watson**, WILLIAM SPENCER, M.B., 44, Chepstow place, Kensington, W. C. 1883-4. *Trans.* 1.

1891 **Weber**, FREDERIC PARKES, M.D., Physician to the German Hospital, Dalston; 19, Harley street, W. *Trans.* 4. *Pro.* 1.

1857 WEBER, SIR HERMANN, M.D., Consulting Physician to the German Hospital; 10, Grosvenor street, Grosvenor square, W. C. 1874-5. V.P. 1885-6. *Sci. Com.* 1889-1902. *Referee*, 1869-73, 1878-84. *Lib. Com.* 1864-73. *Trans.* 6.

1895 WELLS, SYDNEY RUSSELL, M.D., 24, Somerset street, Portman square, W.

1903 WEST, CHARLES ERNEST, 132, Harley street, W.

Elected

1877 WEST, SAMUEL, M.D., Assistant Physician to St. Bartholomew's Hospital; Senior Physician to the Royal Free Hospital; 15, Wimpole street, Cavendish square, W. C. 1894-5. *Lib. Com.* 1892-4. *Trans.* 7.

1888 WETHERED, FRANK JOSEPH, M.D., Assistant Physician to the Hospital for Consumption, Brompton; 83, Harley street, Cavendish square, W. *Trans.* 1.

1881 WHARRY, ROBERT, M.D., 7, Cambridge gate, Regent's park, N.W.

1891 WHITE, CHARLES PERCIVAL, M.B., B.C., 22, Cadogan gardens, S.W.

1881 WHITE, WILLIAM HALE, M.D., Physician to, and Lecturer on Materia Medica at, Guy's Hospital; 65, Harley street, Cavendish square, W. C. 1900-2. *Referee*, 1888-97, 1899-1900. *Trans.* 4.

1890 WHITE-COOPER, W. G. O., M.B., 5, Courtfield road, Gloucester road, S.W.

1897 WHITFIELD, ARTHUR, M.D., 21, Bentinck street, Manchester square, W. *Trans.* 1.

1899 WHITING, ARTHUR J., M.D., 142, Harley street, W.

1902 WIGHTWICK, FALLON PERCY, M.D., 9A, Upper Brook street, W.

1890 WILLCOCKS, FREDERICK, M.D., Physician to Out-Patients, and Lecturer on Materia Medica and Therapeutics, at the Charing Cross Hospital; Physician to the Evelina Hospital for Sick Children; 14, Mandeville place, Manchester square, W.

1865 Willett, ALFRED, Consulting Surgeon to St. Bartholomew's Hospital; Surgeon to St. Luke's Hospital; 6, Oxford square, Hyde park, W. *Trustee*, 1892-1903. C. 1880-1. V.P. 1890-1. P. 1902-4. *Referee*, 1882-9, 1892-1902. *Bldg. Com.* 1889-92. *Ho. Com.* 1892-8. *Cent. Com.* 1904-5. *Trans.* 2.

Elected

1887 WILLETT, EDGAR, M.D., 22, Queen Anne street, Cavendish square, W. *Trans.* 1.

1902 Willett, JOHN ABERNETHY, M.B., 26, Upper Wimpole street, Cavendish square, W.

1888 WILLIAMS, CAMPBELL, 18, Queen Anne street, W.

1866 Williams, CHARLES THEODORE, M.V.O., M.A., M.D., *Trustee for Debenture-holders;* Consulting Physician to the Hospital for Consumption and Diseases of the Chest, Brompton; 2, Upper Brook street, Grosvenor square, W. C. 1884-5. V.P. 1900-2. *Referee,* 1888-1900. *Lib. Com.* 1880-3. *Ho. Com.* 1900-2. *Sci. Com.* 1889-1902. *Trans.* 6.

1881 WILLIAMS, DAWSON, M.D., Physician to the East London Hospital for Children; 2, Agar street, Strand, W.C. C. 1905-6. *Trans.* 1.

1901 WILLIAMS, LEONARD, M.D., Physician to the French Hospital, 8, York street, Portman square, W.

1905 WILLIAMSON, HERBERT, M.B., B.C., 45, Weymouth street, Portland place, W.

1903 WILLIAMSON, OLIVER K., M.A., M.D., 50, Upper Berkeley street, W.

1887 WOOD, THOMAS OUTTERSON, M.D., Senior Physician to the West End Hospital for Nervous Diseases; 40, Margaret street, Cavendish square, W.

1892 WRIGHT, Sir ALMROTH EDWARD, M.D., Ch.B., 7, Lower Seymour street, W. *Referee.* 1906—. *Trans.* 2.

1890 WYNTER, WALTER ESSEX, M.D., Physician to the Middlesex Hospital; 27, Wimpole street, W.

Elected

1904 YOUNG, ROBERT ARTHUR, M.D., B.Sc., Assistant Physician to the Middlesex Hospital, and to the Brompton Hospital, 41, Wimpole street, W.

1906 YOUNG, SAMUEL LEGGATE OXFORD, M.B., B.C., St. Bartholomew's Hospital, E.C.

LIST OF RESIDENT FELLOWS

ARRANGED ACCORDING TO

DATE OF ELECTION

1849 C. H. F. Routh, M.D.
1854 Sir Alfred B. Garrod, M.D., F.R.S.
1856 Jonathan Hutchinson, F.R.S.
Timothy Holmes.
Alonzo H. Stocker, M.D.
1857 Sir Hermann Weber, M.D.
Henry Cooper Rose, M.D.
Henry Walter Kiallmark.
1859 Wm. Howship Dickinson, M.D.
Richard Barwell.
1860 William Ogle, M.D.
Thomas Bryant, M.Ch.
John Couper.
1861 William Spencer Watson, M.B.
1862 Edmund Symes Thompson, M.D.
Reginald Edward Thompson, M.D.
George Cowell.
1863 Sydney Ringer, M.D., F.R.S.
Sir Thomas Smith, Bart., K.C.V.O.
Arthur B. R. Myers.
William Sedgwick.
1864 Thomas William Nunn.
1865 James Edward Pollock, M.D.
George Fielding Blandford, M.D.
Sir Dyce Duckworth, M.D., LL.D.
Frederick W. Pavy, M.D., F.R.S.
John Langton.
1865 Alfred Willett.
Sir Alfred Cooper.
1866 Samuel Jones Gee, M.D.
Charles Theodore Williams, M.D., M.V.O.
Heywood Smith, M.D.
Sir William Selby Church, Bart., K.C.B., M.D.
1867 Sir R. Douglas Powell, Bart., K.C.V.O., M.D.
F. Howard Marsh.
1868 H. Charlton Bastian, M.D., F.R.S.
Sir W. H. Broadbent, Bart., K.C.V.O., M.D., F.R.S.
Thomas Buzzard, M.D.
Walter Butler Cheadle, M.D.
T. Henry Green, M.D.
George Eastes, M.B.
1869 Joseph Frank Payne, M.D.
Arthur E. Sansom, M.D.
Thomas Laurence Read.
1870 J. Warrington Haward.
Sir Edgcombe Venning.
Clement Godson, M.D.
Reginald Harrison.
1871 William Cayley, M.D.
Sir T. Lauder Brunton, M.D., F.R.S.

1871 J. Hughlings Jackson, M.D., F.R.S.
Philip Frank, M.D.
1872 Charles S. Tomes, M.A., F.R.S.
Sir William Bartlett Dalby, M.B.
1873 Frederick Taylor, M.D.
Norman Moore, M.D.
Sir William R. Gowers, M.D., F.R.S.
Jeremiah MacCarthy.
Henry T. Butlin.
1874 Alfred Lewis Galabin, M.D.
John Mitchell Bruce, M.D.
Henry Morris, M.A.
William Laidlaw Purves.
William Harrison Cripps.
Herbert William Page, M.C.
Frederic Durham, M.B.
William Robert Smith, M.D.
1875 Thomas Crawford Hayes, M.D.
Waren Tay.
Fletcher Beach, M.B.
1876 Sir Thomas Barlow, Bart., K.C.V.O., M.D.
Albert J. Venn, M.D.
1877 Sir Felix Semon, K.C.V.O., M.D.
Sidney Coupland, M.D.
Francis Warner, M.D.
William Ewart, M.D.
Alfred Pearce Gould, M.S.
Rickman J. Godlee, M.S.
Alban H. G. Doran.
George Ernest Herman, M.B.
Samuel West, M.D.
George Allan Heron, M.D.
Joseph A. Ormerod, M.D.
P. Henry Pye-Smith, M.D., F.R.S.
Sir William Henry Bennett, K.C.V.O.
1878 Sir Jas. Crichton-Browne, M.D., F.R.S.
Fred. T. Roberts, M.D.
Clinton T. Dent.
John H. Morgan, C.V.O.
Donald W. Charles Hood, C.V.O., M.D.
1879 Malcolm A. Morris.
A. E. Cumberbatch, M.B.
Edmund Owen.
Arthur E. J. Barker.
Sir Fredk. Treves, Bart., G.C.V.O., C.B.
Andrew Clark.
Francis Henry Champneys, M.D.
1879 William Watson Cheyne, C.B., F.R.S.
George Henry Savage, M.D.
Henry Hugh Clutton, M.B., M.C.
Frederic S. Eve.
William Henry Allchin, M.D., F.R.S.
1880 Robert Alex. Gibbons, M.D.
David Ferrier, M.D., F.R.S.
Edmund Distin Maddick.
Jas. John Macwhirter Dunbar, M.D.
William Appleton Meredith, M.B., C.M.
Malcolm Macdonald McHardy.
A. Boyce Barrow.
William Murrell, M.D.
George Ogilvie, M.B.
Charles Edward Beevor, M.D.
Thomas Colcott Fox, M.B.
George Henry Makins, C.B.
1881 Francis de Havilland Hall, M.D
Robert Wharry, M.D.
Richard Clement Lucas, B.S.
Sir Stephen Mackenzie, M.D
William Hale White, M.D.
Eustace Smith, M.D.
Percy Kidd, M.D.
Oswald A. Browne, M.D.
W. Bruce Clarke, M.B.
Dawson Williams, M.D.
George Lindsay Johnson, M.D.
Henry Edward Juler.
Jonathan F. C. H. Macready.
C. B. Lockwood.
1882 Ernest Clarke, M.D., B.S.
George Robertson Turner.
Howard Henry Tooth, C.M.G., M.D.
Charles R. B. Keetley.
Anthony A. Bowlby, C.M.G.
Amand J. McC. Routh, M.D.
Seymour J. Sharkey, M.D.
William Lang.
Henry Radcliffe Crocker, M.D.
Sir James Reid, Bart., G.C.V.O., K.C.B., M.D.
1883 Edwin Clifford Beale, M.A., M.B.
James Kingston Fowler, M.D.
James Frederic Goodhart, M.D.
Walter H. H. Jessop, M.B.
Walter Edmunds, M.C.
Sir Victor A. Horsley, F.R.S.
Dudley Wilmot Buxton, M.D.

1883 John James Pringle, M.B.
Henry Roxburgh Fuller, M.D.
Wilmot Parker Herringham, M.D.
Augustus Waller, M.D., F.R.S.
William Pasteur, M.D.
John Bland-Sutton.
Robert Marcus Gunn, M.B.
1884 George Newton Pitt, M.D.
Charles Stonham, C.M.G.
Stanley Boyd, B.S.
William Arbuthnot Lane, M.S.
Sidney Harris Cox Martin, M.D., F.R.S.
Thomas Wakley, jun.
F. Swinford Edwards.
James Johnston, M.D.
George Richard Turner Phillips.
Bilton Pollard.
1885 Alexander Haig, M.D.
Theodore Dyke Acland, M.D.
Frederick Walker Mott, M.D., F.R.S.
James Berry, B.S.
John Cahill, M.D.
John Poland.
A. C. Butler-Smythe.
Charles Alfred Ballance, M.S.
Walter S. A. Griffith, M.D.
John Edward Squire, C.B., M.D.
John D. Malcolm, M.B., C.M.
Phineas S. Abraham, M.D.
1886 Robert Maguire, M.D.
Harrington Sainsbury, M.D.
Cuthbert Hilton Golding-Bird, M.B.
Lauriston Elgie Shaw, M.D.
Charters James Symonds, M.S.
Robert Boxall, M.D.
Allan Ogier Ward, M.D.
Archibald Edward Garrod, M.D.
Stephen Paget.
William Radford Dakin, M.D.
Samuel Herbert Habershon, M.D.
Arthur H. N. Lewers, M.D.
1887 Walter George Spencer.
Thomas Outterson Wood, M.D.
Edgar William Willett, M.D.
Henry Lewis Jones, M.D.
Francis George Penrose, M.D.
Hugh Percy Dunn.
Frederic William Hewitt, M.V.O., M.D.
James Barry Ball, M.D.
1887 Gilbert Richardson, M.D.
D'Arcy Power, M.B.
John Gay.
James Calvert, M.D.
Percy J. F. Lush, M.B.
1888 Robert Henry Scanes Spicer, M.D.
Jonathan Hutchinson, jun.
Campbell Williams.
James Donelan, M.B., M.Ch.
John Anderson, M.D., C.I.E.
Laurie Asher Lawrence.
Arthur Pearson Luff, M.D., B.Sc.
Albert Carless, M.S.
Frederick C. Wallis, M.B., B.C.
Charles James Cullingworth, M.D.
Edmund Cautley, M.D., B.C.
H. Montague Murray, M.D.
Frank Joseph Wethered, M.D.
Edmund Wilkinson Roughton, B.S.
Frederick William Cock, M.D.
1889 Montagu Handfield-Jones, M.D.
David Henry Goodsall.
Raymond Johnson, M.B.
John Fletcher Little, M.B.
Henry Work Dodd.
George Lindsay Turnbull, M.D.
Sidney Phillips, M.D.
Henry Percy Dean, M.S.
William Hunter, M.D.
J. Inglis Parsons, M.D.
Bernard Pitts, M.C.
Robert Percy Smith, M.D., B.S.
Herbert R. Spencer, M.D., B.S.
Nestor Isidore Chas. Tirard, M.D.
Arthur William Mayo Robson.
1890 John Rose Bradford, M.D., F.R.S.
Charles D. B. Hale, M.D.
Sir Edwin Cooper Perry, M.D.
Morton Smale.
Frederick Willcocks, M.D.
William T. Holmes Spicer, M.B.
Henry Walter Syers, M.D.
Seymour Taylor, M.D.
W. G. O. White-Cooper, M.B.
William A. F. Bateman.
James Jackson Clarke, M.B.
Leonard G. Guthrie, M.D., B.Ch.
G. William Hill, M.D., B.Sc.
Edward Law, M.D., C.M.
Sir Patrick Manson, K.C.M.G., M.D., C.M., F.R.S.
Humphry D. Rolleston, M.D.
Walter Essex Wynter, M.D.
Edward Lawrie, M.B.

1891 Herbert P. Hawkins, M.D., B.Ch.
Cyril Ogle, M.A., M.D.
Arthur F. Voelcker, M.D., B.S.
Herbert T. Herring, M.B., B.S.
Ernest Muirhead Little.
Henry Charrington Martin, M.D.
Frederick William Andrewes, M.D.
Alfred Eddowes, M.D.
Herbert Morley Fletcher, M.D.
William Heaton Hamer, M.D.
William Bromfield Paterson.
Holburt Jacob Waring.
Frederic Parkes Weber, M.D.
F. E. Batten, M.D.
Thomas Jessopp Bokenham.
Norman Dalton, M.D.
Philip R. W. De Santi.
Percy W. Dove, M.B.
William J. Gow, M.D.
Paul Frank Moline, M.B.
Edward Percy Paton, M.S.
James Samuel Risien Russell, M.D.
Charles Percival White, M.B., B.C.
W. Page May, M.D.
Charles Ernest Baker, M.B.

1892 J. Dundas Grant, M.D.
R. J. Bliss Howard, M.D.
Thomas Horrocks Openshaw, C.M.G., M.S.
William Bezly Thorne, M.D.
W. H. Russell Forsbrook, M.D.
John Harold, M.B.
John Alfred Masters, M.D.
Gustave Schorstein, M.B.
Charles Sempill de Segundo, M.B.
John Tweedy.
J. S. Selwyn-Harvey, M.D.
StClair Thomson, M.D.
Henry Rayner, M.D.
H. Marmaduke Page.
Sir Almroth Edward Wright, M.D.

1893 James Taylor, M.D.
Howard Barrett.
Robert Cozens Bailey, M.S.
Henry Albert Caley, M.D.
Arthur Edward Giles, M.D., B.Sc.
D. Watkin Roberts, M.D.
Leonard A. Bidwell.
Frédéric F. Burghard, M.D., M.S.
John H. Drysdale, M.D.
William McAdam Eccles, M.S.
Vaughan Harley, M.D.
George Herschell, M.D.

1893 Arnold Lawson.
Guthrie Rankin, M.D.

1894 Richard Gill.
Joseph Sefton Sewill.
Thomas Vincent Dickinson, M.D.
Alexander Morison, M.D.
L. Hemington Pegler, M.D.
Herbt. Furnivall Waterhouse, C.M.
Percy Furnivall.
R. L. Langdon-Down, M.B., B.C.
Allan Macfadyen, M.D.
Ernst Michels, M.D.
Wm. Rivers Pollock, M.B., B.C.
Charles Slater, M.B.
G. H. Ward-Humphreys.

1895 Charles Arthur Parker.
Sydney Russell Wells, M.D.
Alfred Milne Gossage, M.B.
Robert Murray Leslie, M.D.
James Galloway, M.D.
David Bridge Lees, M.D.
Arthur G. Phear, M.D.
Edward Erskine Henderson, M.B.

1896 Joseph Lockhart Downes, M.B.
Edward Wilberforce Goodall, M.D.
James Ernest Lane.
George Alex. Sutherland, M.D.
Charles Buttar, M.D.
P. J. Freyer, M.D., M.Ch.
Percival Horton-Smith Hartley, M.V.O., M.D.
Thomas William Shore, M.D.
William Aldren Turner, M.D.
Charles Hubert Roberts, M.D.
Charles R. J. Atkin Swan, M.B.
James Kingston Barton.
J. Walter Carr, M.D.
John H. Dauber, M.A., M.B., B.Ch.
Alexander Grant Russell Foulerton.
L. Vernon Jones, B.A., M.D., B.Ch.
Henry Betham Robinson, M.S.
Horace George Turney, M.D.
Ernest Waggett, M.B., B.C.
Frederick Joseph Waldo, M.D.
Hugh Walsham, M.D.
William Edward Lee, M.D.

1897 Comyns Berkeley, M.B., B.C.
William Arthur Brailey, M.D.
James Cantlie, M.B.
Raymond H. Payne Crawfurd, M.D.
Francis Whittaker Tunnicliffe, M.D.
Arthur Whitfield, M.D.
Edward Stainer, M.B.

1897 A. P. Beddard, M.D.
G. F. Blacker, M.D.
W. S. Colman, M.D.
F. W. Goodbody, M.D.
R. Hutchison, M.D.
Harold Low.
Christopher Addison, M.D.
1898 L. A. Dunn, M.S.
E. Hurry Fenwick.
Sir A. Downing Fripp, C.B., M.V.O., M.S.
A. Corrie Keep, M.D.
A. C. Latham, M.D.
J. B. Lawford.
Sir John McFadyean.
H. Murray Ramsay.
J. F. H. Broadbent, M.D.
A. Stark Currie, M.D.
James Morrison, M.D.
Thomas J. Horder, M.D.
F. W. Robertson, M.D.
S. Jervois Aarons, M.D.
Willmott Evans, M.D., B.S., B.Sc.
John Murray.
W. Adams Frost.
C. R. C. Lyster.
Samuel Noble Bruce.
Cuthbert Chapman Gibbes, M.D.
H. Stringfellow Pendlebury, M.B.
William Turner, M.B.
Alexander Crombie, C.B., M.D.
Thomas Herbert Kellock, M.D.
1899 James Hugh Thursfield, M.D.
Lindley Marcroft Scott, M.D.
Louis Bathe Rawling, M.B.
Arthur J. Whiting, M.D.
Edward Farquhar Buzzard, M.D.
Greville Macdonald, M.D.
George Jones, M.B.
Herbert Campbell Thomson, M.D.
Thomas Morison Legge, M.D.
William John Ritchie Simpson, M.D.
Karl Fürth, M.D.
Purves Stewart, M.D.
George Edward Shuttleworth, M.D.
1900 Clive Riviere, M.D.
H. Roe Walker.
Richard Lake.
Percy Flemming, M.D., B.S.
John Shields Fairbairn, M.B.
Aslett Baldwin.
Charles Ryall.
William Hern.
1900 Cecil Huntington Leaf, M.B.
James Harry Sequeira, M.D.
Harold Batty Shaw, M.D.
Charles Herbert Thompson, M.D.
John William Thomson Walker, M.B.
Cecil Price-Jones, M.B.
1901 Sir Hugh Reeve Beevor, Bart., M.D.
J. Brunton Blaikie, M.D.
Herbert John Paterson, B.C.
George Henkell Drummond Robinson, M.D.
Elmore Wright Brewerton.
Thomas Rupert Hampden Bucknall, M.S., M.D.
William Douglas Harmer, M.B.
Henry George Plimmer.
Lionel Vernon Cargill.
T. N. Kelynack, M.D.
Leonard Williams, M.D.
T. J. P. Hartigan.
1902 J. P. Lockhart Mummery, B.A.
James Stansfield Collier, M.D., B.Sc.
Robert Salusbury Trevor, M.B., B.C.
Edward Arthur Saunders, M.B., B.Ch.
Ralph Vincent, M.D.
Herbert French, M.D.
Arthur Evans, M.S.
James Kerr, M.D., D.P.H.
Donald John Armour, M.B.
David Barty King, M.D., Ch.B.
Hector William Gavin Mackenzie, M.D.
John Abernethy Willett, M.B.
Thomas Crisp English, B.S.
Louis W. Sambon, M.D.
Joseph Blumfeld, M.D., B.C.
Ernest Beddoe Hulbert, M.D.
Harold L. Barnard, M.S.
Fallon Percy Wightwick, M.D.
1903 Edmund Ivens Spriggs, M.D.
Otto F. F. Grünbaum, M.B., B.C.
Samuel William Carruthers, M.D.
John Russell Ryan, M.D., B.Ch.
Oliver K. Williamson, M.D.
William Lawrence Ascherson, M.B., B.C.
Harold Burrows, M.B., B.S.
Leonard S. Dudgeon.
Evelyn Arthur Rich.
Fleming Mant Sandwith, M.D.

1903 Charles Gordon Watson.
Charles Ernest West.
Charles Bolton, M.D.
James Sherren.
1904 Harold Shuttleworth Barwell, M.B.
William Philip Sutcliffe Branson, M.D.
John Howell Evans.
Thomas Matheson Ness, M.B.
Henry Edmund Symes Thompson, M.D.
Joseph Arthur Arkwright, M.D.
Richard William Brimacombe, M.D.
H. Overton Hobson, M.D.
Thomas Wright Parkinson, M.D.
Robert Arthur Young, M.D., B.Sc.
Charles Joseph Harrison, M.D., B.S.
1905 William Carnegie Brown, M.D.
Percy John Cammidge, M.B.
Herbert Lightfoot Eason, M.D., M.S.
John Fawcett, M.D.
Herbert J. Scharlieb, C.M.G., M.D., B.S.
William Henry Battle.
1905 Herbert Sherwell Clogg, M.B., M.S.
William Foster Cross.
Thomas Jefferson Faulder.
George Ernest Gask.
William Sampson Handley, M.S.
Henry Head, M.D., F.R.S.
Frederick John McCann, M.D.
Harry Edwin Bruce Bruce-Porter, M.D.
Sydney Richard Scott.
Arthur Ralph Thompson.
Herbert Williamson, M.B., B.C.
William Cecil Bosanquet, M.D.
Francis Frederick Muecke, M.B., B.S.
A. W. Ormond.
John George Pardoe, M.B., C.M.
Frederick William Price, M.B.
1906 Thomas Guy Macaulay Hine, M.B., B.C.
Gerald S. Hughes, M.B., B.S.
Kenneth W. Goadby.
Cyril Alfred Rankin Nitch, M.S.
J. D. Rolleston, M.D.
Samuel Leggate Orford Young, M.B., B.C.

NON-RESIDENT FELLOWS

Elected

1877 **Abercrombie,** *John*, M.D., Consulting Physician to, and late Lecturer on Forensic Medicine at, Charing Cross Hospital; Augill Brough, Westmorland. C. 1896-8. *Referee*, 1898-1906. *Trans.* 2.

1866 *Allbutt, Thomas Clifford*, M.D., LL.D.Glasgow, F.R.S., Regius Professor of Physic, University of Cambridge; Consulting Physician to the Leeds General Infirmary; St. Rhadegund's, Cambridge. *Trans.* 4.

1903 *Amsden, Walter*, Lexden House, Seaford, Sussex.

1884 *Anderson, Alexander Richard*, Surgeon to the General Hospital, 5, East Circus Street, Nottingham. *Trans.* 1.

1905 *Anderson-Berry, David*, 23, Grosvenor crescent, St. Leonard's-on-Sea.

1880 *Appleton, Henry*, M.D., Charlbury, Oxford.

1896 *Bagshawe, Frederic*, M.D., J.P., 35, Warrior Square, St. Leonard's-on-Sea.

1902 *Bailey, William Henry*, M.D., Featherstone Hall, Southall, Middlesex.

1905 *Bain, William*, M.D., Straythorpe, York place, Harrogate.

1891 *Balgarnie, Wilfred*, M.B., The Dutch House, Hartley Wintney, Winchfield.

1896 *Ball, Sir Charles Bent*, M.D., Ch.M., 24, Merrion square North, Dublin.

Elected

1866 *Banks*, SIR JOHN, K.C.B., M.D., LL.D., D.Sc., Physician in Ordinary to H.M. the King in Ireland; Physician to Richmond, Whitworth, and Hardwicke Hospitals; Regius Professor of Physic in the University of Dublin; 45, Merrion square, Dublin.

1900 *Bardswell*, NOEL DEAN, M.D., King Edward the Seventh's Sanatorium, Midhurst, Sussex. *Trans.* 2.

1882 *Barker*, FREDERICK CHARLES, M.D., Surgeon-Major, Bombay Medical Service.

1881 *Barnes*, HENRY, M.D., LL.D., F.R.S. Ed., Consulting Physician to the Cumberland Infirmary; 6, Portland square, Carlisle.

1860 *Bealey*, ADAM, M.D., M.A., Felsham Lodge, Felsham road, St. Leonard's-on-Sea, Sussex.

1896 *Belben*, FRANK, M.A., M.B., Redlands, Knyveton road, Bournemouth.

1880 *Bennett*, ALEXANDER HUGHES, M.D. (Travelling.)

1889 *Bentley*, ARTHUR J. M., M.D., Mena House, Pyramids, Cairo, Egypt.

1872 *Beverley*, MICHAEL, M.D., Consulting Surgeon to the Norfolk and Norwich Hospital; 54, Prince of Wales road, Norwich.

1865 *Bickersteth*, EDWARD ROBERT, Consulting Surgeon to the Liverpool Royal Infirmary; 2, Rodney street, Liverpool. *Trans.* 1.

1892 *Bickersteth*, ROBERT ALEXANDER, M.A., M.B., Assistant Surgeon to the Liverpool Royal Infirmary; 10, Rodney street, Liverpool.

1901 *Bisshopp*, FRANCIS R. B., M.D., Parham House, Tunbridge Wells.

1900 *Blake*, WILLIAM HENRY, M.D.Brux., Bedford Lodge, West Wickham, Kent.

1865 *Blanchet*, HILARION, 35, Conillard street, Quebec, Canada.

Elected

1904 *Bossan, Emile,* M.D., 19, Boulevard Dubouchage, Nice, France.

1869 *Bourne, Walter,* M.D. (Travelling.)

1870 *Bowles, Robert Leamon,* M.D., Consulting Physician to the Folkestone Hospital and Physician to St. Andrew's Home, Folkestone; Prior's Mesne, Lydney, Gloucestershire. C. 1897-9. *Sci. Com.* 1896-1902. *Trans.* 3.

1874 *Bradshaw, A. F.,* C.B., Surgeon Major-General, 111, Banbury road, Oxford.

1899 *Bradshaw, Thomas Robert,* M.D., 51, Rodney street, Liverpool. *Trans.* 2.

1900 *Braine-Hartnell, James Christopher Reginald,* Napier House, Cheltenham.

1899 *Bremridge, Richard Harding,* Bangkok, Siam (c/o R. Bremridge, 17, Bloomsbury square, W.C.)

1876 *Bridges, Robert,* M.B., Manor House, Yattendon, Newbury, Berks.

1867 *Bridgwater, Thomas,* M.B., LL.D., Hooke Hall, Uckfield, Sussex.

1892 *Bronner, Adolph,* M.D., Senior Surgeon to Bradford Eye and Ear Hospital; Laryngologist to Bradford Royal Infirmary; 33, Manor row, Bradford.

1894 *Brook, William Henry Breffit,* M.D., B.S., 8, Eastgate, Lincoln.

1899 *Brooksbank, Hugh Lamplugh,* M.B., B.C., 5, College road, Windermere.

1888 *Browne, Henry Langley,* Moor House, West Bromwich.

1881 *Browne, John Walton,* M.D., Surgeon to the Belfast Royal Hospital; Surgeon to the Belfast Ophthalmic Hospital; 10, College square N., Belfast.

1864 *Buckle, Fleetwood,* M.D., Merton Lodge, Merton road, Southsea.

1904 *Butcher, William Deane,* Holywood, Cleveland road, Ealing, W.

Elected

1891 *Campbell, Henry Johnstone*, M.D., 36, Manningham lane, Bradford.

1900 *Carlton, T. B.*, Brinklow, near Coventry.

1888 *Carter, William Jeffreys Becher*, Aliwal North, Cape Colony.

1898 *Cave, Edward John*, M.D., Bath.

1884 *Chaffey, Wayland Charles*, M.D., Physician to the Royal Alexandra Hospital for Children; 18, Palmeira square, Hove, Sussex.

1885 *Chapman, Paul Morgan*, M.D., Physician to the Hereford General Infirmary, 1, St. John street, Hereford. *Trans.* 1.

1881 *Chavasse, Sir Thomas Frederick*, M.D., C.M., Senior Surgeon to the Birmingham General Hospital; 22, Temple row, Birmingham. *Trans.* 3.

1873 *Chisholm, Edwin*, M.D., 44, Rosslyn gardens, Darlinghurst, Sydney, New South Wales.

1890 *Childs, Christopher*, M.D., D.P.H., Knight of Grace of St. John, Boscarn, Looe, Cornwall.

1896 *Christopherson, John Brian*, M.D., B.C., late Assistant Demonstrator of Anatomy at St. Bartholomew's Hospital; late Surgeon to Seamen's Hospital, Albert Dock; c/o P.M.O., Egyptian Army, Cairo.

1892 *Clark, James Charles*, 10, Kimbolton road, Bedford.

1897 *Clark, W. Gladstone*, Buluwayo.

1888 *Clarke, Robert Henry*, M.B., Oakfield, Warlingham, Surrey.

1857 *Coates, Charles*, M.D., Consulting Physician to the Bath Royal United Hospital; 10, Circus, Bath.

1893 *Cole, Robert Henry*, M.D., Moorcroft, Hillingdon, Uxbridge.

1905 *Collinson, Harold*, 24, Park Square, Leeds.

1891 *Cook, Herbert George*, M.D., B.S., 22, Newport road, Cardiff.

Elected

1899 *Corrigan, William Jenkinson*, Cloughmore, Splott avenue, Cardiff.

1891 *Coumbe, John Batten*, M.D., 64, Caeran road, Newport, Mon.

1892 *Cross, Francis Richardson*, M.B., Ophthalmic Surgeon to the Bristol Royal Infirmary, and Surgeon to the Bristol Eye Hospital; Worcester House, Clifton, Bristol.

1874 *Davidson, Alexander*, M.D., Consulting Physician to the Liverpool Royal Infirmary; Emeritus Professor, University College, Liverpool; 2, Gambier terrace, Liverpool.

1878 **Davy**, *Richard*, Consulting Surgeon to the Westminster Hospital; Burstone House, Bow, North Devon. *Trans.* 1.

1882 *Dawson, Yelverton*, M.D., Heathlands, Southbourne-on-Sea, Hants.

1889 *Delépine, Sheridan*, B.Sc., M.B., C.M., Professor of Pathology, Owens College, Manchester. *Trans.* 1.

1899 *Douglas, Archibald Robert John*, M.B., B.S., Bellevue, Commissioner road, Rangoon, Burma.

1902 *Douty, E. H.*, M.D., La Madeleine, Cannes.

1867 *Drage, Charles*, M.D., Hatfield, Herts.

1898 *Dreschfeld, Julius*, Stanley House, Wilmslow road, Withington, Manchester.

1885 *Drummond, David*, M.D., 7, Saville place, Newcastle-on-Tyne.

1880 *Drury, Charles Dennis Hill*, M.D., Bondgate, Darlington.

1899 *Drury, Edward Guy Dru*, M.B., B.S., Grahamstown, South Africa.

1871 *Dukes, Clement*, M.D., B.S., Physician to Rugby School, and Senior Physician to the Hospital of St. Cross, Rugby; Sunnyside, Rugby, Warwickshire.

Elected

1867 *Dukes, Major Charles*, M.D., Clarence Villa, Torrs park, Ilfracombe, North Devon.

1889 *Duncan, John*, M.D., St. Petersburg, Russia.

1872 *Eager, Reginald*, M.D., Northwoods, near Bristol.

1887 *Easmon, John Farrell*, M.D., Assistant Colonial Surgeon, Gold Coast Colony, and Acting Chief Medical Officer of the Colony; Accra, Gold Coast, West Africa.

1906 *Edgecombe, Wilfrid*, M.D., Rodney house, Victoria avenue, Harrogate.

1898 Edkins, J. S., M.B., Brambles, Watford road, Northwood, Middlesex.

1887 *Elliott, John*, 24, Nicholas street, Chester.

1868 *Ellis, James*, M.D., The Sanatorium, Anaheim, Los Angeles County, California.

1889 *Elliston, William Alfred*, M.D., Stoke Hall, Ipswich.

1903 *Etlinger, Frederick Kincaid*, Cotswold Sanatorium, nr. Stroud, Gloucestershire.

1875 *Fagan, John*, Consulting Surgeon to the Belfast Royal Hospital; Graigavenue, Monasterevan, Queen's Co.

1897 *Fagge, Thomas Henry*, M.D., Villa de la Porte Rouge, Monte Carlo.

1869 *Fairbank, Frederick Roy ston*, M.D., Westcott, Dorking.

1872 *Fayrer, Sir Joseph*, Bart., K.C.S.I., LL.D., M.D., F.R.S. Surgeon-General; Physician Extraordinary to H.M. the King; late Physician to the Secretary of State for India in Council, and President of the Medical Board at the India Office; Kt. of Grace of St. John; Belfield, Woodlane, Falmouth. C. 1888. *Referee*, 1881-7.

1902 *Fennell, Charles Henry*, M.A., M.D., County Asylum, Hellingly, Sussex.

1872 *Fenwick, John C. J.*, M.D., Physician to the Durham County Hospital; Long Framlington, Morpeth.

1903 *Ferguson, George Bagot*, M.D., M.Ch., Cheltenham.

Elected

1864 *Folker, William Henry,* Consulting and late Hon. Surgeon to the North Staffordshire Infirmary; Bedford House, Hanley, Staffordshire.

1903 *Forbes, Norman Hay,* 6, South grove, Tunbridge Wells.

1896 *Forestier, Henri,* M.D., Aix-les-Bains, Savoie, France.

1892 *Foster, Michael George,* M.A., M.D., Villa San Giovanni, San Remo.

1884 *Franks, Sir Kendal,* M.D., c/o J. H. Franks, Esq., C.B., Dalriada, Blackrock, co. Dublin. *Trans.* 2.

1903 *Freeborn, John C. R.,* 38, Broad street, Oxford.

1876 *Furner, Willoughby,* M.D., Surgeon to the Sussex County Hospital; Brunswick square, Brighton.

1885 *Gamgee, Arthur,* M.D., LL.D., F.R.S., Emeritus Professor of Physiology in the Owens College, Victoria University, Manchester; Montreux, Switzerland.

1867 *Garland, Edward Charles,* Yeovil, Somerset.

1879 *Garstang, Thomas Walter Harropp,* Edge Mount, Altrincham.

1884 *Gibbes, Heneage,* M.D., Health Officer, Detroit, Michigan, U.S.A.

1897 *Gibson, George Alexander,* M.D., D.Sc., 3, Drumsheugh Gardens, Edinburgh.

1897 *Gilford, Hastings,* Norwood House, King's road, Reading. *Trans.* 2.

1893 *Gordon, William,* M.B., M.C., The Old Rectory, Goring-on-Thames, Oxon.

1890 *Gordon, William,* M.D., Barnfield Lodge, Exeter. *Trans.* 3.

1898 *Granville, Alexander,* The Sanitary Department, Ministry of the Interior, Cairo, Egypt.

1898 *Gray, J. A.,* M.B., Wadham Lodge, Uxbridge road, Ealing, W.

1889 *Greene, George Edward Joseph,* M.A., D.Sc., F.L.S., Monte Vista, Ferns, County Wexford.

Elected

1875 *Greenfield, William Smith*, M.D., Professor of Pathology and Clinical Medicine in the University of Edinburgh; 7, Heriot row, Edinburgh. *Sci. Com.* 1879. *Referee*, 1881.

1900 *Greer, William Jones*, 19, Gold Tops, Newport, Mon.

1889 *Griffiths, Joseph*, M.A., M.D., C.M., Reader in Surgery in the University of Cambridge; Surgeon to Addenbrooke's Hospital; 63, Trumpington street, Cambridge. *Pro.* 1.

1905 *Grünbaum, Albert Sidney Frankau*, M.D., The Drive, Roundhay, Leeds.

1889 *Gubb, Alfred S.*, M.D., Mustapha Supérieur, Algiers.

1904 *Hall, Arthur John*, M.A., M.B., B.C., 342, Glossop road, Sheffield.

1870 *Hamilton, Robert*, Consulting Surgeon to the Royal Southern Hospital, Liverpool; Magherabuoy, Portrush, co. Antrim, Ireland.

1864 Harley, *John*, M.D., F.L.S., Hon. Physician to St. Thomas's Hospital; Consulting Physician to the London Fever Hospital; Beeding, Pulborough, Sussex. S. 1875-7. C. 1879-80. V.P. 1895-7. *Referee*, 1871-4, 1882-95. *Sci. Com.* 1879. *Trans.* 10.

1880 *Harris, Vincent Dormer*, M.D., Consulting Physician to the City of London Hospital for Diseases of the Chest, Victoria Park; the Royal National Hospital for Consumption and Diseases of the Chest, Ventnor; the Metropolitan Dispensary and the Morley House Convalescent Institutions, St. Margaret's Bay and Sandgate, etc.; Woodrouffe House, Milford-on-Sea, near Lymington, Hants. *Referee*, 1899-1906.

1905 *Hathaway, Frank John*, M.D., Langholm, Osborne road, Windsor.

1890 *Haviland, Frank Papillon*, M.D., B.C., 57, Warrior square, St. Leonard's-on-Sea.

1885 *Hawkins, Francis Henry*, M.D., Physician to the Royal Berkshire Hospital; 73, London street, Reading. *Trans.* 1.

Elected

1900 *Hafford, Ernest James*, M.D., c/o The Agent, Claude's Ashanti Goldfields, Limited, Cape Coast Castle, Gold Coast.

1860 **Hayward**, *Henry Howard*, Consulting Surgeon Dentist to St. Mary's Hospital; 16, Blakesley avenue, Ealing, W. C. 1878-9.

1891 *Hayward, John Arthur*, M.D., 23, The Grange, Wimbledon Common, S.W. *Pro.* 1.

1899 *Hillier, A. P.*, M.D., Markyate Cell, near Dunstable, Beds.

1899 *Hind, Henry*, Blytheholm, Harrogate.

1900 *Hobhouse, Edmund*, M.D., 12, Second avenue, Brighton.

1894 *Holland, James Frank*, M.D., St. Moritz, Engadine, Switzerland.

1868 *Hollis, William Ainslie*, M.D., Physician to the Sussex County Hospital; 1, Palmeira avenue, Hove. *Trans.* 1.

1905 *Hort, E. C.*, San Remo, Italy.

1905 *Howard, Alan Campbell Palmer*, M.D., C.M., c/o Bank of Montreal, 22, Abchurch lane, Lombard street, E.C.

1881 *Howard, Henry*, M.B., Medical Officer of Health, Williamstown, Melbourne, Victoria.

1903 *Hulbert, Henry Louis Powell*, M.A., M.B., B.C., The Vicarage, Towcester, Northants.

1898 *Hulke, S. Backhouse*, Ivy House, Walmer, Kent.

1882 *Humphry, Laurence*, M.D., 3, Trinity street, Cambridge.

1883 *Jacobson, Walter Hamilton Acland*, M.Ch.Oxon., Consulting Surgeon to Guy's Hospital; Lordine Court, Ewhurst, Hawkhurst, Kent. C. 1902-3. *Referee*, 1895-1902. *Lib. Com.* 1896-1902. *Trans.* 2.

1883 *Jenkins, Edward Johnstone*, M.D., The Australian Club, Sydney, New South Wales.

1881 *Jennings, William Oscar*, M.D., 74, Avenue Marceau, Paris.

1876 *Jones, Leslie Hudson*, M.D., Limefield House, Cheetham hill, Manchester.

Elected

1875 ***Jones, Philip Sydney***, M.D., Consulting Surgeon to the Sydney Infirmary; 10, College street, Sydney, New South Wales. [Agents: Messrs. D. Jones & Co., Wool Exchange, Coleman Street, E.C.]

1865 ***Jordan, Furneaux***, Consulting Surgeon to the Queen's Hospital, Birmingham; 10, Ferndale, Teignmouth.

1890 ***Kerr, J. G. Douglas***, M.B., C.M., 6, The Circus, Bath.

1884 ***Keser, Jean Samuel***, M.D., Villa Colatel, Chemin Vinet, Lausanne, Switzerland.

1898 ***Klefstad-Sillonville, O.***, M.D., Aix-les-Bains, Savoie.

1889 ***Lancaster, Ernest le Cronier***, M.B., B.Ch., Assistant Physician to the Swansea Hospital; Hon. Physician to the Swansea and South Wales Institution for the Blind; Winchester House, Swansea, S. Wales.

1873 ***Larcher, O.***, M.D., Laureate of the Institute of France, of the Medical Faculty, and Academy of Paris, etc.; 97, Rue de Passy, Passy, Paris.

1862 ***Latham, Peter Wallwork***, M.D., Downing Professor of Medicine, Cambridge University, 1874–94; Senior Physician to Addenbrooke's Hospital, Cambridge; 17, Trumpington street, Cambridge.

1905 ***Lawson, David***, M.D., Nordrach-on-Dee, Banchory, Scotland. *Trans.* 2.

1880 ***Laycock, George Lockwood***, M.B., C.M., Melbourne, Victoria, Australia.

1892 ***Lazarus-Barlow, Walter Sydney***, M.D., Fernholme, Woodside Park, Finchley, N.W. *Sci. Com.* 1892—1902.

1886 ***Lediard, Henry Ambrose***, M.D., Surgeon to the Cumberland Infirmary; 35, Lowther street, Carlisle. *Trans.* 1.

1882 ***Ledwich, Edward l'Estrange***, Anatomist to the Royal College of Surgeons, Ireland; 30, Upper Fitzwilliam street, Dublin.

1905 ***Leedham-Green, Charles***, M.D., 31, Frederick road, Edgbaston, Birmingham.

1883 ***Leeson, John Rudd***, M.D., C.M., Clifden House, Twickenham, Middlesex.

Elected

1869 *Legg, John Wickham*, M.D. C. 1886. *Referee*, 1882-5. *Lib. Com.* 1878-85. *Trans.* 2.

1879 *Levy, Alfred G.*, M.D., (*temporary address*) 41, Devonshire street, Portland place, W. *Trans.* 1.

1905 *Lewis, Frank Benjamin*, Springfield House, 144, London road, St. Leonard's-on-Sea.

1898 *Lindsay, James*, M.A., M.D., 15, College square East, Belfast.

1889 *Little, James*, M.D., Physician to the Adelaide Hospital; 14, Stephen's Green North, Dublin.

1894 *Lowe, Thomas Pagan*, 16, The Circus, Bath.

1889 *MacAlister, Donald*, M.A., B.Sc., M.D., LL.D., D.C.L., President of the General Medical Council, Consulting Physician to Addenbrooke's Hospital; Linacre Lecturer and Tutor, St. John's College; University Lecturer in Medicine, St. John's College, Cambridge.

1887 *Macdonald, George Childs*, M.D. (Address uncommunicated.)

1876 *Mackey, Edward*, M.D., Physician to the Sussex County Hospital; Senior Physician to the Royal Alexandra Hospital for Sick Children; 1, Ventnor villas, Hove.

1854 *Mackinder, Draper*, M.D., 12, Park View Villas, Hove, Sussex.

1891 *Manby, Sir Alan Reeve*, M.V.O., M.D., Surgeon Apothecary to His Majesty's Household at Sandringham and to T.R.H. the Prince and Princess of Wales at Sandringham; East Rudham, Norfolk.

1894 *Marriott, Charles William*, M.D., Aubrey House, Bath road, Reading.

1892 *Martin, Christopher*, M.B., C.M., Surgeon to the Birmingham and Midland Hospital for Women; 35, George road, Edgbaston, Birmingham.

1899 *Martyn, Gilbert John King*, M.D., 8, Gay street, Bath.

1883 *Maudsley, Henry Carr*, M.D., 22, Collins street, Melbourne, Victoria.

1897 *Merry, William Joseph Collings*, M.D., B.Ch., 2, Chiswick place, Eastbourne.

Elected

1898 **Millard**, *William Joseph Kelson*, M.D., Trediden, Hewlett road, Cheltenham.

1895 **Mills-Roberts**, *Robert Herbert*, C.M.G., Hafod-ty, Llanberis, North Wales.

1904 **Mitchell**, *Thomas Walker*, M.B., C.M., Hadlow park, Tonbridge, Kent.

1896 **Moore**, *Sir John*, M.D., 40, Fitzwilliam square west, Dublin.

1904 **Morgan**, *William Pringle*, M.B., B.Ch., Rostrevor, Seaford, Sussex.

1891 **Morris**, *Graham*, Wallington, Surrey.

1894 **Morse**, *Thomas Herbert*, All Saints' Green, Norwich. *Trans.* 1.

1902 **Moynihan**, *Berkeley George Andrew*, M.S., 33, Park square, Leeds. *Trans.* 3.

1899 **Mundy**, *Herbert*, Florida road, Durban.

1892 **Myddelton-Gavey**, *E. Herbert*, 16, Broadwater Down, Tunbridge Wells.

1881 **Nall**, *Samuel*, M.B., Dryhurst Lodge, Disley, Stockport.

1889 **Napier**, *Francis Horatio*, M.B., Cape Town.

1870 **Neild**, *James Edward*, M.D., Lecturer on Forensic Medicine and Psychological Medicine in the University of Melbourne; 21, Spring street, Melbourne, Victoria.

1905 **Nettleship**, *Edward*, Nutcombe Hill, Hindhead, Haslemere.

1902 **Newland**, *Henry Simpson*, M.B., Ch.B., Adelaide, South Australia.

1895 **Newsholme**, *Arthur*, M.D., 11, Gloucester place, Brighton. *Trans.* 1.

1868 **Nicholls**, *James*, M.D., Trekenning House, St. Columb, Cornwall.

1905 **Norman**, *George*, M.B., B.S., "Brendon," Palmerston road, Buckhurst hill, Essex.

1847 **Nourse**, *William Edward Charles*, Norfolk Lodge, Thurloe road, Torquay.

Elected

1870 *Oldham, Charles Frederic*, India [Agents: Messrs. Grindlay and Co., 55, Parliament street].

1896 *Oliver, George*, M.D., Riversleigh, Farnham, Surrey; and Harrogate.

1883 *Oliver, Thomas*, M.A., M.D., Professor of Physiology, University of Durham; and Physician to the Newcastle-on-Tyne Infirmary; 7, Ellison place, Newcastle-on-Tyne. *Trans.* 2.

1890 *Ord, William Wallis*, M.D., The Hall, Salisbury.

1885 *Ormsby, Sir Lambert Hepenstal*, M.D., Lecturer on Clinical and Operative Surgery and Surgeon to the Meath Hospital and County Dublin Infirmary; Surgeon to the Children's Hospital, Dublin; 92, Merrion square West, Dublin.

1894 *Osborn, Samuel*, Knight of Grace of St. John; Maisonnette, Datchet, Bucks.

1904 *Osler, William*, M.D., Regius Professor of Medicine in the University of Oxford; 7, Norham gardens, Oxford.

1887 *Paget, Charles Edward*, Medical Officer of Health to the County Council of Northamptonshire; County Hall, Northampton.

1887 *Pardington, George Lucas*, M.D., Glynlin, Tunbridge Wells.

1873 *Parker, Robert William*, Consulting, late Senior, Surgeon to the East London Hospital for Children and to the German Hospital; Caryll Hurst, West Grinstead, Sussex. C. 1888-9, 1899-1901. S. 1895-8. *Bldg. Com.* 1889-92. *Referee*, 1891-5. *Lib. Com.* 1885-87, 1892-5, 1898-9. *Ho. Com.* 1892-5, 1899—1901. *Trans.* 4.

1885 *Parker, Rushton*, M.B., B.S., Professor of Surgery, University College, Liverpool (Victoria University); Surgeon to the Liverpool Royal Infirmary; 59, Rodney street, Liverpool.

1891 *Parkin, Alfred*, M.S., M.D., 24, Albion street, Hull. *Trans.* 1.

Elected

1903 *Pearson, S. Vere*, M.B., The Sanatorium, Mundesley, Norfolk.

1879 *Peel, Robert*, 120, Collins street East, Melbourne, Victoria.

1874 *Penhall, John Thomas*, The Cedars, Broadwas-on-Teme, Worcester.

1897 *Perram, Charles Herbert*, M.D., 55, Bromham Road, Bedford.

1879 *Pesikaka, Hormasji Dosabhai*, 43, Hornby road, Bombay.

1878 *Philipson, Sir George Hare*, M.D., D.C.L., Professor of Medicine in Durham University; Consulting Physician to the Newcastle-upon-Tyne Royal Infirmary; 7, Eldon square, Newcastle-upon-Tyne.

1898 *Phillips, L. C. Powell*, Kasr-el-Aini Hospital, Cairo.

1867 **Pick**, *Thomas Pickering*, Consulting Surgeon to St. George's Hospital; The Nook, Great Bookham, Surrey. C. 1884-5. V.-P. 1893-4. *Referee*, 1882-3, 1891-93. *Sci. Com.* 1870, 1889-1904. *Lib. Com.* 1879-81.

1891 *Pierce, Bedford*, M.D., The Retreat, York.

1841 **Pitman**, *Sir Henry Alfred*, M.D., Consulting Physician to St. George's Hospital; Cranbrook, Byculiah park, Enfield, N. L. 1851-3. C. 1861-2. T. 1863-8. V.P. 1870-1. *Referee*, 1849-50. *Lib. Com.* 1847.

1905 *Plummer, Harry Beddoes Wetherell*, 54, Birmingham road, West Bromwich.

1892 *Powell, Herbert Andrews*, M.A., M.D., M.Ch., Piccards Rough, Guildford.

1867 **Power**, *Henry*, Consulting Ophthalmic Surgeon to St. Bartholomew's Hospital; Bagdale Hall, Whitby. C. 1882-3. V.P. 1892-3. *Referee*, 1870-81, 1891-2. *Sci. Com.* 1870, 1889-1904. *Lib. Com.* 1872-8.

1897 *Quartey-Papafio, Benjamin William*, M.D., Accra, Gold Coast, West Africa.

Elected

1857 *VON RANKE, HENRY,* M.D., 3, Sophienstrasse, Munich.

1890 *RANSOM, WILLIAM BRAMWELL,* M.D., Physician to the Nottingham General Hospital; The Pavement, Nottingham. *Trans.* 1.

1854 *RANSOM, WILLIAM HENRY,* M.D., F.R.S., Consulting Physician to the Nottingham General Hospital; 17, Park Valley, Nottingham. *Trans.* 1.

1905 *RASHLEIGH, JOHN COSMO STUART,* M.D., Throwleigh, Okehampton, Devon.

1902 *RAW, NATHAN,* M.D., B.S., 66, Rodney street, Liverpool.

1884 *REID, THOMAS WHITEHEAD,* M.D., Surgeon to the Kent and Canterbury Hospital; St. George's House, Canterbury, Kent.

1901 *REISSMANN, CHARLES HENRY,* M.D., B.C., B.Sc., St. Peter's, College Green, Adelaide, South Australia.

1881 *RICE, GEORGE,* M.B., C.M., Sutton, Surrey.

1906 *RICKETT, GERALD RUSSELL,* M.B., B.C., Babraham, Cambridge.

1889 *RIVERS, W. H. RIVERS,* M.D., St. John's College, Cambridge.

1871 *Roberts, DAVID LLOYD,* M.D., F.R.S.E., Consulting Obstetric Physician to the Manchester Royal Infirmary; Physician to St. Mary's Hospital, and Lecturer on Clinical Obstetrics and Gynæcology at the Owens College, Manchester; 11, St. John street, Manchester.

1889 *ROBERTS, LESLIE,* M.D., 46, Rodney street, Liverpool.

1888 *Robinson, FREDERICK WILLIAM,* M.D., C.M., Huddersfield.

1885 *ROCKWOOD, WILLIAM GABRIEL,* M.D., Colombo, Ceylon.

1898 *Rogers, LEONARD,* I.M.S. [care of Messrs. Thomas Cook and Son, 9, Old Court House street, Calcutta.]. *Trans.* 3.

elected

1863 *Rowe, Thomas Smith*, M.D., Consulting Surgeon to the Royal Sea-Bathing Infirmary; Union crescent, Margate, Kent.

1891 *Ruffer, Marc Armand*, M.D., The Quarantine Board, Alexandria.

1867 *Sandford, Folliott James*, M.D., V.D., late Surgeon-Major, 2nd Batt. S.V.L.Infy., now Hon. Surgeon-Major; Surgeon to the Market Drayton Dispensary and Consulting Physician to the Market Drayton Cottage Hospital; Market Drayton, Shropshire.

1899 *Sandilands, John Edward*, M.D., Bonvile, Winchester.

1886 *Saundby, Robert*, M.D., LL.D., Physician to the General Hospital, and Consulting Physician to the Hospital for Women, and to the Eye Hospital, Birmingham; Professor of Medicine, Mason University College; 140B. Great Charles street, Birmingham.

1883 *Schäfer, Edward Albert*, LL.D., F.R.S., Professor of Physiology in the University of Edinburgh. C. 1899-1900. *Referee*, 1888-99. *Sci. Com.* 1889-1904. *Trans.* 1.

1861 *Scott, William*, M.D., Senior Physician to the Huddersfield Infirmary; Melbourne House, Huddersfield.

1897 *Semple, Edward*, M.D., Grove house, Fenstanton, Hunts.

1887 *Sidebotham, Edward John*, M.B., Erlesdene, Bowdon, Cheshire.

1857 *Siordet, James Lewis*, M.B., Villa Cabrolles, Mentone, Alpes Maritimes, France.

1891 *Smith, G. Cockburn*, M.D., 14, South road, Newton Abbot.

1902 *Smith, Harry Lyon*, M.D., Woodfield House, Uppingham, Rutland.

1886 *Smith, Howard Lyon*, Buckland House, Buckland Newton, Dorchester.

1894 *Smith, Robert Shingleton*, M.D., B.Sc., Senior Physician to the Bristol Royal Infirmary, and Emeritus Professor of Medicine, University College, Bristol, also Consulting Physician to the Bristol Dispensary; Deepholm, Clifton Park, Clifton, Bristol.

Elected

1894 *Smith, Thomas Rudolph*, M.B., B.C., Blytheholm, Stockton-on-Tees.

1873 Smith, *W. Johnson*, Consulting Surgeon to the Seamen's Hospital Society, Woodlands, Willingdon, Sussex.

1868 *Solly, Samuel Edwin*, Colorado Springs, Colorado, U.S.A.

1875 *Spitta, Edmund. Johnson*, 41, Ventnor Villas, Hove. C. 1903-5.

1896 *Stephens, John William Watson*, M.B., B.C., The Johnston Laboratory, The University, Liverpool.

1891 *Stevens, Surg.-Capt. Cecil Robert*, M.B., B.S., I.M.S., Eden Hospital, Calcutta.

1884 *Stewart, Edward*, M.D., Brook House, East Grinstead.

1906 *Stewart, Ian Struthers*, M.D., 15, Merchiston place, Edinburgh. *Trans.* 1.

1879 *Stirling, Edward Charles*, M.D., Senior Surgeon to the Adelaide Hospital; Lecturer on Physiology in the University of Adelaide, South Australia [care of Messrs. Elder and Co., 7, St. Helen's place].

1897 *Strangeways, T. S. P.*, Department of Medicine, The University, Cambridge.

1871 *Strong, Henry John*, M.D., J.P., Consulting Surgeon to the Croydon General Hospital; Colonnade House, The Steyne, Worthing.

1905 *Sutcliffe, William Greenwood*, 7, Dalby square, Margate.

1890 *Sympson, E. Mansel*, M.D., B.C., Surgeon to the Lincoln County Hospital; Deloraine Court, Lincoln.

1886 *Teale, Thomas Pridgin*, M.B., F.R.S., Consulting Surgeon to the Leeds General Infirmary; 38, Cookridge street, Leeds.

1898 *Thomas, J. Lynn*, C.B., Surgeon to the Cardiff Infirmary; Consulting Surgeon to the Hamadryad Hospital; Green Lawn, Pen-y-lan, Cardiff.

Elected

1891 *Thomson, John Roberts*, M.D., Monkchester, Bournemouth.

1904 *Thorburn, William*, M.B., B.S., 2, St. Peter's square, Manchester. *Trans.* 1.

1883 *Thursfield, Thomas William*, M.D., Physician to the Warneford and South Warwickshire General Hospital; Selwood, Beauchamp square, Leamington.

1880 *Tivy, William James*, 5, Victoria square, Clifton, Bristol.

1881 *Treves, William Knight*, Surgeon to the National Hospital for Scrofula; 31, Dalby square, Cliftonville, Margate.

1867 *Trotter, John William*, formerly Surgeon-Major, Coldstream Guards; 4, St. Peter's terrace, York.

1873 *Turner, George Brown*, M.D., Camden House, Hemel Hempsted, Herts.

1894 *Turner, Philip Dymock*, M.D., Sudbury, Ryde, Isle of Wight.

1891 *Tweed, Reginald*, M.D., Hembury Fort Cross, Honiton, Devon.

1881 *Tyson, William Joseph*, M.D., Senior Medical Officer of the Victoria Hospital, Folkestone; 10, Langhorne Gardens, Folkestone.

1900 *Uhthoff, John Caldwell*, M.D., Wavertree House, Hove, Brighton.

1868 *Walker, Robert*, Clovelly, Bideford.

1867 *Wallis, George*, Consulting Surgeon to Addenbrooke's Hospital; 6, Hills road, Cambridge.

1899 *Walters, Frederick Rufenacht*, M.D., Crooksbury Sanatorium, Farnham, Surrey.

1883 *Walters, James Hopkins*, Surgeon to the Royal Berkshire Hospital; 15, Friar street, Reading.

1899 *Warde, Wilfred Brougham*, M.D., 13, Lonsdale Gardens, Tunbridge Wells.

Elected

1861 *Waters, A. T. Houghton*, M.D., Consulting Physician to the Royal Infirmary; 69, Bedford street, Liverpool. *Trans.* 3.

1874 *Wells, Harry*, M.D., San Ysidro, Buenos Ayres, S. America.

1882 *Wharry, Charles John*, M.D., 14, Ewell road, Surbiton, Surrey.

1897 *White, Charles Powell*, Pathological Department, Victoria University, Manchester.

1881 *Whitehead, Walter*, F.R.S. Ed., Senior Surgeon to the Manchester Royal Infirmary, Manchester and Salford Lock Hospital, and Manchester and Salford Skin Hospital; Professor of Clinical Surgery, Owens College, Victoria University; 499, Oxford road, Manchester. *Trans.* 1.

1885 *Whitla, Sir William*, M.A., M.D., Professor of Materia Medica and Therapeutics, Queen's College, Belfast; Physician to, and Lecturer in Medicine at, the Belfast Royal Hospital; Consulting Physician to the Ulster Hospital for Women and Children; Consulting Physician to the Belfast Ophthalmic Hospital; 8, College square north, Belfast.

1870 *Wilkin, John F.*, M.D., Rose Ash Court, South Molton, Devon.

1883 *Willans, William Blundell*, Much Hadham, Herts.

1859 *Williams, Charles*, Senior Surgeon to the Norfolk and Norwich Hospital; 48, Prince of Wales road, Norwich.

1872 **Williams**, *Sir John*, Bart., K.C.V.O., M.D., Physician-Accoucheur to H.R.H. the Princess of Wales, Physician to H.R.H. the Princess Beatrice; Emeritus Professor of Obstetric Medicine, University College, London; Consulting Obstetric Physician to University College Hospital; Plâs Llanstephan, Carmarthenshire. C. 1891. *Referee*, 1878-90. *Lib. Com.* 1876-82.

Elected

1903 *Williamson, Richard Ernest*, M.B., C.M., Romagna House, Otley, Yorkshire.

1890 *Wills, William Alfred*, M.D., late Assistant Physician to the Westminster Hospital; late Senior Physician to the North-Eastern Hospital for Children; Rotherhill, Stedham, Midhurst.

1887 *Wilson, Arthur Hervey*, M.D., 504, Broadway, Boston, U.S.A.

1906 *Wilson, H. Douglas*, M.D., 3, Ripon road, Harrogate.

1889 *Wise, A. Tucker*, M.D., Montreux, Switzerland.

1885 *Wolfenden, Richard Norris*, M.D., Rougemont, Seaford, Sussex.

1905 *Wollaston, Alexander Frederick Richmond*, M.B., B.C., c/o Messrs. Smith, Mackenzie & Co., Mombasa, British East Africa.

1892 *Woodhead, German Sims*, M.D., Professor of Pathology in the University of Cambridge; 6, Scrope terrace, Cambridge.

1899 *Wynter, Andrew Ellis*, M.D., Oakfield House, Clifton, Bristol.

1905 *Young, Eric Ernest*, M.B., M.S., The Infirmary, Stoke-on-Trent.

SERVICE FELLOWS.

1903 BENTHAM, ROBERT, Royal Naval Hospital, Malta.

1905 HOLT, MAURICE PERCY, 67B, Shooter's Hill, Blackheath, S.E., and c/o Messrs. Holt, 3, Whitehall place, S.W.

1904 KELLIE, GEORGE JEROME, Sirur, Poonah District, c/o Messrs. H. S. King & Co., 9, Pall Mall, S.W.

1905 KILKELLY, CHARLES RANDOLPH, Osborne, Isle of Wight.

1903 LEICESTER, JOHN HOLDICH, M.D., B.S., c/o Messrs. Grindlay & Co., 11, Hastings street, Calcutta.

1904 *Pollock*, CHARLES EDWARD, Royal Naval Hospital, Malta [c/o Messrs. Holt & Co., 3, Whitehall Place, S.W.].

1903 RANKING, ROBERT MAURICE, M.B., B.C., Hanover House, Tunbridge Wells.

1903 SMITHSON, ARTHUR ERNEST, M.B., B.C., Barberton, Transvaal, c/o Sir C. R. McGrigor, Bart., & Co., 25, Charles Street, St. James's Square, S.W.

1905 SPENCER, CHARLES GEORGE, M.B., Kent Lodge, 52, The Avenue, Kew Gardens, S.W.

1903 TAYLOR, SIR WILLIAM, K.C.B., M.D., C.M., Queen Anne's Mansions, St. James's park, S.W.

Corrected to 31*st July*, 1906.

ANNUAL GENERAL MEETING

Held at 20, *Hanover Square, W., on Thursday, March* 1*st*, 1906, *at* 5 *o'clock.*

Sir R. Douglas Powell, Bart., President, in the chair.

G. Newton Pitt, M.D., Stephen Paget, } Hon. Secs.

Present—30 Fellows.

The President appointed Dr. Symes Thompson and Mr. Frederic Durham to act as scrutineers, and declared the ballot for officers and other members of Council open till 6 o'clock.

The President called upon the Honorary Secretary to read the

Report of Council.

The Council had so recently to congratulate the Fellows on the position the Society had attained at its Centenary, that it seems needless to repeat these congratulations in the Annual Report of the Council, further than to place officially on record the entire success with which the programme, sketched in last year's Report, was carried out. Full details of the proceedings may be found in the volume of the 'Transactions' lately issued to the Fellows. The Council would like, however, to refer in this Report to the

great honour that was paid to the Society (unique in the history of medical societies) by H.R.H. the Prince of Wales in accepting its Honorary Fellowship, and dining with the Fellows at the Centenary Banquet.

Since the last Annual Report was issued 37 Fellows have been elected, including 17 Resident, 16 Non-resident, and 3 Service. Against this the Society has to regret that by death or resignation the Roll of Fellows has been reduced by the loss of 2 Honorary Fellows and 20 Fellows. At the date of presenting this Report the Roll of Fellows includes 30 Honorary Fellows and 845 Fellows; making a total of 875.

The Council desire to remind Fellows that, in addition to the papers which have been put down for reading at ordinary meetings, the regulations of the Society provide for the exhibition and demonstration of interesting cases, new apparatus, and, in fact, of anything likely to be of interest to the Fellows. It is only necessary to arrange with the Honorary Secretaries beforehand, and if they are notified in time such demonstrations will be announced in the Journals along with the papers; but even up to the last moment suitable exhibits may be received, and a room will be set apart for them for half an hour before the ordinary meeting.

The suggestion made by the President in his Annual Address last year as to a Union of Medical Societies was promptly followed up by the Council, and, as far as possible, the various steps taken are set forth in the reports, included under this heading in the last volume of 'Transactions.'

It may be mentioned here that the Council have under consideration the advisability of applying for a supplemental Charter, to amend and extend the provisions of the existing Charter.

During the year the Secretary called attention to the large back stock of 'Transactions,' of which, long since, all active sale had stopped, and which were costing the Society a considerable amount for storage. As no complete sets existed, the Council gave authority for the

disposal of these volumes, first inviting the Fellows to purchase whatever volumes they might want at 2*s*. each. A few Fellows have availed themselves of this privilege, but a considerable stock remains, which will be disposed of this summer.

As some dissatisfaction with the method of conducting the ballot for new Fellows had been expressed, the Council have decided, tentatively, to adopt the following plan. At the next Ballot the scrutineers will be appointed beforehand, and will be in attendance a quarter of an hour before the ordinary meeting begins, and the ballot will close at 8.45, before the reading of papers. It is hoped that this will enable a larger number of Fellows to record their votes without disturbance of the ordinary business of the meeting.

Last spring, during the visit of our French *confrères*, the Council invited them to consider themselves at home in the Society's house, and, during the week, special rooms were set apart for their reception; periodicals, writing accommodation, light refreshments, and cigarettes being provided for their use. This courtesy seemed to be greatly appreciated, and a warm telegram of thanks was received from the party as it left our shores.

The Council has to record with great satisfaction two legacies that have been received during the past year, one of £500 from Mr. F. J. Gant, our late Fellow, and one of £100 from his wife, Mrs. F. J. Gant.

It would perhaps be invidious to call special attention to any of the papers read during the past session, but the Society may be congratulated on the success of the Discussion on Appendicitis. This was very largely attended, and was continued over three meetings. The report appears in the volume of 'Transactions,' and will, in a few days, be published separately.

Although not technically a "special discussion," the discussion on the Opsonic Index in relation to the Administration of Tuberculin (T. R.) might also be referred to. The subject was first presented to the Society in a paper

by Drs. Lawson and Stewart, but, in order that it might be dealt with completely, the Hon. Secretaries arranged that it should be introduced by Professor Wright, upon whose original work it was founded, and also for two supplementary papers, detailing their experience of Dr. Wright's method, by Dr. Bulloch and Mr. Pardoe. The discussion on these papers was carried over two meetings.

The Honorary Treasurers report:

"The past year has been of an exceptional character. The visit of our professional brethren from France and the celebration of the Centenary of the Society have caused an unusual demand upon our funds, and the year's income has been exceeded by a sum of £185 2*s.* 11*d.*

"The income and expenditure account shows that this excess of expenditure over income is due to the Centenary. The ordinary working of the Society, including the expenses connected with the reception of our friends from France, was met by the year's income, and left a balance of £205 16*s.* 2*d.*, notwithstanding that the rental income of the Society was diminished to the extent of £436 by the expiration of the Berners Street lease.

"The Society has received during the year two legacies, one of £100, from Mrs. Gant, and by the liberality of Mr. Gant an additional sum of £500, to which certain conditions are attached.

"Notwithstanding the extraordinary expenditure of the year the unusually large sum of £751 7*s.* 6*d.* was devoted to the Library in addition to £62 spent on the new catalogue.

"The debenture debt has been reduced by £300 since the previous statement.

"The Honorary Treasurers view with great satis-

faction the considerable increase which has taken place in the number of the Annual Subscriptions."

The Honorary Librarians report:

"Since the issue of the last report the cabinet containing the new card catalogue has been fitted up in the Library. The re-numbering of the books has now been accomplished, and the transference of the accession numbers to the cards will shortly be completed.

"A subject index of books and pamphlets added to the Library during the year 1905 has been made on cards, and will be kept up to date.

"The number of books and pamphlets added to the Library during the year 1905 was 737, of which 368 were presented by Fellows and other donors.

"The number of books borrowed by Fellows was 3512, and the number of Fellows and others visiting the Library during the year amounted to 3843.

"From Lewis's Library 311 volumes were borrowed during the year.

"A selection, from our own shelves, of nearly 150 works published in and about 1805 was included in the Centenary Exhibition, and to these was added a collection of upwards of 70 books and pamphlets on vaccination printed and published between the years 1801—1806, kindly lent by the Royal College of Physicians.

"The general work of the Library has progressed satisfactorily."

The House Committee reports:

"During the past year the whole of the Society's premises were surveyed by Mr. John Belcher,

A.R.A., who prepared a specification for necessary repairs. Estimates for these were procured from three firms of high standing, and the work was entrusted to Messrs. Simpson and Sons, who gave the lowest estimate, and were highly recommended by Mr. Belcher. Opportunity was taken at the same time to re-paint the whole of the exterior, as well as to do a considerable amount of interior painting, and the House Committee have satisfaction in reporting that the premises are now in thorough repair and in excellent condition.

"Rooms let on lease to tenants have not been dealt with by the Committee, but as these rooms are all let to tenants who are responsible under their leases for their good condition, the Committee do not feel it necessary, or desirable, to interfere with them.

"In view of the possibility of increased accommodation being required if the proposed scheme of amalgamation should be carried into effect, the Secretary was authorised to take steps to settle how far the Society could go in raising its premises behind. After some negotiation with the City authorities, who are the owners of the leasehold portion of our premises, and with the adjoining neighbours, this point was satisfactorily settled, and to test it a light screen was erected on the roof of the library to represent the sky-line of proposed additions. This was slightly modified to meet the objections of a neighbour, and your Committee are now in a position to report that very considerable additions can be made to the back premises and additional rooms built over the Library whenever the Council desires to put the work in hand.

"As the North Room has for some time been very largely used for meetings, it was found that it

was insufficiently ventilated for this purpose, and occasionally complaints were made by tenants. Your Committee invited Dr. Glover Lyon to examine the room, and to advise as to the best means of ventilating it, and on his advice the work was carried out by Messrs. Shone and Ault with entire success. The room is now ventilated by means of two powerful electric fans, one of which provides a constant supply of fresh air, tempered in winter by means of radiators, and the other extracts the vitiated air. That the result is satisfactory is proved by the fact that the Council of the Balneological and Climatological Society, the tenant which had most cause to complain, passed a hearty vote of thanks for the improved ventilation."

The Society is deeply indebted to Mr. MacAlister for his unremitting labours in connection with the Centenary Celebration; and his most efficient supervision of all their arrangements.

RICHARD DOUGLAS POWELL, *President.*
G. NEWTON PITT, } *Hon. Secretaries.*
STEPHEN PAGET, }

The PRESIDENT asked the Hon. Treasurer to read the audited statement of accounts.

Sir WM. CHURCH (Hon. Treasurer).—Those who have the accounts in their hands will see that the figures differ very little from those of last year. I think that it must be satisfactory to the Society that, notwithstanding that it was an unusual year and an unusually expensive one, yet the income of the Society was equal to meeting all the ordinary expenses of the Society, including those connected with the visit of our French friends, and still there is a balance of £205 16*s.* 2*d.* in hand. That I am

afraid is not an available balance because you will see the extraordinary expenditure of the year amounted to £391. Therefore, of course, taking the ordinary expenditure with the extraordinary we are slightly in debt for the past year. I should like to call attention also to one or two points in the balance-sheet of our assets and liabilities. One figure there is which perhaps Fellows will not understand. If they look at the liabilities they will see on that side that against the balance of £29,868 3*s*. 8*d*. there is an amount written off of £515 15*s*. 9*d*. That perhaps needs explanation. We really thought, sir, it was wise to write off as a complete loss the whole of the balance of expense with regard to Climate and Baths Reports and also the Report of the Suspended Animation Committee, and that together with £60 which is written off the value of the Epidiascope amounts to £515 15*s*. 9*d*. I do not think I have anything else to tell Fellows unless anyone wishes for information on any of the figures, when either I or Mr. Haward will be very glad to give it.

Dr. C. T. Williams.—I would like to ask the Treasurer one or two questions. I see he has mentioned 'Climates and Baths.' From what he told us we gather that the amount has been written off. I notice that very few copies have been sold—£4 3*s*. 4*d*. is put down. I should like to know whether any means are taken to increase the sale of the book. It is a volume that I personally have some interest in. I contributed to one, and I edited the second volume. There are many Fellows of this Society and some people outside who have spoken to me about it, and they consider it a very valuable piece of work, particularly the first volume. But unless it is advertised I do not see how it can sell. Those medical men who want information about the climates of Great Britain and Ireland and the Baths, should be very glad to possess the books. A great many do not know of its existence. I have shown the volumes to several people, who have purchased them and find them very

useful. I should say that a little advertising would help the sale very much. I should also like to know whether there is in contemplation the provision of a Sinking Fund beyond what we are doing as regards our debentures. I know that the past year has been a very expensive one, and we must not expect our Treasurers to give more than £300 which has already been expended on the liquidation of the debt, but I should like to see that debt going down a lot more. Sir William Church has told us lots of times that it ought to be paid by the next generation and not by this, or something to that effect, but I cannot help thinking that as this generation incurred the debt of £33,000 odd they ought to do a little more towards liquidating it. I sincerely hope next year when we have less expenses (this Centenary has been a very expensive one) something more can be done. It seems to me that if we are spending £300 a year to liquidate a debt of £33,000 this is slow business. Moreover, we get very large rents, and these ought to go in great part towards the liquidation of the debt, but we are spending them in improving the Society. It does not seem to me quite the right thing. I know it is an old story of mine, but I still feel it very strongly, and I believe, certainly two of my co-trustees who are bond-holders think, that the liquidation ought to be proceeded with much more rapidly. Surely £300 a year as a Sinking Fund for £33,000 is a very slow process. Otherwise I have nothing to say. Everything is very admirably put forward, and I am very happy in seconding the adoption of the Report.

Mr. Goodsall.—The amount being written off the debentures is not sufficient. To pay off your debt within thirty years (I believe the debentures have to run for thirty-two) you will require £659 invested at 3 per cent. compound interest; so that paying off £1500 in six or seven years is not sufficient to liquidate that debt. I had a conversation with Mr. Belcher, your architect, and

he tells me that this building will require pulling down and rebuilding in about fifty years;* so that you want, after you have paid off the debentures, to put by £600 a year at least in order to provide funds for that. Then another matter I should like to refer to relates to 'Climates and Baths.' The balances carried forward at the end of the year are spent on things which do not appear, so far as I can see, in the accounts. Now, it seems to me that in properly kept accounts the balances carried forward at the end of each year should be shown either at the bank or it should be shown how they have been spent. Now, 'Climate and Baths' stood in your books on the 31st December, 1899, at £138 10*s.*; 1900, £137 19*s.* 6*d.*; 1901, £128 0*s.* 7*d.*; 1902 they were increased to £339 1*s.* 6*d.*, and out of that increase only £43 6*s.* 9*d.* was taken from the income of that year. Then for 1903 it stood at £320 15*s.* 9*d.*, in 1904 at the same amount, and in 1905 you write it off as a bad investment. What I think is that the accounts should be improved by reverting to what was in force in 1899, viz. a cash statement showing the cash balances the Society hold.

Sir WILLIAM CHURCH.—I am not prepared, sir, to go into the question that Mr. Goodsall has raised. I am not an accountant, and I cannot say what force there is in what Mr. Goodsall has advanced. We used formerly to publish a cash statement. It was discontinued because it was impossible to get the Fellows of the Society at the Annual Meeting to understand the difference between the cash statement and the Assets and Liabilities Account of the Society; and by the advice of the accountants, who I believe have properly kept our accounts now for a great number of years, it was thought better that the cash statement should not be submitted at this meeting. Such a cash statement can very easily be drawn out at any

* *It should be noted that Mr. Belcher denies this statement, and affirms that in his opinion the building is perfectly sound.*

time, and I have no doubt that if Mr. Goodsall wishes it and the Council direct it, I mean if the Council follow his advice, it can easily be made out even for the past year; at all events, it can easily be done in future years. Then, with regard to paying off the debentures, the Treasurers only do that which the Council direct them. The Treasurers are only your servants, and if the Council direct us to pay off so much a year we shall have to do it. Since I have had the honour of being a Treasurer there was one Council which directed us to pay off as much as we could. The Society at that time had a large floating debt, and I discouraged then the idea of paying off debentures until we had paid off our floating debt. That debt has for some years, I am happy to say, been extinguished, and it is in the hands of the Council to direct us how many debentures we are to endeavour to pay off each year. I would remind you that you should look upon your debenture interest as your rent. We are here in freehold property. Look at your debenture interest as the rent which you pay for it. Not only do you have the satisfaction of living in and enjoying the property yourselves, but it is a property which you see is bringing you in over £2690 a year. I do not see why the working of the Society should be at all crippled in a great hurry to pay off that debt. The debt, of course, will not be extinguished in the thirty years in which Dr. Williams and Mr. Goodsall are anxious it should be; but with property of the nature you hold, to me it is self-evident that at the end of the thirty years you will have no difficulty in raising a fresh mortgage to pay off the balance of the old one.

With regard to a Sinking Fund, you know, sir, although the Society does not, that the Treasurers have a proposal on this point, which, owing to the amount of other business that has been before the Council, they have not had the opportunity of laying before them; but both Mr. Haward and I are strongly of opinion that there should be a Sinking Fund, and we have arranged a method. I

hope you are not going to devote too large a sum to that Sinking Fund. Then with regard to 'Climates and Baths,' it was not an "investment," but a scientific report. We had to pay for it, and the accounts which Mr. Goodsall quotes were accurate for the years that they were given. With regard to advertising the 'Climates and Baths,' Fellows have forgotten that they have all received notice (I think more than once) that these volumes can be had on exceptionally easy terms if they like to write and ask for them. We did not think of advertising largely in the public press, but we have advertised in the medical press. We have also taken the trouble to write to the mayors and corporations of all the towns which are connected with watering places and baths, and told them if they liked to remit us the necessary amount for the volumes we would be happy to send them. The Treasurers, therefore, have taken some steps to try and get rid of the books. The Society entered into the business, knowing it would be an unremunerative expense for the sake of science, and not with any idea of a commercial "investment" as seems to be supposed by Mr. Goodsall. The subject is of great importance, and without this action on the part of this Society those two volumes, which are undoubtedly extremely valuable, would never have been in existence. The same remark applies to our 'Report on Resuscitation from Drowning.' Therefore, so far from the Society being to blame for an unprofitable investment, I believe that from a scientific point of view it has been very profitable to the Society.

Another thing that has often been said in this room is that we unduly estimate the market value of the Library, and that the bulk of the books added every year are not worth very much. We did consider that the books which were presented to us and bought were worth something, and one half of the value of the ones that were bought were credited to the Library, but that has ceased for a good many years. For the last five years nothing has been added to our assets account for the books that

were purchased or for those presented to the Library. Mr. Mac Alister tells me that you can value the books presented yearly at about half the value of the books purchased, excluding periodicals. But in spite of this during the last year we have put down the whole of the expenditure on books and written it off. Put it down to a depreciation account if you like to so regard it; in that case the value of bought and presented books may be considered a set-off against the depreciation of the old books.

Sir R. Douglas Powell.—I have nothing to add to the explanation given by the Honorary Treasurer and the remarks with regard to the balance-sheet. I would like to point out, however, that the Society is only pledged to the payment of £100 a year off the debenture debt, and I suppose the trustees of the debenture holders, who, presumably, were zealous for the debenture holders' interests, were responsible for that suggestion. As a matter of fact, this year we paid off £300, so I think, considering that it has been rather a hard year, we seem to have done our duty fairly well. If no other Fellow wishes to make any remarks, I will put it to the meeting:

"That the Report of the Council, together with the Treasurers' statement of accounts, be adopted."

Carried.

The President then read his Address (see p. cxi).

Sir Edgcombe Venning.—I have the honour to propose a resolution, which I am sure will be received with great pleasure by everyone present. It is:

"That the best thanks of this Society be given to the President, Sir Richard Douglas Powell, for his valuable services during his term of office, and that he be requested to allow the Address just delivered to be printed in the 'Transactions.'"

Mr. A. B. R. MYERS.—I rise, sir, with very great pleasure to second this proposal. This last year has been one of immense interest, and the work attaching to the office of this year must have been doubly great. The Centenary itself must have been a source of very great labour to you, and the success of it was unquestionable; also the visit of our French *confrères*. All these matters must have taken up an immense amount of your time. This meeting is a momentous one, because it may be the last at which one can propose and second a vote of thanks to the President of the Royal Medical and Chirurgical Society. One feels almost sad, therefore, at this perhaps dying meeting of the Society, and possibly next year the vote of thanks will be proposed to the chairman of a section of an unnamed Society.

Carried.

The PRESIDENT.—I am deeply grateful to Sir Edgcombe Venning and Mr. Myers and the Fellows present for the very kind manner in which this proposal has been made and accepted. I can only say that I have been so well supported by my colleagues in the past year that I have found my labours infinitely less than I expected to find them. I sympathise with Mr. Myers in his reference to the ending of the present Society. We must drop a few tears over the old Society when it goes. We only hope that upon its ashes will be built an increasingly useful institution.

Dr. C. T. WILLIAMS moved:

> "That the best thanks of the Society be given to the retiring Vice-Presidents, Sir William Broadbent, Mr. Butlin, and Mr. Pearce Gould, for their valuable services during their respective terms of office."

Seconded by Dr. HOWARD TOOTH, and carried.

Dr. F. ROBERTS.—Mr. President and Gentlemen,—The motion that I have to submit to you I am sure will be accepted most cordially:

"That the best thanks of the Society be given to the retiring Honorary Treasurer, Mr. Warrington Haward, for his most valuable services in that office for a period of nearly eleven years."

We have listened to some criticisms about the Treasurers' report this evening, which show that the position is no sinecure, and that it involves a good deal of work and responsibility, and, on that account more especially, we owe a great debt of gratitude to Mr. Haward. But I also observe that he has been actively and almost continuously in office since 1885, first as Member of Council, then as Secretary, and then as Treasurer for eleven years. I think we are showing our appreciation of his services today by electing him President of the Society, a position which, I am sure, he will fill as worthily as he has filled other positions in the past. I have the very greatest pleasure in proposing this vote of thanks.

Seconded by Mr. GOODSALL, and carried.

Sir THOMAS SMITH.—I have great pleasure in acceding to the request that I should move a vote of thanks to the Honorary Secretary, viz.:

"That the best thanks of the Society be given to the retiring Honorary Secretary, Dr. G. Newton Pitt, for his valuable services during his term of office, and particularly for his special services during the Centenary."

The Society is very, very greatly indebted to Dr. Newton Pitt for his services, and our obligations cannot be discharged by a mere vote of thanks. I can only say that his service has been exceptionally long, and exceptionally arduous, particularly with regard to the Centenary and the Committees being held now with a view to amalgamation. I need not say, sir, we shall never get a more urbane, genial, or indefatigable Secretary than the gentleman who is just retiring.

Seconded by Dr. BUZZARD.

The PRESIDENT.—I would remind the Society that this is the fourth year that Dr. Newton Pitt has served the Society as Honorary Secretary. We felt that during the Centenary year his experience of the Society and its affairs would be of great value to us, and I am quite sure that we did not make any mistake about that. I have much pleasure in putting this resolution to the Society.

Carried.

Dr. OUTTERSON WOOD.—Mr. President and Fellows, I rise to propose a vote of thanks to the Members of the Council of this Society. The duties of the Members of the Council are many and onerous, and much of the success of a large and important Society such as this is depends upon the careful attention to detail given by Members of Council in connection with the many subjects of varied interest that come before them. The important proceedings of the last year connected with the Centenary and the visit of our French *confrères* and the question of the amalgamation have all added to the labours of the Council. I beg leave to propose:

> "That the best thanks of the Society be given to the retiring Members of the Council for their valuable services during their respective terms of office."

Seconded by Dr. MURRELL.

The PRESIDENT.—I have much pleasure in putting this vote to the Fellows.

Carried.

The PRESIDENT called upon the scrutineers to announce the result of the ballot, which was as follows:

President.—J. Warrington Haward.

Vice-Presidents.—Thomas Buzzard, M.D.; Joseph Frank Payne, M.D.; Herbert William Page, M.C.; W. Harrison Cripps.

Hon. Treasurers.—Sir William Selby Church, Bart., K.C.B., M.D.; Alfred Pearce Gould, M.S.

Hon. Secretaries.—Howard Henry Tooth, C.M.G., M.D.; Stephen Paget.

Hon. Librarians.—Norman Moore, M.D.; Rickman John Godlee, M.S.

Members of Council.—Theodore Dyke Acland, M.D.; Edwin Clifford Beale, M.B.; Sidney H. C. Martin, M.D., F.R.S.; George Ogilvie, M.B.; William Pasteur, M.D.; John Bland-Sutton; Andrew Clark; Clinton Thomas Dent; Walter H. H. Jessop, M.B.; Henry Roxburgh Fuller, M.D.

The PRESIDENT.—I have now the honour to ask the President elect, Mr. Warrington Haward, to come forward and take my place.

The PRESIDENT elect was installed by the retiring President and presented with the Badge and Master-key. Taking the chair he briefly addressed the meeting:—I feel very deeply indebted for the great honour which you have conferred upon me by electing me your President, an honour of which I desire to express my keen appreciation, and for which I desire most sincerely to thank you. I should like also to thank Dr. Roberts for the kind way in which he proposed the vote of thanks to me on my retiring from the Treasurership, and for the kind way in which it was accepted by the Society. Having had the pleasure of acting with Sir William Church as my colleague I need hardly say that the duties of Treasurer were very much lightened in consequence of my having the advantage of his great experience. Although our labours were certainly somewhat arduous, yet I hope that, in spite of the criticisms which have been made the finances of the Society have not suffered during our Treasurership. Gentlemen, the gratification which I feel at this signal mark of

your confidence in electing me President is greatly mitigated by the remembrance of the responsibilities which attach to the office. And when I think of the distinguished men who have preceded me, and especially of the way in which you, Sir Richard, have conducted the affairs of the Society during the two eventful years of your Presidency, I cannot but feel acutely conscious of my own deficiencies. However, I know that I shall have the willing help of the officers of the Society, and I will venture to claim this, that since the time when, a great many years ago, I was your Secretary, and more recently as Treasurer and in other capacities, I have at least had some opportunity of becoming familiar with the work of the Society, and I would also claim this, that no one can more earnestly desire to promote its welfare and prosperity, to which you may be assured I will do my best.

(A) Income and Expenditure Account for the Year ending 31st December, 1905

Expenditure	£	s.	d.	£	s.	d.
Rent, Rates, Taxes, and Insurance ...	187	10	6			
Salaries of Staff and Accountant ...	706	2	10			
House Servants, Cleaners, etc. ...	363	4	4			
Lighting, Warming, and Cleaning ...	261	14	4			
Printing, Stationery, Stamps and Telegrams	282	15	11			
Meeting Expenses	47	15	10			
Miscellaneous Disbursements ...	95	13	3			
				1944	17	0
Repairs, Alterations, etc. ...				195	19	3
Depreciation of Fixtures, Fittings, etc.				76	9	8
Library Purchases and Expenses ...	751	7	6			
Work on New Catalogue ...	62	0	0			
				813	7	6
Interest on Debentures				1005	9	0
'Transactions'				367	0	4
Audit Fee				10	10	0
Architect's Fees				2	2	0
Law Costs				9	9	0
Telephone				18	2	3
Lift Charges				35	9	8
Balance, being excess of Income over Expenditure during the year ...				205	16	2
				£4684	11	10

Extraordinary Expenditure.

(1) *Centenary, Stamps, Circulars, etc.*	14	9	11			
Centenary Volume ...	186	17	2			
Honorarium to Editors of Centenary Volume ...	105	0	0			
Honorarium to Secretary ...	52	10	0			
Hon. Fellowship (Centenary) Diplomas	21	13	0			
				380	10	1
(2) *Contribution to Expenses of Amalgamation Committee* ...				10	10	0
				£391	0	1

W. S. CHURCH) Hon.

Income	£	s.	d.	£	s.	d.
459 *Annual Subscriptions at* £3 3s.	1445	17	0			
151 *do.* £1 1s.	158	11	0			
				1604	8	0
Composition Fees				39	18	0
Entrance Fees				119	14	0
Rents Receivable				2697	12	9
Sale of 'Transactions'				80	11	8
„ 'Climates and Baths' ...				4	3	4
Interest on New South Wales Stock ...				12	11	4
Legacy (Mrs. Gant)				100	0	0
Miscellaneous Receipts				7	5	9
Fees for use of Epidiascope ...				18	7	0
				£4684	11	10

Mr. Gant's Legacy (to be invested) ... 500 0 0

Audited and approved,

NEWSON-SMITH, LORD & MUNDY,
Chartered Accountants.

LIABILITIES.

	£	s.	d.
3 *per Cent. First Mortgage Debentures* . .	33,300	0	0
[The Debenture Debt has been reduced by £300 since the previous statement, by the Redemption of Three Debentures.]			
Sundry Liabilities	1,064	14	3
Mr. Gant's Legacy (to be invested) . . .	500	0	0
Balance, being Surplus of Assets over Liabilities, viz.—			
Balance, 31st Dec., 1904. . £29,868 3 8			
Less Amount written off 515 15 9			
29,352 7 11			
Excess of Income over Expenditure for the year 1905 . 205 16 2			
£29,558 4 1			
Less Extraordinary Expenditure in year . . . 391 0 1			
	29,167	4	0
	£64,031	18	3

ASSETS.

			£	s.	d.
Freehold and Leasehold Property			51,566	11	6
Fixtures, Fittings, and Furniture	1,343	11 9			
Additions during year . .	186	1 6			
	£1,529	13 3			
Less 5 per cent. written off for depreciation of Fixtures, etc., and £60 written off Epidiascope . . .	136	9 8			
			1,393	3	7
Engravings . . . . (as per Valuation of Mr. F. B. Daniell, Aug. 19, 1896).			555	0	0
Contents of Library (as per Valuation, Dec. 31, 1901) .			8,792	14	7
Investment—"Permanent Endowment Fund" . . . (New South Wales 4 per Cent. Inscribed Stock).			326	7	3
Sundry Debtors. Legacy (Mr. Gant)	500	0 0			
Do., Rents and Outstanding Subscriptions . . .	448	19 8			
			948	19	8
Cash at Bank and in hand .			449	1	8
			£64,031	18	3

Audited and approved,

NEWSON-SMITH, LORD & MUNDY,
Chartered Accountants.

8th February, 1906.

W. S. CHURCH,
J. WARRINGTON HAWARD, } *Hon. Treasurers.*

PERMANENT ENDOWMENT FUND.

[Established and contributed to by the Donations of Fellows.]

From	Sir Richard Quain	£100
„	Mr. Edward Law Hussey	50
„	Sir Richard Douglas Powell	100
„	Mr. Edwin Unwin Berry	124
„	Dr. Fitzpatrick	5
		£379

Invested in New South Wales Inscribed 4 per Cent. Stock amounting to £330 16*s.* 3*d.*

MARSHALL HALL MEMORIAL FUND.

[Being the amount subscribed for a Memorial to Marshall Hall. Every five years the accumulated interest is given as a Prize for the best published work on Nervous Diseases.]

	£	*s.*	*d.*		£	*s.*	*d.*
Consols on Dec. 31st, 1904	600	19	6	Consols in trust on 31st Dec., 1905	615	11	1
Interest for 1905 (added to Fund)	14	11	7				
	£615	11	1		£615	11	1

Accounts examined and Bank certificates obtained.

NEWSON-SMITH, LORD, MUNDY & CO.,
Chartered Accountants,
8th February, 1906.

LIST OF PAPERS.

N.B.—The Council of the Royal Medical and Chirurgical Society deem it proper to state that the Society does not hold itself in any way responsible for the statements, reasonings, or opinions set forth in the various papers which, on grounds of general merit, are thought worthy of being published in the *Transactions*.

ADDRESS

OF

SIR RICHARD DOUGLAS POWELL, Bart.
K.C.V.O., M.D.

PRESIDENT,

AT THE

ANNUAL MEETING, MARCH 1st, 1906

In the year that has gone by we have been busy looking back upon the achievements of the past century, looking forward to possible developments in the future, and doing the work that has come to hand.

We have suffered the loss of ten Fellows by death, and of two honorary Fellows, and how great that loss has been I have endeavoured to show in the brief and too-imperfect references to them that I have made.

The past Centenary year, however, will ever be memorable for the election into the Honorary Fellowship of the Society of H.R.H. the Prince of Wales, and we shall always look back with grateful appreciation of the honour conferred upon us by H.R.H.'s presence at our Banquet and by the warm recognition of the century's work of the Society in the cause of Medicine and for the welfare of the public,

which graced the eloquent and sympathetic speech with which he favoured us on that occasion.

We have also in the past year received an encouraging accession of new Fellows. The financial position of the Society is good and the generous contributions to the Centenary Celebration Fund has enabled our treasury to bear all the ordinary expenses of the year and yet to contribute more largely than usual to the Library and to the repayment of Debentures.

I would take this opportunity to remind the Fellows that however materially well-to-do this Society may be or may become its real prosperity must depend upon the number and *esprit* of its Fellows, and that it is by the continual accession of new Fellows to more than replace those that are gone, that its intellectual wealth, as well as its material prosperity, are maintained. It is within the power of each Fellow to bring the claims and advantages of the Society under the notice of colleagues and friends, and to invite them into the Fellowship.

It is very gratifying to the Council to be able to record such a complete success for our Centenary celebration in May last, and I beg here formally but very sincerely to express the indebtedness of the Society to the various organisation sub-committees of the Council, to the Honorary Secretaries, to Mr. MacAlister and his staff of officials, including Miss Williamson, for their zeal and industry, which made everything pass off so well. One of our Honorary Librarians, Mr. Godlee, took great interest and pains in securing through his friend, Mr. Ashbee, a very handsome design for the Honorary Diplomas, and we have to thank Mr. Partridge, the son of a former President of the Society, for a very artistic design for the Banquet Table cards. I must also again express our thanks to our Honorary Librarian, Dr. Norman Moore, and to our Honorary Secretary, Mr. Stephen Paget, for the production of the Centenary volume, recording the doings of our Society within the hundred years, upon which the festival celebration was based and justified.

The ordinary work of the Society has included many interesting and valuable papers fully on a level with those of former years. It may, I think, be affirmed that the Discussion on Appendicitis brought together a mass of statistical information, and a volume of well-matured experience, that could scarcely have been at the command of any Society but this, and that it has settled, for many years to come, the lines, both of Medical and Surgical procedure with regard to the most critical aspects of Appendix disease.

Another series of papers, very amply illustrated, brought fully before the profession the question of a rational and scientific method upon which the treatment of tuberculosis by tuberculin should be based. It was contended that the tuberculin treatment of tuberculosis should be effected upon lines in common with those upon which the treatment of certain other diseases, that have their origin in the actions of specific organisms, was founded, viz. measures calculated to increase the bactericidal influence of the blood serum upon such organisms, thus permitting of greater phagocytic activity on the part of the white corpuscles. The treatment of tuberculosis by tuberculin, originated by Koch, was so far an empiricism that it was in advance of any ordered reasoning, it was a speculative treatment, although based, it is true, upon the promptings of his great discovery. The treatment now again initiated necessarily awaits further experience in order that its limitations may be better defined, its co-ordination with other measures of treatment, surgical and medical, more clearly recognised, and, above all, in order that a more easily recognisable clinical index may be attained, which will enable the treatment to be safely carried out without constant and expensive, and often unattainable, reference to the bacteriological expert.

We were also favoured in the Marshall Hall Prize Essay, which was communicated to us at a special meeting in the Centenary week, with a remarkable output of prolonged, patient, and, I may truly say, self-sacrificing

work—for much of the vivisectional experiments were made upon the author himself—which has advanced our knowledge in an important manner, especially with regard to the phases of loss and restoration of sensation in cases of nerve injury and repair.

In working power then, as in finance, the Society may be truly said to be in a sound condition.

With regard to the question which I raised in my first annual address, and which was so cordially and generously accepted for consideration by this Society and by many others, viz. that of a possible Union of the Central London Medical Societies for greater economy and more comprehensive and efficient work, I may say that the scheme is still in progress; very many committee meetings have been held under the presidentship of Sir William Church, and much has been done towards the attainment of a working plan of amalgamation. The negotiations have been delicate and sometimes difficult; but in the existence of what I believe to be a conviction amongst the members of the different Societies, that in Union we shall find strength and greater efficiency in forwarding the interests of Medical Science, and with the impetus of will (and I hope good-will) power amongst them, I believe that the Union will be triumphantly effected. It is quite clear that, before any actual coalition of the Societies in agreement takes place, very careful estimates, based on exact valuations of the assets of each Society, must be made, in order to place the new Society on a sound financial foundation. The up-keep of the new Society must depend upon the subscriptions of Fellows and Members, and with a large Fellowship there can be no anxiety on this head. The income-producing property must be estimated on realisable assets only, and probably reserved as a fund for special scientific requirements. The market value of books and museums can scarcely enter into such estimates; yet, nevertheless, the library, which should be the best in the world, must be a chief attraction, and the most really valuable asset of such a society. I have no misgivings

myself as to the possibility of bringing about this much needed union.

Apart, however, from any amalgamation scheme, and indeed perhaps as a part of any such scheme, my experience as a past Secretary, and as now, alas, also a past President of this Society, leads me to say that I think the Society needs some expansion and development in certain directions which were indeed contemplated at its foundation. Its meetings have long been too exclusively of a formal kind. Undoubtedly the two great objects of the Society are a perfect Medical and Scientific Library and the production of first-rate papers and discussions, which its resources enable it to publish and illustrate with every necessary fulness. But the Society did not originally contemplate that every meeting should, so to speak, be a full-dress one. It had in view instructive conversational meetings over an interesting case, a new discovery, or a new method of treatment, and I venture to think that if an evening were sometimes devoted to the conversational consideration of a few interesting cases, specimens, or demonstrations of objects of medical interest, such as one sees to be the nucleus of a group of busy brains at odd corners at the Royal Society Soirée, it would not be misspent; and that a more formal paper read at some subsequent meeting on a subject thus less formally ventilated would meet with more sympathetic and full consideration. The organisation of these less formal gatherings would no doubt involve some extra work, skill, and enthusiasm on the part of the Honorary Secretaries, but those qualities may be safely reckoned upon and have never been found wanting. There used in my day at the Pathological and Clinical Societies to be a clique of working pathologists and clinicians who met together at one another's houses after the formal meetings of the Societies, and discussed informally the events of the evening. They were interesting, entertaining, often lively meetings, and, I think, useful. Certain lessons of the evening were sometimes inculcated with

greater emphasis than could be done at a public gathering. I remember that the editors of some of the journals were conspicuous members, and, although they left their note-books behind, I have no doubt they acquired some useful information of the trend of medical thought at those informal gatherings.

I think there might be found within our Society's premises a room for post-Medico-Chirurgical gatherings of this kind consisting of members qualified by a certain standard of fellowship and work at the Society. I believe such an inner or outer circle properly organised on liberal lines would attract Fellows and stimulate them to good work in the Society. And the same remark would apply to any new society that might or may be founded upon its association with other societies.

It only remains for me now to say how keenly I have appreciated the friendly and courteous support I have always received from the Council and Fellows of the Society during the somewhat difficult year of office that I have now again completed. I shall always treasure the memory of my Presidentship as one of my proudest attainments as well as of my most pleasant experiences.

The Council has reported to you the loss we have suffered by the death of ten Fellows and two Honorary Fellows, and my first duty is to give a brief account of their lives and work.

Hermann Nothnagel, M.D., Honorary Fellow, Professor of Clinical Medicine, University of Vienna. Our distinguished Honorary Fellow, Professor Nothnagel, whose somewhat early death has left a serious gap in medical science was born in 1841. Professor Nothnagel was a pupil of Traube and Virchow, and was of the best type of physician and clinical teacher, his instruction and practice being based upon a most profound knowledge of pathology. With this great qualification in the background he also made a special study of therapeutics, and he wrote one of the best of modern text-books on that subject;

and amongst his later achievements he edited a treatise in twenty-four volumes on special pathology and therapeutics. To all these literary and teaching labours he added the wear and tear of a very large practice. He was a good as well as a great physician, and gave without stint of his talents and labour to the poor. He was made a Member of the House of Lords in 1902 by the Emperor of Austria, who sent a warm message of sympathy to his relatives at his death on July 6th. He was known to have early cardio-vascular degeneration, and he died suddenly in bed from heart failure having spent the day in active work.

Besides his work on therapeutics Dr. Nothnagel will perhaps be best remembered by his writings on vaso-motor neuroses, angina pectoris vaso-motoria, and tachycardia.

Rudolph Albert von Kölliker, M.D., Professor of Anatomy in the University of Würzburg. Honorary Fellow 1868. Our venerated Honorary Fellow, Rudolph Kölliker, died on November 23rd, 1905, of pneumonia, aged 88. The name of Kölliker was familiar to the oldest of us in student days, and up to 1899 he was an almost continuous contributor of learned papers on histological and allied subjects, amounting, as he himself states in his memoirs published in that year, to 245 in number.

At the age of twenty-seven he became Professor of Physiology and Comparative Anatomy at Zurich, and three years later he was called to Würzburg as Professor of Physiology, and subsequently of Anatomy. A pupil of Johannes Müller he was in the commencement of responsible work in 1838 and 1839, when Schleiden and Schwann were contributing to the world the results of their researches into the histology of vegetable and animal cell structures. He may be said to have carried on and developed with the improving penetration of microscopical powers the work of these scientists and of Henle up to the

time of modern histological physiology or pathology. It must have been an interesting life to have taught through this period, and to have seen his work accepted by his friends, Professors Sharpey, Owen, Grant, Bowman, Wharton, Jones, and others in this country, and by innumerable followers, including Professor Virchow, in his own.

He became a rather frequent visitor to England and Scotland in the fifties, and had a sincere reverence for Professor Sharpey, who may be said to have introduced his histological teaching into this country. He must have been well versed in our language, for it is said that he fell asleep over 'Tom Jones' when on a visit to Professor Goodsir, and nearly met his death through blowing out the gas without turning it off.[1] He delivered the Croonian Lecture before the Royal Society in 1862.

Modern readers may jump the times of Kölliker, as they will of Burdon-Sanderson, taking their work as read and incorporated in more modern text-books, but the historian of literature will ever place their contributions to histology, physiology, and pathology as the foundation of much of the real knowledge of to-day and hereafter in these sciences. An adequate sketch of Kölliker's long life and doings is impossible in the space allowed me. I may quote from the admirable account of him in the 'British Medical Journal' that he published 108 papers on histology, two on anatomy, sixteen on physiology, fifty-two on embryology, five on Darwinism, nineteen on comparative anatomy, and five on miscellaneous subjects, and we may be sure that all were good. He was a great athlete and an ardent Alpine climber, a picturesque and handsome figure in the world of science.

Edwin Thomas Truman, M.R.C.S., who died in April last, aged 86, was Surgeon-Dentist to H.M. Household, an office he had held for more than fifty years. He was

[1] 'British Med. Journal,' obituary notice, Nov. 18th, 1905.

a member of the Institute of Electrical Engineers, and made an important improvement in the manufacture of gutta percha, which rendered it more serviceable as an insulator for electrical cables. He also contributed some practical papers to dental science. He was a great collector of old books and engravings. He had been a Fellow of this Society since 1859, but had not contributed to its 'Transactions.'

Eustace Talbot, M.A., M.B.Cantab., M.R.C.P., and Casualty Physician, St. Bartholomew's Hospital. Dr. Eustace Talbot died on May 26th, 1905, at the early age of thirty-one years of appendicitis of which he had previously experienced a mild attack some twelve years ago. He was the youngest son of the Rt. Hon. J. G. Talbot, M.P. for Oxford University, and was educated at Winchester and Trinity College, Cambridge. He entered St. Bartholomew's Hospital on leaving Cambridge in 1896, and after qualification became resident at the Royal Hospital for Diseases of the Chest, which he relinquished in order to return to St. Bartholomew's as House Physician to Sir William Church. While holding this appointment he was attacked with hæmoptysis, and spent the following winter at Davos, whither he returned frequently in the following years. In 1903 his health was fully re-established, and he was elected to the office of Casualty Physician at St. Bartholomew's early in 1904. He also held the post of Medical Officer to the Sun Life Assurance Office, and of Assistant Physician to the Royal Hospital for Diseases of the Chest, and had recently been elected to a post in the Medical School at St. Bartholomew's.

In him St. Bartholomew's Hospital and the medical profession in general sustained a great loss. He was not only an extremely careful and sagacious clinician, but his social qualities and his personal charm would have assured him a prominent position in the future. His influence and example at his own school were certain to

have found a wider sphere in the process of time. His personal friends were numerous, and there was none whose admiration and respect he did not easily win.

Frederick James Gant, F.R.C.S., Consulting Surgeon to the Royal Free Hospital, a former Vice-President of this Society. Born in London December, 1825, Mr. Gant was delicate in early life and whilst still a youth lost both his parents. He began life as an assistant to a chemist in East London, but afterwards entered as a student at University College Hospital, took the membership of the Royal College of Surgeons at twenty-four and became a Fellow twelve years later.

In 1852 he commenced practice as a surgeon, and lectured on Physiology at the Hunterian School of Medicine for a year and, on that school ceasing to be, he became attached to the Royal Free Hospital, and lectured there on Anatomy and Physiology. He went out to the Crimea as Civil Surgeon, and for his services received a medal and clasp. He returned at the end of the war to the Royal Free Hospital, and it was from his experience at that Hospital that his professional writings emanated. These were chiefly of the nature of text-books on general surgery, although he made a special study of disease of the prostate and bladder. It is stated in the notice of him in the 'Lancet' that in his work on the 'Science and Practice of Surgery,' published in 1871, he was, perhaps, the first to recognise and give an account of Lister's antiseptic methods, which had been in use in Glasgow some five years, but had not yet penetrated south of the Tweed. After some hesitation he took an active interest in the medical education of women, and his clinical teaching of those who attended the Royal Free Hospital from the London School of Medicine for Women was greatly appreciated between the years 1878 and 1890.

Mr. Gant was a broad-minded man who, deprived of definite academic education owing to the early death of

his parents, and, perhaps, his own delicacy in early life, had yet acquired by his industry and determination a considerable professional position, and also attainments outside his professional work. He had a somewhat controversial turn of mind, and was very definite and determined in his opinions, but always took in very good part the somewhat lively controversy to which their expression sometimes gave rise in this and other Societies.

He was very loyal to this Society of which he was for two years Vice-President, and we have this day recorded his very handsome legacy of £500.

Mr. Gant was also President of the Medical Society in 1880, and Lettsomian Lecturer in 1871.

Perhaps Mr. Gant may be best remembered by his demonstration of the extensive fatty degeneration or infiltration of the tissues, especially of muscles including the heart, which was produced by the over-feeding of animals in preparation for the Smithfield cattle show about 1857. The value of his researches was recognised by letters from the Prince Consort, the Duke of Richmond, and others interested in cattle. He contributed to our 'Transactions' on "Excision of Joints," vols. liii, lvi, lxiii.

Mr. Gant married in 1859 Miss Matilda Crawshay, who died in 1899, whose character seems to have inspired him in his sketch of the heroine in his book on 'Perfect Womanhood.' Mrs. Gant, who warmly followed all the interests of her husband's life, has also bequeathed to this Society a legacy of £100. They had one child who died in infancy.

Mr. Gant's later life was a suffering one during which, however, long after giving up the profession, he still continued to interest himself in literature. He published volumes on 'The Lord of Humanity,' 'The Mystery of Suffering,' Our Dead Selves to Higher Things,' and that above quoted on 'Perfect Womanhood.' Also a somewhat embittered volume on 'Mock Nurses of the Latest Fashion.'

Dr. William Ogle, of Derby, died in that town on May 16th, 1905, after a long illness, at the age of 81. He was a son of the vicar of a parish near Boston, Lincolnshire. He was educated at Rugby in the time of Dr. Arnold, and was a Fellow of St. Catherine's College, Cambridge. He studied medicine, however, at the University of Edinburgh and in Dublin, and then came to London to practise, his first appointment being to the Royal Pimlico Provident Dispensary. He took the M.D. of Cambridge in 1858, and became a Fellow of the Royal College of Physicians ten years later. He was elected Physician to the Derby Infirmary in 1860, and continued in that office for thirty years, when he became Consulting Physician. In 1894 he became a Justice of the Peace for the county. Dr. Ogle did a considerable consulting practice in Derby and the neighbourhood. He organised the Nursing and Sanitary Institution of Derby, and devoted much time to its development. He wrote papers on Preventive Medicine.

Dr. Ogle was a man of deep religious convictions, and a staunch supporter of the Young Men's Christian Association. He married in 1860 Miss Margaret Lambert, of Bradford, who survives him. His two sons, the Rev. Hugh Lambert Ogle, of Plumstead, Kent, and the Rev. Philip Douglas Ogle, vicar of Nottingham, also survive him.

With his strong character and simple faith he was much loved and respected by friends and patients.

He contributed two papers to our 'Transactions':— 1. "On the Pathology of the Cervical Portion of the Sympathetic Nerves," lii. 2. "On Anosmia," liii.

Christopher Heath, F.R.C.S., Consulting Surgeon, University College Hospital; formerly Emeritus Professor of Clinical Surgery, University College; and President of the Royal College of Surgeons, and a Vice-President of this Society.

Born in London 1835, Christopher Heath was educated at King's College School, and later at the College and

Hospital. He took the Membership of the College of Surgeons in 1856 and the Fellowship in 1861. The grandson of a surgeon in the Royal Navy, he also served with the Fleet in the Crimean War, and ever carried with him something of the brusqueness and build of a naval officer of old times. He commenced work in London as a Teacher of Anatomy, and was Demonstrator at the Westminster Hospital, and later Lecturer on Anatomy and Assistant Surgeon.

In 1866 he migrated to University College Hospital, where he was appointed Assistant Surgeon and Teacher of Operative Surgery in 1866, and Holme Professor of Clinical Surgery and full Surgeon in 1875.

'Heath's Practical Anatomy' was already a well-known work, and remained the text-book for many generations of students. His 'Manual of Minor Surgery' was another handbook of the utmost practical help to innumerable students. His Jacksonian essay on "The Injuries and Diseases of the Jaws," for which he was awarded the prize, gained for him great reputation as a practical surgeon. He became a Member of Council of the Royal College of Surgeons in 1881, and President in 1895 and 1896, and delivered the Hunterian oration on "John Hunter considered as a Great Surgeon" in 1897; also the same year the Lane Medical Lectures at San Francisco. Some papers on the "Treatment of Intra-thoracic Aneurysm by the Distal Ligature" in 1871 and 1898, contributed to our 'Transactions,' attracted considerable attention.

Mr. Christopher Heath's reputation was gained by his clear and incisive teaching. His language was always well chosen, terse, vigorous; his method very direct and clinical. No doubt he acquired his great clearness and power from his profound knowledge of anatomy and long practice as a demonstrator in the dissecting room. He was also an exceedingly dexterous operator having been much associated with that most brilliant operating surgeon of his day, Sir William Fergusson. Christopher Heath

indeed, may be regarded in this respect as in touch rather with the old pre-chloroform operating days in which rapidity, precision and style were more considered. The more minutely dissecting and less showy methods consequent upon the complete establishment of anæsthesia, the perfect control of hæmorrhage, and the anti- and aseptic methods of the present time, were only possible in his later professional life, and, although versatile and quick in grasping most essential points, he was apt to regard modern methods as somewhat "finicking." We are, perhaps, with assured familiarity of aseptic methods, witnessing a reversion to some of the rapidity and style in operating, such as characterised a former generation of surgeons, and which, by saving time and shock to the patient, may still further diminish mortality.

Mr. Christopher Heath thoroughly understood students and knew how to impart to them the knowledge they required, and how to instil into them practical lessons of life-enduring value. Of handsome presence, cheery, breezy manner, he was truly an upright and a downright man, a true friend, and a generous but strenuous opponent. He had served on the Council of this Society, 1880; as Vice-President, 1889; Library Committee, 1870–3; and he contributed four papers to the 'Transactions.'

Dr. John William Ogle, of London, a member of an old family coming originally from Northumberland, was a widely-distinguished man. Educated at Wakefield and at Trinity College, Oxford, he graduated M.A. at Oxford in 1851 and M.D. in 1857, became a Fellow of the Royal College of Physicians in 1855, and was successively Censor, Senior Censor, Harveian Orator in 1880, and Vice-President of the College in 1885. Dr. John Ogle was member and corresponding member of innumerable learned medical societies and an Associate Fellow of the College of Physicians of Philadelphia. His medical education was chiefly at St. George's Hospital, and it was at that hospital that he laboured as assistant, and full physician for

twenty years until about 1876 when failing health obliged him to lessen the strain of work and he retired from the active duties of the hospital, although continuing in private practice for many years afterwards. With Mr. Timothy Holmes he edited the first volumes of the 'St. George's Hospital Reports' for eight years from 1866, and those volumes and the few which succeeded them contained many brilliant articles and much valuable and well-arranged clinical matter. Dr. Ogle was an advanced Churchman. He lived through the Tractarian times at Oxford, and his scholarship and religious views brought him into close and sympathetic relationship with Gladstone, Keble, Dean Church, and others. Dr. Temple and Dr. Benson, both Archbishops of Canterbury were intimate friends.

Dr. John Ogle was a very dignified, yet singularly gentle and attractive, personality, and a successful and an inspiring clinical teacher, and what is still more rare an excellent examiner. He contributed no formal treatise to medical science, but he made many and valuable contributions to the 'Transactions of the Pathological Society' and to the 'St. George's Hospital Reports,' and he was the author of a monograph on "Puncturing of the Abdomen for the relief of Tympanites," and contributed four papers to the 'Transactions' of this Society. Many who were students and are now long since in practice bear the impress of his sound teaching, his accurate scholarship, and his great humanity.

William O'Neill, M.D., M.R.C.P., Fellow of the Royal Medical and Chirurgical Society; Fellow of the Royal Academy of Medicine in Ireland. Born in 1830 in co. Leitrim, the youngest son of parents of good stock on both sides, Dr. O'Neill was educated at Trinity College, Dublin, and at King's College, Aberdeen, and graduated M.D. Aberdeen in 1859, and M.R.C.P., 1877. He settled at once in practice in the town of Lincoln, and became physician to the Lincoln General Dispensary, and in due

course attained to large practice in the town and in consultation in the county.

Besides his professional work and numerous writings in the medical journals, Dr. O'Neill was learned in archæology and art. He was a member of the Archæological and Architectural Societies, and a great authority on pottery. He wrote pamphlets on Derby China, on old Pottery, Dresden and Sèvres Porcelain, and on Bow and Chelsea Porcelain. He also contributed articles on Roman remains in Lincolnshire on "Sanitary work of the Romans in Lincoln," and a brochure on the Coronation Chair in Westminster Abbey, in which he traces the history of the stone, which is the basis of the chair to early Greek times, and through the earliest historic times of North Ireland as the "Lia Fail" or Stone of Destiny, held in great veneration by the Irish for sixteen or eighteen centuries, and used in the coronation of the Kings of Ireland. Dr. O'Neill also wrote on botanical, religious, and sociological subjects.

He was an energetic and courteous physician and a deeply-learned and cultivated man. Dr. O'Neill was unmarried. He died October 27th, 1905, aged seventy-five, and his funeral at Canwick was attended by many residents and his medical brethren of Lincoln.

Pearson Robert Cresswell, C.B., V.D., F.R.C.S.E., died on the 22nd November, 1905, at Dowlais, Merthyr Tydvil, Glamorganshire, the place of his life's work, at the age of seventy-one.

Mr. Cresswell, the son of a solicitor, was born and bred at Worcester, and went in early life to Australia, returning, however, to London for his medical studies. He was trained at the Middlesex Hospital, and was house surgeon there for twelve months. He went to Merthyr Tydvil as surgeon to the Dowlais Iron Works, and remained in that mining district for forty-five years. He was specially interested in surgery, and by his post-graduate studies required for taking his Fellowship of

the Edinburgh College of Surgeons late in 1873 was enabled to grasp the details of the antiseptic methods which he early began to use in the Dowlais Workmen's Hospital and the Merthyr General Hospital.

Mr. Cresswell took up ambulance work, and taught first-aid to the wounded for many years, and instituted an edition of the 'Manual of the St. John's Ambulance Association,' translated into Welsh by some friends. He was elected an Honorary Associate of the Order of St. John of Jerusalem. He took an active part also in the local affairs of the British Medical Association, and was a member of the administrative Council.

Mr. Cresswell was a Justice of the Peace for Glamorgan, and President of the South Wales Branch of the English Church Union. He rendered great services to the volunteer movement which was started in his time, became assistant surgeon in 1860 in the 2nd Glamorgan Rifles, and later became a combatant officer of the Volunteer Battalion of the Welsh Regiment, in which regiment he ultimately attained the rank of colonel. He worked zealously in raising this regiment to over 2000 in strength, and he took the most prominent part in organising a Welsh volunteer force for the front in the South African War. For his military services he was made Companion of the Most Honourable Order of the Bath in 1898.

Mr. Cresswell was twice married, and of his family one son, Dr. Stuart Cresswell, was associated with him at Merthyr, and another, Dr. Frank Cresswell, is in practice at Cardiff.

He was brought back to his native county and buried near Malvern. Truly he lived a strenuous life, and will long be remembered as an enlightened surgeon and a strong man.

Sir John Scott Burdon-Sanderson, Bart., LL.D., M.D. Edin., F.R.S., late Regius Professor of Medicine at Oxford, died November 23rd, 1905, aged 77. Born at Jesmond, Northumberland, December 21st, 1828, he was

of an old county family. He was educated at home and at the Universities of Edinburgh and Paris, and settled in London in 1855, successively holding the following offices: Medical Officer of Health for Paddington, 1856—1867; Inspector, Medical Department, Privy Council, 1860—1865; Assistant and full Physician, Brompton Hospital, Assistant Physician, Middlesex Hospital, 1860—1870; Superintendent, Brown Institution, 1871—1878; Professor of Physiology, University College Hospital, 1874—1882; Waynflete Professor of Physiology, Oxford, 1882—1895; Regius Professor of Medicine, Oxford, 1895—1904; President of the Pathological Society of London, 1903—1905.

He was Harveian Orator at the Royal College of Physicians in 1876, and received the Baly Medal for his researches in physiology in 1880, and was Croonian Lecturer, Royal Society, in 1891. He also received the Medal of the Royal Society for his researches in physiology and pathology. He served on three Royal Commissions—on Hospitals, 1883, on Meat and Milk in Relation to Consumption, 1890, on the University of London, 1892—1894. He was created a Baronet in 1899.

Of the many offices held by Sir John Burdon-Sanderson, those relating to public health, which occupied the first ten years of his London career, 1856—1867, and those relating to physiology and pathology in London and Oxford from 1871 to the end of his busy life, were the principal fields of his work, which was essentially that of a physiologist pressing his inquiries on into the domain of pathology. Burdon-Sanderson's bent of mind was not such as to have enabled him ever to attain eminence as a physician, and his attachment to the staffs of the Middlesex and Brompton Hospitals over a period of ten years was chiefly useful in giving a more practical insight into the conditions of health and disease which were so much the scene of his inquiries.

He was a great student of life—a biologist both in the animal and vegetable world—and a profound exponent of

the processes of life in healthy function as demonstrated by physiology, and its perversions in disease as studied in pathology. Sanderson was one of the earliest advocates in this country of the use of mechanical and electrical methods in the study of health and disease processes. He was the earliest worker with the sphygmograph of Marey in the sixties, and later with the cardiograph, and used both instruments in his clinical work at his two hospitals. Still more recently, indeed up to the time of his death, he closely studied the electrical reaction and resistance of tissues. In one of his latest addresses, that to the Pathological Society as President in 1904, he insists upon the great importance of employing the methods of physical chemistry in aid of experimental inquiries into the origin of infective processes.

Intimately acquainted with the literature of Europe of the sciences, Sir John never actually arrived at any great discovery, such as might have earned undying fame for a more speculative, if a less profoundly learned, man. It is probable that his great initiative in many directions, his great power of formulating data for new work, and his inspiriting training and encouragement of younger men will not have built for him a name beyond their memory. But he was none the less happy in his work, and Science has been none the less profoundly served, enriched, and advanced by his having lived in her cause. His researches on artificial tuberculosis in relation to the pathology of phthisis and his article in 'Holmes' System of Surgery' on "Inflammation" are the best remembered of his writings, and were of great value and authority in their time, but are even now past the period of more than historical usefulness and interest.

Of commanding stature, with magnificently proportioned head, and handsome, delicately-cut features, Sir John Burdon-Sanderson was a man of calm and philosophic temperament, with a courtly dignity and kindliness of manner, and an entire absence of cynicism or satire that rendered him peculiarly attractive to younger men, and

capable of stimulating them to their best work. He was singularly absent-minded in the ordinary affairs of life, and many humorous stories are current about him which are too well known to many of the Fellows here for me to quote.

Sir John married a sister of the late Lord Herschell, who survives him. A large and representative gathering attended the funeral service at Magdalen College Chapel. He was buried at Wolvercote Cemetery, near Oxford.

John Abernethy Kingdon, F.R.C.S., a former Vice-President of this Society, died on January 5th, aged seventy-seven. His father was in large practice in the City, and John Abernethy was his God-father. He was educated at St. Paul's School and at St. Bartholomew's, where he was House Surgeon to Sir William Lawrence. He took the M.R.C.S. in London in 1849, and the Fellowship in 1861. He was elected a Fellow of the Royal Medical and Chirurgical Society in 1861, and served on the Council, and in 1872–3 as Vice-President. He served on the Committee appointed by the Society to investigate the action of drugs when used subcutaneously.

Mr. Kingdon was a man of singularly dignified presence, and his remarkably fine head and countenance could not fail to attract notice in any assembly. He had a wide and profound knowledge of human nature. He was Surgeon for many years to the City of London Truss Society, and was very zealous in his work for the interests of that Society. He contributed a valuable paper to this Society on "The Causes of Hernia," which was published in the forty-seventh volume of our 'Transactions,' and he had made a profound study of this malformity. He was a member of the Grocers' Company, and Master in 1883, and did much to direct the charitable expenditure of that ancient and beneficent Guild. Another interest of Mr. Kingdon was the Abernethian Society of St. Bartholomew's, which he did much to restore to its present flour-

ishing state. He was chiefly engaged professionally as Medical Officer to the Bank of England, and all the Insurance Medical Reports of the Bank were drawn up by him. He was an admirable examiner for several Insurance Offices.

He slept peacefully out of life, dying from heart failure in the midst of his official duties, and was buried in Highgate Cemetery. Mr. Kingdon was never married.

PROPOSED UNION OF MEDICAL SOCIETIES.

In continuation of the record of this movement printed in last year's volume, the Hon. Secretaries of the Committee, Messrs. Latham and Pendlebury, have been good enough to supply the following statement recording the progress of the movement to July 17th, 1906.

A meeting of the Committee of Representatives of the various Societies was held at 20, Hanover Square, on December 19th, 1905.

Sir William Church read from the chair replies (page cxxxiv *et. seq.*) which had been received from twenty-three societies on the subject of the Report of the Committee of Representatives as amended and adopted on July 19th, 1906. All these societies agreed as to the feasibility of union, but made varying conditions with regard to their acceptance of the Report.

After some discussion, and after hearing the opinion of some of the ladies in the profession, it was decided that on the formation of the new Society women should become members of sections only, but that this decision should be without prejudice to their position in the Society in the future.

The following resolutions were carried:

(1) That an Organising Committee, consisting of the members of the late Executive Committee, together with representatives of the Pathological and Obstetrical Societies, be appointed to consider the replies that have been received from the various societies, and to take such steps as they may think fit to formulate a definite scheme of amalgamation. That this Committee have power to add to its number.

(2) That it be an instruction to the Organising Committee that circulars be sent to all members of those societies which have given a conditional assent to the scheme of amalgamation for the purpose of ascertaining whether, in the event of

amalgamation taking place, they would be prepared to join as Fellows of the proposed new Society, or as members of a section or sections.

(3) That the necessary expenditure which has been incurred, and which will have to be incurred, in promoting the scheme of amalgamation be defrayed by funds to be contributed from the societies which have given a conditional assent to the scheme in proportion to the number[1] of members constituting such societies.

The Organising Committee held a number of meetings from February to July, 1906. At the commencement of its sittings the Committee had before it the annexed suggestions (page cxlviii) from the Hon. Secretaries, which were discussed in detail. A number of sub-committees were then appointed to negotiate with delegates of the various societies with regard to the various objections raised by these societies to the Report of July 19th, 1905.

A Finance Sub-Committee was also appointed to investigate thoroughly the finance of the proposed new Society.

The Organising Committee fully considered the reports of its various sub-committees, and then passed unanimously the annexed Report (page clii). This Report was considered on July 17th, 1906, by the Committee of Representatives of various societies. Sir William Church, in the chair, pointed out that the first meeting of members of the societies, held at the Royal College of Physicians, was to consider the feasibility of union, and that, as the outcome of that meeting, the Committee of Representatives was appointed. The Committee of Representatives appointed an Executive Committee to go more thoroughly into the feasibility of the union, and to outline some scheme of union if such were found possible. This Executive Committee reported that a union was feasible on certain lines, and the Report was confirmed by the Committee of Representatives on July 19th, 1905. Thereupon an Organising Committee was appointed to draw up a definite and as far as possible a detailed scheme of union. The Report of the Organising Committee was now before the Committee of Representatives, and, if approved, would be sent to the societies to act upon or not as they thought fit.

The Report was adopted unanimously by the Committee of Representatives with a few verbal alterations, as shown in the footnotes of the Report.

Those societies which approve of the Report and decide to join the proposed union will appoint a representative before December 7th next to sit upon a Committee which shall act as the Council of the new Society and deal with the necessary details of the amalgamation.

[1] This was altered by the Organising Committee to the more just proportion of "income of such Societies from subscriptions."

REPLIES OF TWENTY-THREE SOCIETIES TO THE REPORT OF THE COMMITTEE OF REPRESENTATIVES (pp. cxxxiv—cxlvii).

The Royal Medical and Chirurgical Society,
20, Hanover Square, W., *November 24th*, 1905.

Dear Sirs,—I have great pleasure in informing you that at a Special General Meeting of this Society, held here yesterday, the enclosed resolution was carried unanimously. For your information I enclose also three copies of your Report, showing in red ink the modifications this Society would like to see adopted.*—Faithfully yours,

J. Y. W. MACALISTER, *Secretary*.

"That the Council be and is hereby authorised to take all such steps and proceedings, and to do all such acts and things as to the Council, in its discretion, shall seem necessary or expedient for carrying into effect the amalgamation of the Royal Medical and Chirurgical Society with any sufficient number (at the discretion of the Council) of the Societies named in the '*Report on the Union of Medical Societies as amended and adopted at the meeting of the General Committee of Representatives of the Societies held on July 19th*, 1905,' or with any other Society, or Societies, either in accordance with the scheme set forth in the Report subject or not (as the Council shall think fit) to the modifications recommended to them or to such (if any) other modifications, amendments, or alterations as to the Council in its discretion shall seem necessary or expedient, or in accordance with such other scheme as the Council in its discretion shall think desirable."

MESSRS. LATHAM and PENDLEBURY.

* *List of Modifications* (*marked in red ink*) *in Copy of Report.*

"*N.B.* It has to be remembered that the Royal Medical and Chirurgical Society has a Debenture Debt of £33,000 which must be paid off or provided for in 1939. On the other hand, its assets are valued at upwards of £60,000.

"1. The new Society shall be called the Royal Society of Medicine.

"2. All moneys, books, premises, and other properties belonging to any of the societies which join the proposed union shall become the property of the new Society, and shall be vested in the Fellows.

"4. The Fellows of the Society shall meet annually for the election of officers and other business, and four or more times a year for the election of Fellows and for such other business as may be desired by the Council.

"7*a*. The election of Fellows shall be on the same lines as are at present followed in the Royal Medical and Chirurgical Society.

"*N.B.*—The Council of the Royal Medical and Chirurgical Society are of opinion that it would be premature at the present time to discuss the list of sections of the new Society.

"11. The general management of the Society shall be under the control of a General Council, consisting of the President, the Presidents of the various sections, two Treasurers, two Librarians, two Secretaries, and eight Fellows. The members of the Council, with the exception of the Presidents of the sections (who are to be *ex-officio* members) shall be elected by the Fellows."

The Medical Society of London,
11, Chandos Street, Cavendish Square, W.,
November 27th, 1905.

To the Honorary Secretary, the Committee *re* the Proposed Amalgamation of London Medical Societies.

Proposed Amalgamation of London Medical Societies.

Dear Sir,—At a special meeting of the Council of the Medical Society of

London, held November 22nd, to consider the proposed amalgamation of London medical societies, the following resolution was passed:

"That whilst re-asserting the desirability of an amalgamation of the various medical societies of London into a Royal Society of Medicine, the Medical Society of London can only agree to join in this effort, provided—

"First, that the financial position of the proposed new body is found to be satisfactory after the financial accounts of the various societies have been thoroughly investigated; and

"Second, that the privileges of the Fellows of the Medical Society are carefully safeguarded."

We shall be glad if you will bring the above resolution before the next meeting of your Committee.

We are, dear Sir, yours faithfully,

J. S. RISIEN RUSSELL, CUTHBERT S. WALLACE, } *Hon. Secs.*

Hunterian Society, London Institution,
Finsbury Circus, E.C., 29, Weymouth Street, W.,
November 25th, 1905.

The Secretaries of the Committee for the Union of Medical Societies.

Dear Sirs,—A Special Meeting of the Council of the Hunterian Society has been held to consider the position of the Society in regard to the proposed amalgamation of medical societies, and we are instructed to lay before you their views as follows:

"(1) The Hunterian Society is one of the oldest of the medical societies in London, and is especially interested in Clinical Medicine and Clinical Surgery, having a considerable membership both among general practitioners and consultants.

"(2) The Council hope that some proposal for affiliation may receive full and early consideration which, whilst preserving the character, individuality, and local usefulness of the Hunterian Society, may give its Fellows the great advantages of a connection with the proposed central Society.

"(3) If the question of the participation of this Society is deferred until after the Union has taken place, the Council would ask that the Fellows of the Hunterian Society should be treated on as favourable terms as those of the uniting societies."

Yours faithfully,

FRED. J. SMITH, *President.*
R. FORTESCUE FOX, *Hon. Secretary.*

Pathological Society of London,
20, Hanover Square, W., *December 9th*, 1905.

Dear Sirs,—I enclose, as you wish, a copy of the amendments, etc., adopted by the Council on November 7th, 1905, in regard to the Report of the Executive Committee as amended July 19th, 1905.

Yours faithfully,

Dr. ARTHUR LATHAM. S. G. SHATTOCK.
Mr. HERBERT S. PENDLEBURY.

These amendments would have finally to be discussed at and passed by a general meeting, which might be summoned at any time for the purpose as circumstances require.

Page 4, par. 1.—"The Council were strong in their view that the title of the proposed Society should *not* be the Royal Society of Medicine."

The resolution took only this negative position.

Page 4, par. 4.—Amendment: "That meetings of the Society, as a whole, should be held at the discretion of the General Council."

Page 6.—At the end of paragraph 10 was added: "Each member shall receive a copy of the publication or publications containing a record of the work done in his section or sections."

Page 6, par. 13.—To this was added: "The selection of all illustrations coming under the cognisance of the Pathological Section, the methods of their reproduction, and the firms employed to reproduce them, shall be in the hands of the Council of the Pathological Section."

At the bottom of page 6 was added: "Should a paper be selected for the 'Transactions,' an abstract of it may previously appear in the 'Proceedings.'"

In par. 15, line 5.—After the words "Editorial Committee" was added: "On which the Pathological Section shall be represented."

Page 7.—The whole of the first paragraph was disagreed to, with the exception of the three last lines, viz. "Authors of papers should have the privilege of suggesting the section or sections before which they wish to read their papers."

In addition to the foregoing the Council adopted the following resolution of a Committee appointed to consider the question of confederation.

"If it shall appear that the financial position of the new Society will allow of an adequate expenditure upon the publication of the Pathological Section, the Pathological Society will be prepared to join the new Society."

The Pathological Society will agree to have its donation list to British, Irish, Colonial, and Foreign Universities curtailed in accordance with the regulations which the new Society may make in this respect for general observance, and will be prepared for the discontinuance of gratuitous copies to contributors, if this practice is not adopted generally by the new Society.

Clinical Society, 20, Hanover Square,
London, W., *December 9th*, 1905.

Dear Sirs,—In reply to your letter of the 6th inst., I have to inform you that the following resolution was unanimously passed at a special general meeting of the Clinical Society of London, held on Tuesday, November 21st ult.:

"That the Clinical Society of London expresses an opinion in favour of the amalgamation of the various medical societies of London, provided that the scheme proposed prove financially feasible."

At the meetings of the Council of the Society at which the Report of the General Committee of the Representatives of the Societies has been discussed, a general expression of opinion was made on the following two points:

(1) That a Clinical Section of the new Society should continue work on the lines which have guided the meetings of the Clinical Society of London in the past.

(2) That it is highly desirable that the 'Proceedings' of this Section should be published in such a form as to continue the existence of the 'Transactions' of the present Society. It was felt that these 'Transac-

tions,' as a record rather of facts than opinions, are of a somewhat special literary value as illustrating the progress of clinical medicine.

I am, dear sirs, faithfully yours,

G. H. MAKINS,

Representative of the Clinical Society of London.

To ARTHUR LATHAM, Esq., M.D., and
H. S. PENDLEBURY, Esq.

Obstetrical Society of London,
20, Hanover Square, W., *December 6th*, 1905.

To the Hon. Secretaries, Union of Medical Societies.

Dear Sirs,—We have the pleasure to inform you that at a meeting of this Society, held on December 4th, 1905, the following resolutions were passed *nem. con.*

(1) "That this meeting is in favour of amalgamation."

(2) "That the Report of the Executive Committee be received and adopted subject to the amendments printed in red ink." (On the copy of Report enclosed.)

We are, dear Sirs, yours very faithfully,

M. HANDFIELD-JONES,
ROBERT BOXALL, } *Hon. Secs.*

[Enclosure.]

"The Council of the Obstetrical Society think that no member of any existing Society should be admitted as a member of the amalgamation until he has paid all arrears of his subscriptions.

"The Council of the Obstetrical Society propose that, for the present, their capital shall remain in the hands of their Trustees, with the addition of others to be appointed, with power—if in the course of five to ten years the financial position of the amalgamation should be assured—to hand it over. In the meanwhile they do not object to instruct these Trustees to hand over the interest.

"As regards books, they think that the Obstetrical Society's library should be kept distinct, under the title of 'The Rigby Library,' the name originally given to it (see 'Obstetrical Transactions,' vol. iii, 1862, p. 29) in memory of its founder and first benefactor, Dr. E. Rigby, jun., and remain the property of their Trustees as defined above.

"The Obstetrical Society has, since 1902, opened its doors to qualified medical women, and could not in honour consent to their exclusion from any of the privileges which they at present possess.

"The Council of the Obstetrical Society think that no Fellow or member should have the power of voting in any section, or sections, except those to which he has been elected.

"The Council of the Obstetrical Society think that the following words should be added after 'sections,' 'but no Fellow of the new Society who is not an elected member of the Section shall have the power to vote in that Section.'

"The Council of the Obstetrical Society think that the Fellows on the roll of the Obstetrical Society at the time of the amalgamation should have access to the Rigby Library, and power to borrow books from it without any extra library subscription.

"The Council of the Obstetrical Society think that each Section having invested capital should be represented by one of its Trustees on the Finance Committee.

"The Council of the Obstetrical Society think that the new 'Proceedings' of the Obstetrical Section should exhibit, for convenience of

reference, evidences of continuity with the present 'Transactions' of the Society, known as the 'Obstetrical Transactions,' and that arrangements for their publication should be left in the hands of the Council of the Section.

"The Council does not think a double publication of its 'Proceedings desirable.

"Other matters may occur to the Council of the Obstetrical Society in the course of the negotiations (some of which are already in view) such as the constitution of the Council of the Obstetrical and Gynæcological section, the mode of election of officers, and similar matters. When such occur the Council will communicate with the Amalgamation Committee."

Anatomical Society of Great Britain and Ireland,
Medical School, Charing Cross Hospital,
London, W.C., *November 8th*, 1905.

Dear Dr. Latham,—At a meeting of the Committee of Management of this Society held the other day, the Report of the Sub-Committee on the Union of Medical Societies was considered, and the Committee *reluctantly* came to the conclusion that, in view of the indefinite proposal in the Report with regard to anatomy, and in view of the scattered membership of this Society, and the smallness of its annual subscription (10s.), it was not possible for them, at present, to recommend the Society to take any action in the matter.

I am, faithfully yours,
CHRISTOPHER ADDISON, *Hon. Secretary.*

Medico-Psychological Association,
36, Queen Anne Street, W., *December 8th*, 1905.

Dear Sir,—In reply to your letter of December 6th, asking if I could give you a reply before December 15th as to the views of the Medico-Psychological Association on the Report of the Executive Committee as amended and adopted, I write to say that the question came before the Council of the Association at its meeting in November, and that a special sub-committee was appointed to consider the matter and report again to the Council at its next meeting in February. The question of union cannot be decided until each of the five Divisions of the Association (Scottish, Irish, Northern, South-Eastern, and South-Western) has had an opportunity of considering the subject, which will then have to be finally considered at at least two general meetings of the whole of the Association.

At present one can say nothing more than that there appear to be very great difficulties in the way of the Association as a whole forming a section of the proposed Academy of Medicine and surrendering its present freedom of action and its duties with regard to many important questions.

Yours faithfully,
Dr. ARTHUR LATHAM, 44, Brook Street, W. R. PERCY SMITH.

36, Queen Anne Street, W., *January 12th*, 1906.

Re Union of Medical Societies.

Dear Sirs,—In accordance with a resolution passed at the meeting of the Council of the Medico-Psychological Association on November 16th, "That a Committee be appointed to confer with the Executive Committee of the proposed union in order to see if objections which at present seem to the Council to be fatal can in any way be met," I write to say that the Com-

mittee thus appointed begs to forward herewith the following list of matters for consideration at the suggested conference between it and the Executive (now Organising) Committee.

1. The constitution of the Association is not merely that of a London medical society, but involves the existence of "Divisions" spread over the whole of the United Kingdom, and which are as follows:
   English Divisions, namely: (*a*) South-Eastern (including London); (*b*) South-Western; (*c*) Northern and Midland.
   Scottish Division.
   Irish Division.

This constitution has been revised quite recently, giving more power to the Divisions, each of which elects its own representatives on the Council of the Association, and holds divisional meetings in addition to the general meetings of the Association. All important questions, such as the present proposal, are referred to the Divisions, and it is highly improbable that the members of these Divisions will consent to form merely a sub-section of one section of the proposed union.

2. The Association is registered under the Companies Act, and therefore any amalgamation with other societies would involve "winding-up" and other legal formalities.
3. Many of the members of the Association would object most strongly to the Journal of the Association ('Journal of Mental Science') being dropped. The Journal is also a source of profit to the funds of the Association.
4. The Association holds certain trust funds for the purpose of awarding prizes to assistant medical officers of asylums, which it could not hand over to another body.
5. The Association has for many years taken an important position with regard to the training, examination, and registration of mental nurses, and a Select Committee of the House of Commons having recently recommended that a separate Register of registered asylum nurses should be kept by the central body, to which should be admitted nurses of good character holding the Association's certificate, we cannot take any step which might in any way interfere with our responsibility in this respect.
6. The Association has a Parliamentary Committee for the purpose of watching legislation in connection with the care and treatment of the insane and matters allied to it. At times, when Bills are passing through Parliament, it is necessary for the Parliamentary Committee to act quickly on its own decision and without reference to a General Meeting of the Association. There might be great difficulties in this if the Association were merely one section of the union.
7. It appears to the Committee that there might be great danger of the work of the Association being at times overruled by the votes of Fellows who might have no knowledge of, or interest in, the special work of the Association.

The Committee would be glad to have the opportunity of discussing these matters with the Organising Committee in time for the result to be laid before the Council of the Association at its meeting at Wakefield on February 23rd next. I am, dear Sirs, yours faithfully,

Dr. A. LATHAM,
H. S. PENDLEBURY, Esq.

R. PERCY SMITH.

Laryngological Society of London,
20, Hanover Square, W., *January 2nd*, 1906.

Dear Sir,—At a Special General Meeting of the Laryngological Society

of London, held Friday, December 1st, 1905, the enclosed reply *re* union of medical societies was proposed and adopted, and I was instructed to forward it to you. Yours faithfully,

Dr. Latham. PHILIP DE SANTI, *Hon. Sec.*

"Union of Medical Societies.

"Dear Sir,—The Laryngological Society of London is prepared to join in an amalgamation, provided chiefly that Laryngology stands as a separate section.

"Before giving adhesion to the scheme as outlined in the Committee's Report the Society, in order to estimate what changes would be necessary in its financial and practical working, would like information on the following points:

"(1) With regard to the disposal of funds, the Society, while not questioning that some method agreeable to all sections will be agreed upon, would like to have some notion, in outline at least, of this part of the scheme.

"For instance: After the annual expenses have been allowed by the Central Council, what power will any section possess over expenditure upon special volumes, illustrations, instruments, or other special purposes?

"(2) With regard to paragraph 8, conferring on a Fellow the privilege to attend all sections, two objections occur to us—one applying to all sections, and one especially to our own Society. Under paragraph 13—'Each section will have the power to make the necessary laws and regulations for the conduct of its business,' is it not possible that a candidate rejected by a section (under paragraph 13) may, by becoming a Fellow, force himself on this particular section under paragraph 8?

"The question especially affecting the Laryngological Society under this paragraph 8 is the possible accession of members many of whom may be unskilled in the use of the laryngoscope. The Society is one for the exhibition of cases only, and it has been found necessary in the past to restrict, in the interest of the patients, the number of possible examiners.

"Each candidate is, under our present rules, required to give evidence of special training before his name is placed before the Society for election. If a large number of Fellows having no special acquaintance with the technique were to attend the meetings, the patients—often private patients—would suffer, the work of the Society would be seriously interfered with, and even its very existence threatened.

"We would suggest that, while Fellows of the new Society who have not been elected members of our special section should enjoy all other privileges of members of the section, the right of examining patients should be restricted to those who had been elected members of our particular section by the section itself. Finally, we may add that, in our opinion, the term 'Royal Academy of Medicine' is preferable to any other.

"C. J. SYMONDS, *President.*

"P. DE SANTI, } *Hon. Secs.*
"H. DAVIS, }

"*December 1st*, 1905."

Odontological Society of Great Britain,
20, Hanover Square, W., *November 3rd*, 1905.

To the Honorary Secretaries of the Committee on Scheme of Amalgamation of London Medical Societies.

Gentlemen,—The questions contained in your letter having been carefully considered by the Council of the Odontological Society, I have embodied their opinion in the following report:

"The Council feel that while the Society would gain in prestige, there are many difficulties in the way of amalgamation according to the scheme proposed.

"The Society is at present in a strong financial position, having accumulated funds to the extent of £5000, as well as a fairly complete library, and a museum of a very representative and comprehensive character; they have also secured premises for the lodgment of their library and museum and provision for holding their meetings, under a lease from the Royal Medical and Chirurgical Society, which has thirty-one years to run and is not terminable by the lessors before that time has expired.

"Judging from the Accountants' Report, few of the other Societies can be in a similarly strong position, for the interest received from investments by the Odontological Society amounts to a third of the whole, and their assets (leaving out of account the library and museum) amount to one eighth of the whole (twenty-two societies contributing £40,000).

"They think that while, doubtless, a great future may lie before the Royal Academy of Medicine, its financial position in the immediate future as indicated by the Accountants' Report appears to be by no means so assured. The feeling existed at the Council that in surrendering their assets the Society would be contributing more than its share, and the privileges conferred seemed hardly commensurate.

"Under the scheme proposed the country members of the Odontological Society would pay the same subscription as at present, but they would be deprived of the use of their museum and of the use of the library, unless they paid an increased subscription, notwithstanding that the Society was handing over a clear income of £122 a year in addition to the members' subscription.

"Whilst anxious to identify itself with a movement which is calculated to advance the true interests of the profession in this country, the Odontological Society feels that its individual interests must be safeguarded on somewhat the following lines:

"(1) The Society's trust funds to be kept intact and safeguarded.

"(2) The museum to be retained.

"(3) The present library to be kept distinct and to be accessible to the country members without increasing their subscription.

"(4) The interest of the trust funds to be allotted to the maintenance of the museum and library.

"For the above reasons the Council cannot help feeling that some scheme of affiliation would be more acceptable to the Society.

"The altered conditions as proposed would no longer necessitate the exercise under the lease of the right to use the meeting-rooms, as that will be common to all the societies included in the amalgamation; the lease will therefore require such modification as to waive this right, whilst retaining a lease of the rooms for the museum and library with a corresponding deduction in the rent.

"If an arrangement of this kind is entered into it will constitute so important an item in the separate expenditure of the Odontological Society that the settlement of the terms of the new lease must constitute a condition precedent to the final adoption of any scheme by the Council of the Odontological Society, for under the scheme of amalgamation the Odontological Society, as a separate body, will have, in the future, no income for the maintenance of its museum and library beyond that which it derives from investments, and it will be necessary to consider whether this will be adequate.

"As an alternative, with regard to the library, whilst the Council of the Odontological Society desires its retention as a separate collection

of books, it might not be necessary that it should be located in a separate room (it might, for instance, occupy a bay in the general library), but this portion of the library should remain accessible to the existing country members of the Odontological Society without their being called upon for an increased subscription.

"If the library, with the foregoing exception, was to be thus treated as a portion of the general library it would, of course, be necessary that it should be kept up to date out of the funds of the Academy of Medicine."

I am requested to make it clear to the Committee that the above represents the opinions of the Council only, and that the matter must finally be laid before a general meeting of the members for decision.

I am, Gentlemen, Yours faithfully,

J. HOWARD MUMMERY,
Representative appointed by the Odontological Society.

British Balneological and Climatological Society,
20, Hanover Square, W., *December 4th*, 1905.

To the Secretaries of the Committee for the Union of Medical Societies.

Dear Sirs,—The Council of the British Balneological and Climatological Society have had under consideration the proposals of your Committee for the Union of Medical Societies. In response to the request of your Committee for a statement of the views of this Society, as one of the Societies included in the proposed union, I am instructed by the Council to submit:

"(1) That they welcome the proposal for a Royal Society or Academy of Medicine, and are prepared to recommend it to their Society on the definite understanding that the subjects of Balneology and Climatology are allowed to form a separate and distinct section. These subjects are sufficiently recognised as to form together an important branch of practical medicine, and should not, therefore, in the opinion of the Council, be relegated to a sub-section. The Society has a distinctive position in Great Britain and Ireland, and of necessity includes a large proportion of country Fellows (about three quarters of its total membership of 380). These are scattered widely amongst the health resorts of the country, and to provide an appropriate centre for all health resort practitioners is one of the main objects of its existence.

"(2) We submit further, therefore, that it is desirable to make some difference in the subscription between town members and country members, because it is obvious that the country members would not be able to utilise the library and premises of the new body as freely as those resident in town.

"(3) The circulation of the 'Journal of Balneology and Climatology, or 'Transactions,' is an essential part of the work of the Society, and we feel that no scheme of amalgamation would be altogether satisfactory which entailed the disappearance or absorption of this publication."

Finally, though we readily admit the advantages to be obtained by the work of amalgamation, and though we are anxious to further the scheme by every means in our power, we feel that it is only by preserving a certain individuality in the proposed larger organisation on the lines above indicated that this Society can hope to continue to fulfil its functions. Yours faithfully,

GEO. W. HAMILTON CUMMING, *President.*
W. V. SNOW, *Chairman of Council.*
SEPTIMUS SUNDERLAND, *Hon. Sec.*
LEONARD WILLIAMS, *Vice-President.*

British Gynæcological Society,
20, Hanover Square, W.,
October 24th, 1905.

Dear Sir,—I had a Special Council of the Gynæcological Society summoned to consider the Executive Committee's Report.

The Council wished to make these comments on the Report:

(1) The Council approves generally of the Report and the conditions contained in it.
(2) The Council approves of the name "Royal Society of Medicine."
(3) *Re* Clause 7, p. 5, the Council thinks the word "*men*" should be deleted and the clause read "the Fellowship of the Society shall be restricted to registered medical practitioners," etc.
(4) Clause 11, p. 6, the membership of Fellows in the two societies (nearly 500 in the Gynæcological alone) warrants a larger representation on the General Council of the Society.
(5) Only very distinguished men are elected Honorary Fellows of the British Gynæcological Society; the Council considers that the present Honorary Fellows should retain the Honorary Fellowship of the Royal Society.

I am also to add that as the British Gynæcological Society is an incorporated society it will be necessary to get the consent of the general body of Fellows before the proposed amalgamation can take place.

To this end it would be desirable that the two Societies—Obstetrical and Gynæcological—should have an understanding as to the conditions under which the union should be carried out.

I remain, Yours very faithfully,
A. LATHAM, ESQ. H. MACNAUGHTON-JONES.

The Neurological Society of the United Kingdom,
15, Upper Berkeley Street, Portman Square, W.,
December 7th, 1905.

Dear Sir,—I beg to inform you that at a Special Meeting of the Neurological Society, held on November 18th, the following resolution was carried:

"That the Neurological Society join in the amalgamation of medical societies, provided that there be a separate Neurological Section in the new Society."

I am, dear Sir, Yours faithfully,
ARTHUR LATHAM, Esq., M.D. LEONARD G. GUTHRIE, *Hon. Sec.*

British Laryngological, Rhinological, and Otological Association,
20, Weymouth Street, Portland Place, W., *November 21st*, 1905.

Gentlemen,—At the General Meeting of the British Laryngological, Rhinological, and Otological Association, held on November 10th, the question of the union of the medical societies was discussed, and the following resolution was passed:

"This Association is in entire accord with the general principle of the union of the medical societies, but finds itself unable to join in the present scheme unless—(1) women practitioners are granted equal rights with men, and (2) the individual sections are given a greater degree of autonomy than is indicated in the report."

I am, Yours truly,
CHICHELE NOURSE.

Dermatological Society of Great Britain and Ireland.

At a Special General Meeting, held at 11, Chandos Street, Cavendish Square, W., on Wednesday, November 22nd, 1905, the following resolutions were carried unanimously:

"That it is desirable (if the details of arrangement can be satisfactorily completed) that the Dermatological Society of Great Britain and Ireland should join the proposed union of medical societies.

"That this Society approves of the scheme for the formation of the new Society as formulated in the Report of the Executive Committee (pages 4–6), as amended and adopted at the meeting of the General Committee of Representatives of the Societies, held on July 19th, 1905.

"That this Society approves of the title of 'The Royal Society of Medicine' for the new Society."

EDWARD STAINER, } *Hon. Secs.*
SPENCER HURLBUTT, }

Dermatological Society of London,
61, Wimpole Street, Cavendish Square, W.,
January 31st, 1906.

Dear Latham,—This Society cordially approves the scheme for the union of the existing medical societies in accordance with the suggestions of the Executive Committee's Report, amended and adopted by the General Committee of Representatives of the Societies held on July 19th, 1905, and is willing to join, provided satisfactory arrangements can be made.

Upon the question as to the proposed name for the new amalgamated Society, a majority voted for the title of "Royal Academy of Medicine."

Believe me, yours sincerely,
E. GRAHAM LITTLE, *Junior Sec., Derm. Soc. Lond.*

West London Medico-Chirurgical Society,
124, Harley Street, W., *September 25th*, 1905.

Union of Medical Societies *re* West London Medico-Chirurgical Society.

Dear Sirs,—In reply to your circular of even date, I take it that under the scheme proposed this Society (West London Medico-Chirurgical Society) cannot take any part.

If I am wrong, perhaps you will inform me, and I would bring the matter before the Society.

Yours truly,
W. MCADAM ECCLES.

Dr. ARTHUR LATHAM, and
H. S. PENDLEBURY, Esq.

British Electro-Therapeutic Society,
22, Queen Anne Street, Cavendish Square, W.,
October 30th, 1905.

Union of Medical Societies.

At the Ordinary Meeting of this Society, held at 11, Chandos Street, on Friday, October 27th, 1905, it was moved by Dr. Lewis Jones, seconded by Dr. Reginald Morton, and carried:

"That the British Electro-Therapeutic Society is in favour of joining the proposed union of the medical societies, but would like to see the establishment of a special Electro-Therapeutic or Physio-Thera-

peutic sub-section in such a united Society, for the reason that such a sub-section would be a meeting-place for members interested in a well-defined sphere of medical work."

REGINALD MORTON, *Hon. Secretary.*

Medical Officers of Schools Association,
33, Harley Street, W., *December 7th*, 1905.

Dear Sir,—In reply to your letter, December 6th, the Council of the Association have considered the matter, but, owing to the rules of the Society, are unable to send any reply until after the General Meeting, which is held in April.

Yours faithfully,
FREDERICK E. BATTEN, *Hon. Sec.*

Life Assurance Medical Officers' Association,
57, Harley Street, W., *December 9th*, 1905.

To the Honorary Secretaries.

Dear Sirs,—At a meeting of the Life Assurance Medical Officers' Association, held on December 6th, I was requested to forward to you for the information of the members of your General Committee a copy of a resolution unanimously adopted at that meeting.

The resolution reads as follows:

"That Dr. Heron be empowered to convey to the Central Committee that this Society will be pleased to join '(in the proposed amalgamation) on condition that it shall maintain its complete autonomy as a separate section.'"

I am, yours very truly,
G. A. HERON.

Medico-Legal Society,
5, Essex Court, Temple, E.C., *December 16th*, 1905.

Dear Sir,—At a meeting of the Council of the Medico-Legal Society it was agreed that:

"The Medico-Legal Society be recognised in the scheme for the amalgamation of the societies, but that it is premature to make any binding proposal."

I shall be at the meeting on Tuesday.

Yours faithfully,
R. HENSLOWE WELLINGTON.

Otological Society,
26, Wimpole Street, W., *October 21st*, 1905.

Re Union of Societies.

Dear Sirs,—On the other side I send you the reply of the Council of the Otological Society to your second question—"Under what conditions your Society (Otological Society) would be prepared to join such a scheme as in the printed report."

Yours very truly,
URBAN PRITCHARD.

Drs. Latham and Pendlebury.

The Council of the Otological Society would recommend the Society to join the Union Scheme on the following conditions:

"1. That there shall be separate Sections for Otology and Laryngology. (*Each section would take Rhinology.*)

"2. That paragraph 8, page 5 of the Report, be amended by adding after 'any of its sections' 'after having been duly elected by the members of such section.'

"3. That paragraph 13, page 6, be amended by adding at the end—'and the election of its own members.'"

The foregoing three amendments are regarded as essential, but the Council recommend the following further alterations:

"4. That the name of the new body should be 'The Royal Academy of Medicine,' and that the sections be called affiliated societies.

"5. To paragraph 5, page 5, adding at the end, 'of the section.'

"6. Page 7. That the first paragraph be omitted, as the Council of the Otological Society consider that the author of a paper should have a voice on the question of the section in which his paper is to be read."

The Society for the Study of Inebriety,
120, Harley Street, W. *December 7th*, 1905.

My dear Sirs,—Thanks for your communication of 6th inst.

The matter has been considered by our Council.

There seems to be difficulty in our being able to comply with suggested requirements, for:

1. Our minimum annual subscription is only 5*s*., which not only allows of attendance at each quarterly meeting, but provides for free delivery of the quarterly journal.
2. Non-medicals are admitted to the Society as Associates.

I am, yours faithfully,
T. N. KELYNACK, *Hon. Sec.*

The Society for the Study of Disease in Children,
50, Wimpole Street, *October 10th*, 1905.

Dear Sir,—In answer to your inquiry as to whether the above-named Society would be willing to join in the amalgamation, I am unable to give any definite answer. The scheme has been before the Council, and they decided that until it was known whether the Royal Medical and Chirurgical Society and the Medical Society could arrange a union it would be useless for this Society to consider the matter. Yours faithfully,

To Dr. LATHAM. R. CLEMENT LUCAS.

Society of Anæsthetists,
20, Hanover Square, W.,
December 7th, 1905.

Dear Sirs,—I have to inform you that the proposed amalgamation scheme has been considered by the Society of Anæsthetists.

The Society of Anæsthetists is willing to join the proposed new Society on the basis outlined in the report on the following conditions:

1. That no Fellow, unless elected a member of the Section, be permitted to vote either for the election of officers or upon any alteration of the Rules of the Section.
2. That women be eligible for the Fellowship of the new Society.
3. That the Council of the Section has the sole right to accept or refuse all papers and communications pertaining to it.

I hope to be present at the meeting on Tuesday, December 19th.

Yours truly,

ARTHUR LATHAM, Esq., M.D. R. J. PROBYN-WILLIAMS.

Epidemiological Society of London,
11, Chandos Street, Cavendish Square, W.,
November 18th, 1905.

Dear Sir,—A Special Meeting of the Epidemiological Society was held on November 10th, 1905, for the consideration of the Report of the General Committee of Representatives on the proposed Union of London Medical Societies, and the conclusions reached were as follows:

"(1) The Epidemiological Society attaches great importance to maintaining continuity of name as well as of work, and from that point of view would strongly advocate the term *Academy* being applied to the united body of societies as a whole, the Epidemiological Society being designated a Society.

"(2) The Epidemiological Society assumes it is contemplated that the election of the Council and Officers (as well as Members) of each Section will be made by the Section itself. I am instructed to enclose a list of the Officers of the Society, showing the basis on which it is organised.

"(3) The success of the meetings and discussions of the Epidemiological Society has been found to depend largely upon the fact that it has been the practice of the Council and Officers of the Society to discriminate among papers offered, to select the subjects best fitted for discussion, and to invite contributions from eminent authorities. This course is, in the opinion of the Society, preferable to that suggested in the sixth paragraph of page 6 of the Report of the General Committee of Representatives.

"(4) The Epidemiological Society attaches great importance to the continuance of the present practice of the Society, namely, that all papers shall be printed in proof before the meetings, and that the papers (and, if deemed of sufficient interest by the Council of the Society, the discussion also) shall appear in full in the Annual Volume, a copy of which is sent to every subscribing member. The Society regards this condition as essential, and desires to suggest further that the Editorial Committee of the united body of Societies should include a representative of each Section.

"(5) The Epidemiological Society, in the event of union, would desire to retain, subject to any formal ratification that may be prescribed, the right to elect Honorary and Corresponding Members, thereby establishing relations with all the leading colonial and foreign epidemiologists.

"(6) The Jenner Medal, which bears the name of the Epidemiological Society, and is awarded by the Society as an exceptional distinction, is identified so closely with epidemiology that—again in the event of union—it seems desirable that the initiative in any future award should still rest with the Section.

"(7) Subject to the foregoing conditions, the Society approves generally the proposed union of medical societies."

Yours truly,
W. H. HAMER, *Hon Sec.*

H. S. PENDLEBURY, Esq., F.R.C.S.,
44, Brook Street, W.

SOME SUGGESTIONS FROM THE HON. SECRETARIES FOR THE CONSIDERATION OF THE ORGANISING COMMITTEE.

DEAR SIR,

In our capacity of Secretaries to the various committees of the above we have received from different sources a number of expressions of opinion concerning the organisation and details of the proposed new society. We therefore venture to formulate some of the conclusions which we have reached concerning the more controversial matters at stake, in the hope that by so doing we may possibly shorten the labours of the Organising Committee.

Yours faithfully,

ARTHUR LATHAM,
HERBERT S. PENDLEBURY.

44, *Brook Street, W.*
February 28th, 1906.

The replies of the various societies, embodying criticism on the scheme as outlined in the Report of the Executive Committee may be analysed as follows:

(1) *Acceptances on Lines which are likely to be met.*

Royal Medical and Chirurgical, Pathological, Clinical, Gynæcological, Neurological, Laryngological, Rhinological and Otological, Dermatological of Great Britain, Dermatological of London, Electro-Therapeutic, Life Assurance Officers, Anæsthetists and Epidemiological 12

(2) *Possible Acceptances on Conditions requiring negotiation.*

Medical, Obstetrical, Laryngological, Odontological, Balneological, Medico-Legal, and Diseases of Children 7

(3) *Probable Refusals.*

Anatomical, Medico-Psychological, and Study of Inebriety 3

With regard to this class it may be stated as extremely probable that the leading anatomists, physiologists, and alienists would be prepared to join corresponding sections *after* the new society was constituted.

The answers to the post-card inquiry so far received show that at least 600 members of our profession are willing to become Fellows of the new society, in addition to the existing 440 Fellows of the R.M.C.S.

We are convinced, from interviews with many individuals and from many letters, that there is a very general feeling in favour of the new society, and especially so on the part of the younger members of the profession.

It would appear that it is possible to form the new society on a lasting basis, although it may not embrace all the societies originally invited.

There are certain difficulties which will have to be met by the Organising Committee:

A.—Those which affect the procedure, etc., of the new society.

B.—Financial.

C.—Objections or suggestions raised by various societies.

A.—*Those which affect the Procedure, etc., of the New Society.*

As examples we would give the method of obtaining a Royal Charter, the name of the new society, the rules and procedure, and the method of election.

We would suggest that such questions should be left for decision until the new society has been formed. If this course were adopted much time and discussion would be saved.

B.—*Financial.*

The assets and financial position of the various societies have been ascertained with some exactitude. The revenue from subscriptions to the new society remains somewhat doubtful. The reply to the post-card referendum is suggestive, but nearly 3000 individuals have not answered. This result is in part due to the fact that some societies have not called general meetings to discuss the question at issue. Those societies which have funds and which consider the financial position of the proposed society not sufficiently sound, may not alter their opinions on the facts obtained by the replies to our post cards.

The following table shows *approximately* the assets of the various societies.

SOCIETIES WITH FUNDS.

		Approximately.
[1] Clinical	£640 Consols	£600
[1] Obstetrical	£600 Consols, £807 L.C.C. 3%, £1641 Midland Railway Debentures, £146 North British Railway	£4500
[1] Odontological	£5200 Consols	£5000
Pathological	£854 Consols	£800
[1] Diseases of Children ...	£288 Consols	£200
[1] Ophthalmological ...	£500 Ramsgate Corporation, £525 East Indian Railway Annuities ...	£1000
[1] British Gynæcological ...	£6 Caledonian Railway Debentures, £270 Grand Trunk Railway Debentures	£270
[2] Medical Society	£637 New Zealand Stock, £277 Victoria Stock, £12,000 Leasehold and Freehold ...£12,914 Less Debentures and Loan ... 2950	10,000
[2] Royal Medical and Chirurgical	£326 New South Wales, Leasehold and Freehold, £51,566...£51,892 Less Debentures, etc.... ... 33,600	18,000

[1] See Appendix B, p. clviii.

[2] Value of contents, etc., is not included.

This table shows that the societies in possession of £1000 or upwards are the Obstetrical, Odontological, Ophthalmological, Medical, and R.M.C.S.

It is worthy of remark that these societies are also the societies which possess libraries.

It is evident from the replies of the societies that the Medical, Obstetrical, and Odontological are not prepared to "pool" their funds under suggested conditions. The Ophthalmological Society has sent no reply to us, but we understand that its members are not in favour of the amalgamation on the lines of the Executive Committee's Report.

A possible way out of the difficulty outlined above would be to place all funds brought into the amalgamation in the hands of three trustees, to be selected by the societies with funds, for a period of five years. If at the end of this time the new society was well established, from a financial standpoint, the funds could be paid over to the new society. If the financial condition of the new society was unsatisfactory at the end of five years, the funds could be paid back to their original owners.

The establishment of such a trust fund would probably save the time of the Organising Committee, and possibly attract certain societies which otherwise would refuse to join. Further, it would only be necessary for the Organising Committee to negotiate with the societies as to the allocation of the interest on the money handed by them to the trust fund, in the matter of grants for specific purposes, such as the upkeep of the Odontological Museum.

The general income of the new society from subscriptions, etc., would naturally be in the hands of its own Finance Committee.

If such a course were adopted, and the Medical Society joined the proposed amalgamation, there would be a further advantage, for the sections of the new society could then meet in both Chandos Street and Hanover Square. If at the end of five years the financial position of the new society proved to be sound, the premises of 20, Hanover Square, could be enlarged and the property in Chandos Street realised.

Against such a course as the formation of a trust fund are the obvious objections that it is expedient rather than business-like, and would lead to increased legal expenses and increased upkeep.

Another point of financial concern is the amount of subscription on the part of country members. If country members are to receive full copies of the 'Proceedings' in addition to other privileges, it is doubtful whether it would be possible to make their subscription lower than that of town members.

C.—*Objections or Suggestions raised by various Societies.*

It is impossible to give any rational sequence to these, hence we take the more important *seriatim*.

(1) The fear on the part of some societies that their corresponding sections might have their business interfered with by fellows would probably be overcome by the following:

"That all members of a society taking part in the amalgamation, who desire to do so, shall become fellows of the society without election."

"That all members of a society taking part in the amalgamation, who desire to do so, shall become members of the corresponding section of the new society without election, whether they join as fellows or not."

"That only original members of a section and those who are subsequently elected as members of it have power to vote on matters directly affecting the affairs of that section."

(2) It is felt by some individuals that those members of the Medical or Royal Medical and Chirurgical Societies who did not wish to become fellows would be harshly treated if they were not allowed to join both the medical and the surgical sections of the new society at one inclusive subscription of £1 1*s*. per annum. There are only 260 members of the two societies who pay as little as £1 1*s*. in subscriptions at present; probably therefore the concession would be made to those who join at the time of the amalgamation.

(3) The admission of women to the fellowship has already been settled on the lines that at present women cannot be admitted as fellows, but that nothing in the Charter shall prevent them from being admitted at some future date.

(4) The Laryngological Society object to any one not a member of the section being allowed to examine the patients shown with a laryngoscope. This would probably be met by the formation of a laryngological club in addition to the section.

(5) The Balneological, Otological, Electro-Therapeutic, and Life Assurance Societies are unlikely to join unless they have separate sections. This point could probably be conceded.

(6) Societies with honorary fellows could be allowed as sections to continue this association with those already elected, but the election of honorary fellows to the new society cannot be dealt with until the society has been constituted.

(7) Societies with libraries are not prepared to debar from the use of them those of their members who join as members and not as fellows. Any arrangement of libraries in separate rooms, or in the bay of the existing library, would be difficult. The question might perhaps be solved on the following lines, without much financial loss:

"Existing members of those societies, viz. R.M.C.S., Medical, Ophthalmological, Obstetrical, and Odontological, which bring libraries into the amalgamation shall have the privilege of using the general library without payment of the yearly library subscription."

(8) There are various objections raised on the questions of papers and publications.

Probably papers will in the first instance have to go to the section suggested by their author. If the Council of the section consider that other sections, or the whole society, might probably join in the discussion, they would have power to communicate with the necessary committees.

One society suggests that all papers should be in proof before being read; such a procedure would tend to prompt publication.

It does not appear feasible that the 'Proceedings' of the new society can be published separately by the sections, or in different forms, which aim at continuity with existing publications. An editorial committee must be formed for this purpose, but the printing, etc., of the 'Proceedings' can be so arranged that a member of any section can keep a record of that section alone.

Societies which own or partly own journals will probably have to make their own arrangements with regard to these, quite apart from the question of amalgamation.

REPORT OF THE ORGANISING COMMITTEE TO THE GENERAL COMMITTEE OF REPRESENTATIVES OF THE SOCIETIES.[1]

YOUR Committee (consisting of Sir William Church, Chairman; Sir R. Douglas Powell, Dr. Champneys, Dr. Garrod, Dr. Head, Mr. Langton, Mr. Goodsall, Mr. Makins, and Mr. Symonds, together with Dr. Latham and Mr. Pendlebury as Honorary Secretaries) held its first meeting on February 8th, 1906, when Sir F. Treves (who, to the Committee's regret, was unable to serve), Dr. Allchin, Dr. Frederick Taylor, and Mr. Laurence Read were co-opted members.

Your Committee carefully considered the replies received from the various societies, which had been requested to give their views on the Report of the Committee of Representatives of December 19th, 1905, and appointed delegates to meet delegates of these societies, to negotiate with regard to any points of difference. The reports of these delegates were considered, and the suggested regulations on page 4 (*now* cliv) *et seq.* form the basis of what your Committee believes will be acceptable to the larger number of societies.

The central ideas of those who first suggested a union of societies were, that such a union would add to the prestige of British medicine, would tend to bring those engaged in special

[1] This Report was submitted at a Meeting of the General Committee of Representatives on July 17th, 1906, and adopted as amended by the alterations which are shown in footnotes.

branches of medicine or surgery into more intimate relations with those whose work was of a more general character, and would be a great convenience to the profession. Your Committee has endeavoured to meet the views of the various societies, whenever it has been possible to do so without destroying the original intentions of the Committee of Representatives. Your Committee would especially draw attention to the suggestions that—

(1) All male members of those societies which take part in the amalgamation can join the new society on its formation as members or fellows without election.

(2) All women members of a society taking part in the amalgamation, who desire to do so, shall become members of the corresponding section or sections of the new society on its formation without election.

(3) Sections of the new society shall be self-governing as far as possible, and shall have direct representatives on the Council of the society and on the Editorial Committee. The expenditure of the individual sections shall be subject to the control of the Finance Committee of the general Council.

(4) Any member of any section shall receive for his subscription a copy of the 'Proceedings,' not only of his own section, but of all sections of the Society.

Your Committee appointed a Finance Sub-Committee, consisting of Dr. Frederick Taylor (Chairman), Dr. Head, Dr. Latham, Mr. Goodsall, and Mr. Pendlebury, The report of this Sub-Committee was adopted *nem. con.* by your Committee, and is incorporated in the following pages.

If both the Medical and Royal Medical and Chirurgical Societies join the proposed union, the number of rooms which would be at once available for meetings, both for the general business of the Society and for other purposes, is as follows: at 20, Hanover Square, two meeting-rooms, and five other rooms, at present occupied by the Odontological and Obstetrical Societies; at 11, Chandos Street, two meeting-rooms and one other room, at present occupied by the Ophthalmological Society. Many of the existing leases of the Royal Medical and Chirurgical Society terminate in 1911, and it is probable that some other tenants could be persuaded to give up their rooms almost immediately if the above accommodation did not prove sufficient.

The Finance Report, with its explanatory appendices, shows that a balance of income over expenditure may be expected to the amount of £1200, for the provision of a fund which may be used for the redemption of existing debentures or for the formation of a building fund. It will be noticed that 1040 individuals, or 57·7 per cent. of those who answered the post-card inquiry (1800), stated that they would join as Fellows, although under present conditions only 1300 (*i. e.* 26 per cent.) of the members of societies (5000), whose accounts have been investigated, pay

more than £1 1*s*. per annum. In estimating the income from those who have not answered the post-card inquiry, no allowance has been made for any individuals becoming Fellows, or joining more than one section, or paying a library subscription. If, however, the 57·7 percentage were maintained amongst those who may be expected to join, although they did not answer the post-card inquiry, the balance of income over expenditure would be increased by (1557 × £2 2*s*.) £3269—*i. e.* would become £4469.

It is necessary to explain why your Committee has included an estimate of income and expenditure excluding the Medical Society. The representatives of the Medical Society on your Committee are not disposed to accept the valuation which has been twice placed on the Royal Medical and Chirurgical Society's property by independent valuers. Accordingly it was suggested that the Presidents of the Medical and Royal Medical and Chirurgical Societies should together appoint a valuer to make a further valuation. The Royal Medical and Chirurgical Society intimated their willingness to agree to this suggestion, provided that the Medical Society would bind itself to join the proposed union in the event of the present valuation of the property of the Royal Medical and Chirurgical Society being confirmed. The Medical Society has had this offer before it for some time, but up to the present has sent no answer.

The expenses of the Executive Committee and of this Committee have been, or will be, met by the various societies which have representatives on the Committee of Representatives, with the exception of the Society for the Study of Disease in Children, which so far has declined to pay its estimated share.

Your Committee is of opinion that a union of societies on the lines laid down in the following pages would be successful, and that the aims of those who initiated the movement would be realised. Your Committee suggests that this Report should be laid before the various societies, and that those societies which approve it should each appoint[1] a representative to form a committee, to draw up rules, and to deal with the necessary formalities of amalgamation. Your Committee further suggests that these representatives should form the first Council of the new society and have power to co-opt other members.

SUGGESTED REGULATIONS, TOGETHER WITH CERTAIN FINANCIAL DETAILS.

Title of Society.

The decision with regard to the title of the new society, and such questions as the election of fellows and rules of procedure, shall be left to the vote of those societies which amalgamate.

[1] At the Meeting of the General Committee on July 17th, 1906, the words "before December 7th next" were inserted here.

Housing.

The society shall be housed at 20, Hanover Square, and at 11, Chandos Street.

Constitution.

The society shall consist of fellows, honorary fellows, members [1] and honorary members.[1]

All male members of a society taking part in the amalgamation, who desire to do so, shall become fellows of the new society without election.

An original fellow of the new society shall have no power to vote in the business of any section unless he is an original member of that section, or unless he has been duly elected to it subsequent to the formation of the new society.

All members of a society taking part in the amalgamation who desire to do so shall become original members of the corresponding section without election, whether they join as fellows or as members.

Members of a society taking part in the amalgamation cannot become members of any section or sections, other than those which correspond to the society or societies to which they belong at present, unless they are duly elected members of such sections after the formation of the new society.

All women members of a society taking part in the amalgamation, who desire to do so, shall become members of sections of the new society in precisely the same manner as male members.

Honorary members of any society taking part in the amalgamation shall retain their present privileges, but the election of honorary fellows of the new society must be left until the society is formed.

The society shall consist of the following sections which represent existing societies, but the society shall have power to add new sections, or to modify existing ones with the consent of the members:

(1) Anæsthetic.
(2) Balneological and Climatological.
(3) Clinical.
(4) Dermatological.
(5) Diseases of Children.
(6) Electro-Therapeutical.
(7) Epidemiological.
(8) Laryngological.
[2] (9) Medical.

[1] At the Meeting on July 17th, after "members" and after "honorary members" the words "of sections" were inserted.

[2] At the Meeting on July 17th a section for Life Insurance was adopted. In the final list therefore it appears as No. 9, Medical as No. 10, and so on.

(10) Neurological.
(11) Obstetrical and Gynæcological.
(12) Odontological.
(13) Ophthalmological.
(14) Otological.
(15) Pathological.
(16) Surgical.
(17) Therapeutical.

It is hoped that in the early future an anatomical and physiological section and a section of preventive medicine may be formed.

The Medico-Psychological Association and the Medico-Legal Society, although not at present able to form sections in the new society, hope to do so in the future.

Finance.

The entire management of the funds of the society shall be in the hands of a finance committee, subject to and acting as a subcommittee of the general council.

Those societies which bring in property, together with a library, namely, the Medical, Royal Medical and Chirurgical, Obstetrical, Ophthalmological, and Odontological Societies, shall each choose a direct representative, who shall have a seat on the first finance committee of the new society.

The invested funds and other property of any society joining in the amalgamation shall at once become the property of the new society.

All funds left in trust for prizes and lectureships shall remain in trust and shall at once become the property of the new society, which shall administer them in the terms of the existing trusts.

Estimate of Income and Expenditure of the New Society with Explanatory Appendices.

Estimate of Income and Expenditure.

I.—Including the Medical Society.

Income.[1]

	£	s.	d.
(*A*) From Subscriptions	6800	0	0
(*B*) From Investments	350	0	0
(*C*) From Rents—			
(*a*) Royal Medical and Chirurgical Society	2000	0	0
(*b*) Medical Society	700	0	0
From Entrance Fees	150	0	0
	£10,000	0	0

[1] An estimated income from advertisements in the 'Proceedings,' amounting to £555, has been ignored for the moment.

Expenditure.	£	s.	d.
Interest on £33,300 Debentures at 3 per cent. R.M.C.S. ...	999	0	0
Interest on £2300 4 per cent. Debentures Medical Society...	92	0	0
(*D*) Maintenance—			
(*a*) R.M.C.S.	2050	0	0
(*b*) Medical Society	900	0	0
Library—			
(*a*) R.M.C.S.	600	0	0
(*b*) Medical Society	25	0	0
(*E*) 'Proceedings' of the new society, 10 issues per annum, including cost of distribution and illustrations	2286	0	0
Editor	500	0	0
Increase of salaried officials (at present £1048)	500	0	0
[1] Additional expenses for printing, stationery, library, sectional meetings, and other contingencies	848	0	0
Balance for Depreciation, Reserve and Building Fund, and Redemption of Debentures	1200	0	0
	£10,000	0	0

[1] On an average of ten years these additional expenses amounted to £457.

(*F*) Estimate of Income and Expenditure.

II.—Excluding the Medical Society.

Income.	£	s.	d.
From Subscriptions	6527	0	0
From Investments...	350	0	0
From Rents...	2000	0	0
Entrance Fees	150	0	0
	£9027	0	0

Expenditure.	£	s.	d.
Debentures R.M.C.S.	999	0	0
Maintenance R M.C.S.	2050	0	0
Library R.M.C.S.	600	0	0
'Proceedings' of new society	2286	0	0
Editor	500	0	0
Increase of salaried officials	500	0	0
Additional meeting expenses, extra printing, stationery, library, and contingencies	848	0	0
Balance	1244	0	0
	£9027	0	0

Appendix A.

Income from Subscriptions of the New Society.

Present reply post-cards show:	£	s.	d.
1040 fellows at £3 3s.	3276	0	0
150 two or more sections	315	0	0
300 one section...	315	0	0
30 one section and Library	63	0	0
1520 total promised per annum	£3969	0	0

Out of 5000, 1800 have replied, viz. 1520, as above; the others are doubtful, dead, gone away, compounded, country, and refusals.

The Medico-Psychological Association will not join at present. This has 500 members who belong to no other society.

There are left, therefore, 5000 − 2300 = 2700 members who will come in as members of sections, or possibly as fellows, if their society joins.

Total income from subscriptions:	£	s.	d.
(1) Promised as above	3969	0	0
(2) Join with their society as members	2835	0	0
	£6804	0	0

N.B.—These figures may be increased, for—

(1) The Medico-Legal Society is not included in these figures, nor the Anatomical, nor the Physiological Society, although either may join in the future.

(2) Many counted above as refusals or doubtful will join if their society joins.

(3) All the fellows of the Royal Medical and Chirurgical Society have not answered the post-card.

(4) A certain proportion of the 2700 included as *members* may reasonably be expected to join as *fellows*.

APPENDIX B.

INVESTMENTS.

	£	s.	d.
Royal Medical and Chirurgical Society, New South Wales Stock	326	7	0
Mr. Gant's Legacy	500	0	0
Gynæcological Society, Railway Stock	255	0	0
Clinical Society, Consols	668	0	0
Obstetrical Society, Consols and L.C.C....	2550	0	0
Odontological Society, Consols	5070	0	0
Ophthalmological Society, Consols	520	0	0
Pathological Society, Consols	800	0	0
Children's Society, Consols	341	0	0
	£11,030	7	0

It is probable that some changes have taken place in these investments since the auditors went through the accounts.

APPENDIX C.

ROYAL MEDICAL AND CHIRURGICAL SOCIETY.

Memorandum re *Tenancies*.

Tenants.	*Rent.*	*Term.*
*1.	£200	21 years from 1890.
2.	170	21 years from 1890.
3.	65	21 years from 1904.
4.	45	Yearly.
*5.	52	Yearly.
6.	230	21 years from 1890.
*7.	105	Yearly.
8.	75	5 years from 1904.

Tenants.	*Rent.*	*Term.*
9.	£15	Yearly.
10.	165	7 years from 1904.
11.	25	Yearly.
12.	350	66½ years from 1890.
13.	150	Yearly.
*14.	42	3 years from 1905.
15.	21	Yearly.
16.	130	21 years from 1890.
*17.	21	3 years from 1905.
*18.	73	Yearly.
19.	70	Yearly.
*20.	12	Yearly.
*21.	273	21, 28, or 35 years from 1901.
22.	26	3 years from 1905.
23.	58	Yearly.
24.	70	3 years from 1902.
25.	160	7, 14, or 21 years from 1902.
26.	162	7, 14, or 21 years from 1902.
	£2765	
Sundry lettings of meeting-rooms, average ...	65	
	£2830	

* Are societies willing to take part in the union after negotiation, and are therefore excluded from our estimate of income from rents.

MEDICAL SOCIETY OF LONDON.

Income derived from Rents and Occasional Lettings.

	£	s.	d.
1. On lease expiring in 1914...	250	0	0
2. „ „ 1915...	160	0	0
3. Annual tenancy	70	7	6
*4. „ „	80	0	0
5. „ „	40	0	0
6. „ „	45	0	0
7. „ „	5	5	0
*8. „ „	16	16	0
*9. „ „	21	0	0
*10. „ „	15	15	0
11. „ „	10	10	0
12. „ „	24	0	0
13. „ „	5	5	0
14. On lease expiring in 1909...	90	0	0
	833	18	6
Occasional lettings	110	0	0
	£943	18	6

* Are societies willing to join in the union after negotiation and are excluded from our estimate.

Income derived from Rents and Occasional Lettings and Fellows' Subscriptions for the past Five Years.

	Fellows' Subscriptions.			*Rents and Occasional Lettings.*		
	£	*s.*	*d.*	£	*s.*	*d.*
1900–1901 Session	532	16	0	 876	16	0
1901–1902 „	552	16	6	 886	0	6
1902–1903 „	543	18	0	 895	12	6
1903–1904 „	599	0	6	 944	18	0
1904–1905 „	603	3	6	 954	1	10

In our estimate of income from rents we have also excluded occasional lettings, though it is probable that this source of income will remain after the new society is formed.

APPENDIX D.

MAINTENANCE.—ROYAL MEDICAL AND CHIRURGICAL SOCIETY.

	£	*s.*	*d.*
Rent, Rates, Taxes, and Insurance	198	0	0
Salaries of Staff and Accountant	704	0	0
House Servants, Porters, Cleaners	352	0	0
Lighting, Warming, and Cleaning	192	0	0
Printing and Stationery, Stamps	251	0	0
Meeting Expenses	43	0	0
Repairs and Alterations	141	0	0
Telephone	15	0	0
Lift	34	0	0
Miscellaneous Disbursements	55	0	0
Audit Fee	10	10	0
Architect's Fees	16	16	0
	£2012	6	0

MAINTENANCE.—MEDICAL SOCIETY.

	£	*s.*	*d.*
Rent, Rates and Taxes	460	0	0
Salaries, Wages, and Annuity	235	0	0
Meeting Expenses	15	0	0
Repairs	20	0	0
Printing	25	0	0
Lighting, Heating, and Cleaning	90	0	0
Miscellaneous	55	0	0
	£900	0	0

APPENDIX E.

MONTHLY 'PROCEEDINGS'—COST.	£	*s.*	*d.*
Cost of composing 256 pages small pica solid, supplying paper, printing, and binding in wrapper (small type footnotes and tabular matter extra). 6,000 copies at £8 8*s.* a sheet of 16 pages	134	8	0
Allowance for corrections at 1*s.* 6*d.* per page	19	4	0
Cost of distribution at 2*d.* a copy	50	0	0
Allowance for illustrations	25	0	0
	£228	12	0

Therefore cost of ten issues ... £2286.

Note.—Number of words per page, 610; estimated output of words 1,561,600. The annual output of words under present conditions is estimated at 1,580,000.

APPENDIX F.

FINANCE, EXCLUDING MEDICAL SOCIETY.

Loss of Income.

	£	s.	d.
260 Fellows of Medical Society belonging to that Society only	273	0	0
Rents, as per estimate Appendix C.	700	0	0
	£973	0	0

Decrease of Expenditure.

	£	s.	d.
Maintenance, as per estimate	900	0	0
Library	25	0	0
Interest on debentures	92	0	0
	£1017	0	0

The society will also be relieved of the redemption of £2300 4 per cent. debentures. But there will be two meeting-rooms and one other room *less* for the purposes of the new Society.

APPENDIX G.

MEMBERS OF VARIOUS SOCIETIES WHO BELONG TO ONLY ONE SOCIETY.

British Balneological and Climatological Society	236
British Electro-Therapeutic Society	107
British Gynæcological Society	320
Clinical Society of London	131
Dermatological Society of Great Britain and Ireland	35
Dermatological Society of London	9
Epidemiological Society of London	121
Laryngological, Rhinological and Otological Association	37
Laryngological Society of London	49
Life Assurance Medical Officers' Association	25
Medico-Psychological Association of Great Britain and Ireland ...	514
Medical Society of London	260
Neurological Society of the United Kingdom	73
Obstetrical Society of London	354
Odontological Society of Great Britain...	364
Ophthalmological Society of the United Kingdom	311
Otological Society	21
Pathological Society of London	219
Royal Medical and Chirurgical Society of London	203
Society of Anæsthetists	52
Society for the Study of Disease in Children	135
Therapeutical Society	137
	3713

General Government of the Society.

The general management of the Society shall be under the control of a General Council, consisting of the President, the Presidents of the various sections, two Treasurers, two Librarians, two Secretaries, and eight other fellows.

The Society shall meet from time according as the Council shall direct—

(1) To discuss the general business of the Society.

(2) To discuss subjects of medical and scientific interest.

After the formation of the new society the fellowship of the society shall be restricted to men who are registered medical practitioners of the British Empire, and to men whose scientific attainments are satisfactory to the General Council.

On the formation of the new society women shall not become fellows, but care shall be taken that nothing in the constitution of the new society shall prevent the society from passing the necessary bye-laws for the purpose of admitting them as fellows in the future.

A fellow shall pay, subject to any future bye-law, an annual subscription of £3 3*s*., and shall have the right to attend all meetings of the society or of any of its sections, and shall have full use of the library. After the society is constituted (*i. e.* after a date to be subsequently determined) a new fellow shall pay an entrance fee.

It is not thought advisable to have a lower subscription for country fellows than for town fellows at present.

Government of Sections.

Each section shall have the power to elect as members of the section such persons as the Council of the section may think fit, provided that the names of the candidates proposed for election be previously submitted by the Sectional Council to the Council of the society for its approval.

Only original members of a section, and those who are subsequently elected as members of it, shall have the power to vote on matters affecting the internal affairs of that section.

Each section shall have power to make the necessary laws and regulations for the conduct of its internal affairs.

In each section the papers shall be submitted to the Council of the section before they are accepted for reading.

The Council of each section shall have sole power to decide whether a paper submitted to it shall be read before that section.

In the event of the Council of a section considering that a particular paper might be discussed with advantage by two or more sections, or by the whole society, it shall have power to transmit the paper to the General Council for this purpose.

Presidents of sections shall be the Vice-Presidents of the society *ex officio* and shall serve on the General Council of the society.

A member of any particular section shall pay, subject to any future bye-law, £1 1*s*. per annum, and shall have the right to

attend all the meetings of his section, but must pay an additional £1 1*s*. per annum if he wishes to have the use of the library, and a further subscription of 10*s*. 6*d*. per annum for each additional section.

It is not thought desirable to have a lower subscription for country members than for town members at present.

In virtue of their bringing their libraries into the amalgamation the existing fellows and members of the Medical, Obstetrical, Odontological, and Ophthalmological Societies shall have the privilege of using the library of the new society without payment of the annual library subscription.

The Odontological library and museum shall be kept separate, and shall be open to members of the Odontological, and to fellows of the new, society.

Fellows of the Medical Society or of the Royal Medical and Chirurgical Society who join the new society as fellows shall be original members of both the medical and surgical sections.

Fellows of the Medical Society who belong to that Society *only* shall be permitted to join both the medical and surgical sections at an inclusive annual subscription of one guinea.

The Presidents of the Medical and Royal Medical and Chirurgical Societies at the time of the formation of the new society shall have seats on the first council in addition to the direct representatives of their Societies.

The first Council shall elect the officers and Councils of the medical and surgical sections of the new society as far as possible from those who hold office at the time of union in the Medical and Royal Medical and Chirurgical Societies.

The governing bodies of other sections shall be elected by the orginal members of the individual sections.

Publications.

There shall be ten monthly issues of a publication to be called 'The Proceedings of the ——— Society.'

The 'Proceedings' shall contain as full a record as possible of the society's work during the previous month, and individual papers shall be condensed only with the sanction of the Council of the section before which they have been read.

The record of the work of the sections shall be adequately illustrated.

The 'Proceedings' shall be printed in such a way that the 'Proceedings' of any section may be bound separately at the end of the year.

As far as possible all papers shall be in proof before being read.

Care shall be taken to respect the exchange list of the present societies when they become sections of the new society.

Each society joining the amalgamation shall send its exchange

list to the editorial committee, which at the end of each year shall forward to those on this list separate copies of the 'Proceedings' of the sections concerned.

Members of sections who desire to do so shall be able to obtain from the editor at the end of each year separately bound copies of the 'Proceedings' of a particular section, provided that they give notice of their wish to do so before the publication of the first copy, and that they pay for the cost of binding.

Societies which own or partly own journals shall make their own arrangements with regard to these quite apart from the question of amalgamation.

It is hoped that when the society has been constituted the most valuable papers may be collected together into an annual volume of 'Transactions.'

The entire management of the publication of the monthly 'Proceedings' of the new society shall be in the hands of an editorial committee.

The editorial committee shall consist of one representative of each section, together with an editor, and shall work in conjunction with the Councils of the various sections.

(*Signed*) W. S. CHURCH,
Chairman.

July 6th, 1906.

ON THE GENERAL PRINCIPLES OF THE THERAPEUTIC INOCULATION OF BACTERIAL VACCINES AS APPLIED TO THE TREATMENT OF TUBERCULOUS INFECTION

BY

A. E. WRIGHT, M.D.Dub.,

SOMETIME PROFESSOR OF PATHOLOGY, ARMY MEDICAL SCHOOL, NETLEY; PATHOLOGIST TO ST. MARY'S HOSPITAL, LONDON, W.

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PART I.

Preliminary Matter.

What I have to say to-night on the subject of the treatment of tuberculous infection by the therapeutic inoculation of tubercle vaccine may conveniently be prefaced (*a*) by a recital of the train of events which supervenes in the blood upon the inoculation of a bacterial vaccine[1] or, as the case may be, upon a succession of such inoculations; (*b*) by a consideration of the principles which may properly guide us in determining in the case of each successive inoculation the dose of vaccine to be administered; (*c*) by a brief account of the manner in which the organism conducts itself when it becomes the victim of a bacterial invasion; and (*d*) by an exposition of the conditions—so far as these are known to us—under which pathogenetic bacteria cultivate themselves in the infected organism.

[1] The term "vaccine" is here and throughout this paper employed to denote a sterilised and standardised suspension of micro-organisms.

Train of Events which follows upon the Inoculation of a Bacterial Vaccine.

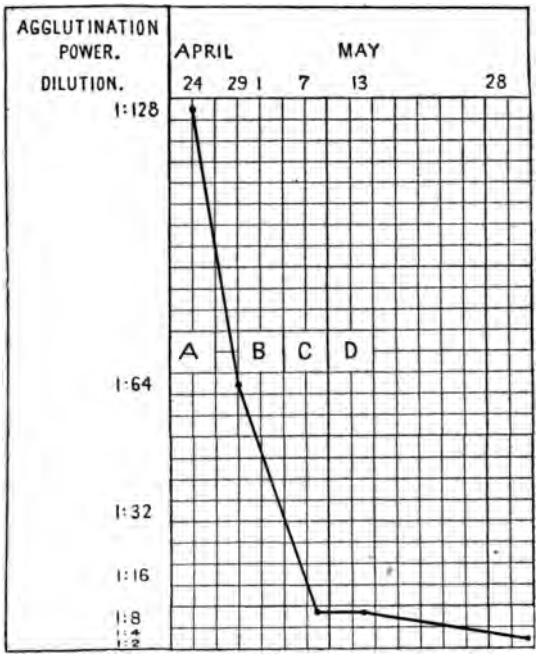
The changes in the antibacterial power of the blood which supervene upon the inoculation of a bacterial vaccine were for the first time investigated by the aid of quantitative methods and upon man in connection with my work on anti-typhoid inoculation. That work has been followed up by similar researches conducted by myself and my pupils and fellow-workers in connection with the inoculation of Malta fever vaccine, tubercle vaccine, plague vaccine, pneumococcus vaccine, staphylococcus vaccine, streptococcus vaccine, gonococcus vaccine, proteus vaccine, and a series of vaccines made from different strains of the *Bacillus coli*. All of these vaccines, with the exception only of the plague vaccine, have come into application in connection with the treatment of the corresponding bacterial infections.

Upon the inoculation of each of these vaccines without exception there has followed one and the same train of events. That train of events is as follows: (1) Upon the inoculation of the vaccine there supervenes a period of intoxication which is characterised by a decline in the antibacterial[1] power of the blood. This "negative phase" is more or less accentuated and prolonged according as a larger or smaller dose of the vaccine is inoculated. In the former case the "negative phase" may disclose itself to clinical observation by a temperature reaction and constitutional disturbance. In the latter case the "negative phase" may be quite unaccompanied by clinical symptoms. (2) Upon the "negative phase" there follows a "positive phase." This phase, whose characteristic feature is an increase in the antibacterial power of the blood, corresponds to a period of increased resistance. The curve whose trace sets forth the changes in the antibacterial power of the blood runs up in many cases into a sharp

[1] The particular anti-bacterial element which was measured was in the large majority of cases the *opsonin*.

peak and sinks away first comparatively rapidly and afterwards more slowly. There is associated in many cases with the climax of the "positive phase" a sense of increased physical vigour and a very pronounced feeling of well-

CURVE I (obtained by Author).

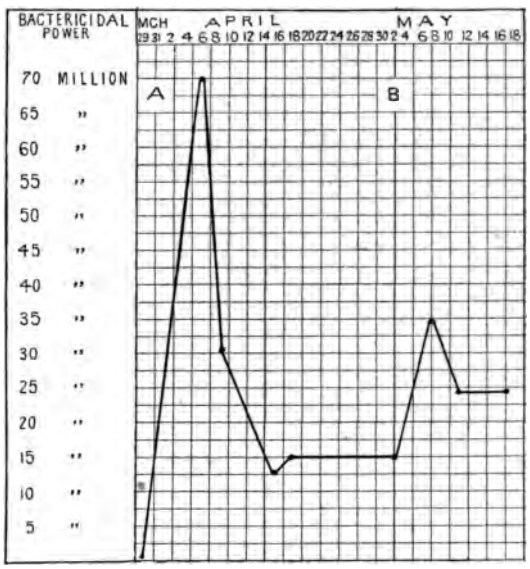


Relating to E. S—, a case of tubercular cystitis, treated by inoculations of new tuberculin (Case 4, p. 33, *infra*), showing that a cumulation in the direction of the negative phase is produced by the inoculation of a series of inappropriately adjusted and inappropriately interspaced doses of a bacterial vaccine. A. Inoculation of 0·01 milligramme of the new tuberculin. B. Inoculation of 0·025 milligramme of the new tuberculin. C. Inoculation of 0·05 milligramme of the new tuberculin. D. Inoculation of 0·2 milligramme of the new tuberculin. The method employed for testing the blood was that described by the Author, 'Lancet,' July 23rd, 1903.

being. 3. After the negative and positive phase which train of events I have ventured to speak of as the "ebb and flow and reflow of the tide of immunity," the blood

may be maintained for a variable period (after tubercle inoculations occasionally for as long as a month) at a somewhat higher level of antibacterial power than before inoculation. Or—and this in connection with inoculations with tubercle vaccine is a more usual event—the antibacterial

Curve II (obtained by Author in conjunction with Capt. W. Glen Liston, I.M.S.).



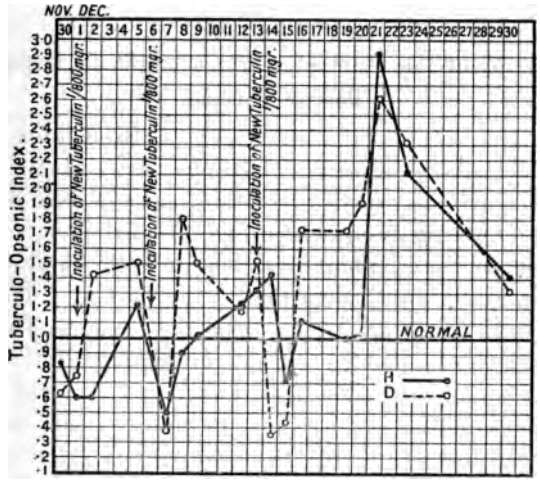
Relating to a rabbit which was being immunised against the typhoid bacillus, showing that a cumulation in the direction of the positive phase may be obtained by the inoculation of appropriately adjusted and interspaced doses of a bacterial vaccine. A. First inoculation; 5 cubic centimetres broth culture of the typhoid bacillus. B. Second inoculation; 5 cubic centimetres broth culture of the typhoid bacillus. The bactericidal power which is charted represents the bactericidal power of, in each case, 1 c.c. of freshly drawn serum. The method employed for measuring the bactericidal power of the blood was that described by the Author, 'Proc. Roy. Soc.,' vol. lxxi, 1902.

power of the blood may over and over again fall back after ten days or a fortnight to the level at which it stood anterior to inoculation.

Train of Events which follows upon the Inoculation of a Series of Doses of a Bacterial Vaccine.

I originally pictured to myself that a cumulative effect in the direction of the negative phase such as is exhibited in the curve here shown (Curve 1) would occur in a regular manner where re-inoculation is undertaken in the negative phase of a preceding inoculation, and that *vice versâ* a cumu-

CURVE III (obtained by Author).



Relating to H and D, two children with tuberculous glands, who were treated with therapeutic inoculations of new tuberculin. The curve shows the condition of the blood in each case before inoculation and the changes in the tuberculo-opsonic power which supervened upon the three first inoculations.

lative effect in the direction of the positive phase such as is exhibited in the companion diagram here shown (Curve 2) would be achieved in a regular manner by re-inoculating in the positive phase of a previous inoculation. Further experience has shown me that, while cumulation in the direction of the negative phase is a phenomenon which must everywhere be reckoned with, it is in connection with inoculations undertaken with tubercle vaccine difficult, if not impossible, to achieve cumulation in the direction of the positive phase.

This is clearly brought out in connection with the two traces in Curve 3, which show the result of an endeavour to achieve in connection with the inoculation of tubercle vaccine a cumulative effect in the direction of the positive phase. In view of this, and a number of similarly unsuccessful endeavours, I have, in connection with the inoculation of tubercle vaccine, put out of my thoughts all idea of cumulating positive phase on positive phase. I am now content to treat each inoculation as an independent event, regulating my dose as described.

Consideration of the Principles which ought to Regulate the Dose of Vaccine.

There appears to be everywhere a fixed idea that to secure the greatest yield of protective substances we ought in each case to begin with a dose which produces a certain amount of constitutional disturbance, and that we ought in subsequent inoculations to employ doses which increase by geometrical progression. This fixed idea rests as a matter of fact upon the preconception that immunisation cannot be either initiated or followed up apart from constitutional disturbance, and on the further preconceptions that the capacity of the organism for immunising response is practically unlimited, and that the yield of antibacterial substances will increase *pari passu* with the dose. This is not so. I obtain almost every day maximal immunising responses from the inoculation of doses of tuberculin which have not produced any constitutional disturbance. Further, I have for periods extending over a year continued to inoculate with doses of new tuberculin corresponding to from $\frac{1}{1000}$ to $\frac{1}{600}$ milligramme of tubercle powder[1] without registering any falling off in the immunising response. Again, I have in some of these cases repeatedly registered worse and not better results whenever larger doses than these were employed. Lastly, I have before my mind the fact that the horses

[1] The doses in this paper have reference in each case to the weight of tubercle powder held in suspension in the new tuberculin as issued.

which are, in connection with the manufacture of diphtheria antitoxin, inoculated with large doses of diphtheria toxin, all sooner or later lose their power of responding to the stimulus of inoculation, and recover that power of response only after a long period of rest.

In view of these facts I would submit that the whole question of dosage requires to be reconsidered. For myself I am day by day more impressed with the fact that the machinery of immunisation can be brought into action by very small stimuli, and that it can very easily be overtaxed. In accordance with these facts I regard it as a matter of great moment, especially in connection with immunisation against tubercle, to employ in every case the smallest doses which will elicit a satisfactory response; to repeat the dose only when the effect of the preceding inoculation is passing off; and to increase the dose only when it becomes clear that the dose previously employed is ceasing to evoke a sufficient immunising response. Acting in accordance with this principle, I now begin with a quantum of tuberculin corresponding to not more than $\frac{1}{10000}$ milligramme of the tubercle powder, and now never advance to doses larger than $\frac{1}{6000}$ milligramme.

I may before passing on just refer to two further points with regard to the dosage of tubercle vaccine. Where on observing the results of a series of inoculations I find that the negative phase phenomena are becoming with each inoculation more pronounced I know that I am exceeding my proper dose. Where, on the contrary, the negative phase phenomena are becoming after each inoculation less well marked I know that I am employing the proper dose and am making good progress. The last point to which I would call attention is this: Where a dose has been administered prematurely, or where too large a dose has been administered, there may result from this, in the case where the positive phase of the previous inoculation has not yet exhausted itself, only the cutting short of that phase, or, as the case may be, the production of a negative phase which is unduly accentuated and which is followed

up somewhat tardily by a positive phase. But the case will also occur where, after the administration of an excessive dose or premature re-inoculation, the positive phase makes default. Where the positive phase is long delayed I take it that the proper policy is not to wait indefinitely for its arrival but to reinoculate again with a smaller dose as soon as ever the blood disturbance has come to rest.

Manner in which the Organism conducts itself when it becomes the Subject of Bacterial Invasion; and Discrimination of Bacterial Infections into (A) Bacterial Infections where the Machinery of Immunisation is Inactive, and (B) Bacterial Infections where the Machinery of Immunisation is called into Action.

Consideration will make it clear that a knowledge of the effects exerted upon the blood by inoculations of bacterial vaccines will not, taken by itself, constitute a sufficient equipment for the physician who desires to come actively to the aid of the organism when invaded by pathogenetic bacteria. It will manifestly be quite out of question for us to assist in an intelligent manner by inoculation until we have ascertained what action, if any, the infected organism is taking with respect to the invading microbes.

While we are only upon the very threshold of knowledge with respect to these subject-matters, certain of the broad general principles have already emerged; and these, inasmuch as they seem to be of absolutely fundamental importance in connection with the treatment of bacterial disease, I will venture to lay before you. It emerges in a very clear manner from the already very many thousands of quantitative estimations of the opsonic power of the blood which I and my fellow-workers have conducted in connection with many forms of bacterial disease, that bacterial infections distribute themselves naturally into two categories. In one class of infections the opsonic power with respect to the infecting micro-organisms hardly varies from day to day, remaining always inferior to that of the normal blood. In another class of infections the opsonic

power is continually fluctuating—the range of variation being from far below the normal to far above the normal. These two categories of infections correspond respectively to *strictly localised* and *systemic infections.*

An explanation of the different findings in these two classes of cases readily suggests itself. We are, I think, warranted in conceiving of the low opsonic power which is found in association with strictly localised infections as a condition which dates back to a period anterior to infection. Further, we are, I think, warranted in attributing the circumstance that the opsonic power of the blood remains, in the case of strictly localised bacterial infections, persistently low, to the default of those immunising stimuli which are supplied by the entrance of bacterial elements into the blood. And again we are, I think, warranted in conceiving of the fluctuation of the opsonic power between high and low, which is found in association with systemic infections, as the expression of a periodic activation and inhibition of the machinery of immunisation, brought about by the conveyance of bacterial elements into the blood, in appropriately or, as the case may be, inappropriately adjusted and interspaced doses.

Our strictly localised, and our systemic, bacterial infections, would in this manner resolve themselves into a category of infections where the stimuli which call forth an increased elaboration of protective substances make default; and into a category of infections where we have to reckon with the delivery of, oftentimes ill-adjusted and oftentimes inappropriately interspaced, auto-inoculations.

In association with this difference between infections which evoke immunising responses and infections which evoke no such responses there emerges a distinction which is of absolutely fundamental importance.

Systemic infections—provided always that the machinery of immunisation is not overtaxed—are infections which terminate ordinarily in death, or in a cure— that cure when it occurs being never indefinitely delayed.

Strictly localised infections do not tend to get well. They are characterised by an altogether indefinite duration.

I need not remind you that, while an acute specific fever will ordinarily run its course within a limit of one, two, or three weeks, a strictly localised infection, such as lupus, may commence in earliest infancy and run on through sixty or even more years, terminating only with the life of the patient.

Conditions under which Pathogenetic Micro-Organisms cultivate themselves in the Interior of an Infected Organism.

With the discovery of the bactericidal properties of the blood of susceptible animals the problem presented itself as to how bacteria could maintain their existence in an organism which was furnished with these bactericidal elements. With the discovery of the agglutinating power of the blood, the parallel problem as to how the infecting micro-organisms can remain unagglutinated in the interior of the organism; and with the discovery of the opsonic power of the blood, the similar problem as to how the infecting micro-organisms can escape phagocytosis in the organism in the presence of leucocytes, presented themselves for solution.

The general problem as to how bacteria can maintain themselves in an organism which is provided with antibacterial substances has been dealt with by Metchnikoff by a procedure similar to that which was adopted by Alexander the Great in the case of the Gordian knot. Metchnikoff's method of dealing with the problem is to contend that bactericidal, agglutinating, and antibacterial elements generally make their appearance in the blood only after this has been withdrawn from the blood-vessels, or phagocytes have dissolved in the blood-fluids. This contention—which is so congenial to everyone who desires to leave out of his reckonings in dealing with bacterial disease everything that relates to the antibacterial power of the blood—seems to me to be in conflict with the whole of the experience which is won by a systematic comparison of the clinical

condition of the patient with the result of quantitative measurements of the antibacterial power of his blood.

I will ask you, therefore, to consider with me whether we have not a very simple solution of the problem before us in the consideration that the infecting micro-organisms cultivate themselves in the organism in every case in regions of *lowered bacteriotropic pressure—i. e.* in regions where antibacterial substances are absent from the tissue fluids or where these contain anti-bacterial substances in diminished quantity as compared with the circulating blood.

This theory, which was first enunciated by me in a paper written in conjunction with Lamb, on "The Distribution of the Agglutinins in the Organism in the Case of Typhoid and Malta Fever,"[1] was shown by us to furnish a key to the explanation of our findings in connection with those infections. Later this theory was shown by Lamb[2] to furnish the key to his findings in connection with the bacteriolysins in spirillum fever. Lastly, in conjunction with Douglas,[3] and afterwards with Reid,[4] I have been able to show that this theory furnishes the key to the distribution of opsonins in the infected organism, in the case of tuberculosis and a large number of other bacterial infections.

Let me try to put the situation before you as I conceive of it in connection with micro-organisms cultivating themselves in the tissues. I conceive that these are cultivating themselves under conditions which do not even remotely resemble those which they would have to confront in the circulating blood. In the case of bacteria in the actual blood-stream all the antibacterial elements of the organism would come into application upon them. In the case of bacteria cultivating themselves in the tissues only those antibacterial elements would come into application which had passed out from the blood in the lymph in the region of infection. Further, inasmuch as lymph, coming in con-

[1] 'Lancet,' December 23rd, 1899.

[2] 'Scientific Memoirs by Officers of the Medical and Sanitary Department of the Government of India,' vol. xii, pp. 96 *et seq.*

[3] 'Proc. Roy. Soc.,' vol lxxiv, 1904, pp. 151 *et seq.*

[4] 'Proc. Roy. Soc.,' 1906.

tact in succession with a number of bacteria, or, as the case may be, with their products, would part with its antibacterial elements to those first encountered, retaining after percolating through a first bacterial nidus to a second, or through the outer portion of such a nidus to its interior, only a residuum of its original antibacterial power; there would come into existence, in particular in the case when the lymph-flow stagnated in the tissues, conditions far more congenial to the cultivation of bacteria than those which obtain in the blood.

Premising that I shall as I proceed, ever and anon, have to recur to the general principles enunciated in this first section of my paper, I may pass on now to consider the application of therapeutic inoculations of tubercle vaccine in connection with the treatment of tuberculosis. It will be convenient to take up first the consideration of the treatment of strictly localised tubercular infections. Examples of such strictly localised tubercular infections are furnished by most cases of lupus, further by the large majority of tubercular invasions of the subcutaneous tissue, lymphatic glands, serous cavities, bone, testes, kidney, bladder, and other internal organs, lastly by many apyrexial cases of phthisis.

PART II.

Treatment of strictly localised Tubercular Infections by the Aid of Therapeutic Inoculations of a Tubercle Vaccine.

In connection with the treatment of cases of strictly localised tubercular infection we have to take into account the following facts: (1) The tuberculo-opsonic power of the blood in these cases appears to be uniformly inferior to that of the normal blood. (2) The immunising stimuli which are required for raising the opsonic power and for maintaining it at a high level here make default. (3) The tubercle bacilli are cultivating themselves in the focus of infection under conditions which are much more favourable

to their growth than those which obtain in the case of the circulating blood. (4) An increase of the opsonic power of the blood can be achieved and maintained by the inoculation of a series of appropriately adjusted and interspaced doses of tubercle vaccine. (5) We have at disposal methods by which we may increase the lymph-flow through the focus or foci of infection in such a manner as to bring the antibacterial elements of the blood into application upon the invading bacteria.

It would be impossible within the limits of space within which I have here to confine myself to bring before you the evidence in support of all the above propositions. So far as it relates to the first four of the above propositions, that evidence has been set forth in detail in a communication to the Royal Society made in conjunction with Douglas[1] and in a further communication made to the same Society in conjunction with Staff-Surgeon S. T. Reid, R.N.[2] I may therefore here limit myself to the consideration of the proposition that we have at our disposal methods for sending through the focus of infection a stream of anti-bacterial lymph.

Discussion of the Means which are available for sending a Stream of Anti-Bacterial Lymph through the Focus of Infection.

The activation of the lymph-stream in the focus of infection supplies the *rationale* of a number of procedures which have been empirically practised. Our grandmothers were wont to activate the lymph-stream in boils—they spoke of it as "drawing the boil"—by the application of hot poultices

[1] Wright and Douglas, "On the Action exerted upon the Tubercle Bacillus by Human Blood Fluids and on the Elaboration of Protective Elements in the Human Organism in response to Inoculations of a Tubercle Vaccine," 'Proc. Roy. Soc.,' vol. lxxiv, pp. 159-180; and 'Lancet,' October 22nd, 1904, p. 1138.

[2] Wright and Reid, "On the Determination of the Presence or Absence of Tubercular Infection by the Examination of the Patient's Blood and Tissue Fluids." This paper was read in November, 1905, and is about to appear in the 'Proc. Roy. Soc.'

followed by sugar-and-soap plasters.[1] The surgeon of these latter days practises the method when he applies hot boric fomentations in connection with the treatment of septic infection associated with lymphangitis. Professor Bier in Germany practises the method when he obstructs the circulation in a limb or, as the case may be, in the head and neck, with a view to achieving an effusion of lymph. The physician, I take it, practises it in connection with the application of his rubefacients and preparations of iodine, and possibly also when he administers expectorants—deeming that he is only "loosening the expectoration." The X ray, the radium, and the radiant heat therapist practise it in connection with the exercise of their particular professions. Lastly, as I think emerges very clearly from the facts which Dr. Bulloch proposes to lay before you, the work of the Finsen light therapist resolves itself into an application of this method.

It seems to me all that is further needed in connection with these methods is that they shall be employed purposefully as means to an end and not blindly as empirical methods. For I conceive that if this were done it would immediately be recognised (*a*) that the douching of a bacterial nidus with a rapidly flowing stream of lymph might in the case where that lymph possesses only very inferior antibacterial properties be associated with risk; (*b*) that the irrigation would always be more effective in the case where the antibacterial power of the blood had previously been raised either by auto-inoculation or artificial inoculation; (*c*) that an ampler lymph-stream could in every case be obtained by administering decalcifying agents (such as citric acid) in such quantities as might suffice to reduce the coagulability and at the same time the viscidity of the blood; (*d*) that in the case where the focus of infection is positioned in a lymphatic gland the blood-stream

[1] Let us reflect in this connection that the hot poultices determined the blood-stream to the focus of infection, that the sugar by its osmotic power drew the lymph through the open boil, and that the soap by decalcifying the lymph prevented it coagulating and forming a scab and so blocking the outlet.

might with advantage be determined not only to the lymphatic gland involved but also to the whole territory which sends its lymph to that gland; (*e*) that in cases where the focus of infection is positioned in the skin, and where the blood-supply to the skin is inefficient, advantage might be taken of any medicinal agent, such as thyroid extract, which increases the cutaneous blood-supply; (*f*) that inoculation of old tuberculin may possibly find a useful incidental application in certain cases of superficial lupus by producing an outflow of lymph through the affected skin; (*g*) that the injection into discharging sinuses of a decalcifying agent dissolved in a concentrated salt or sugar solution may possibly be found useful in causing an irrigation of such sinuses by lymph; and, lastly, (*h*) that if the therapeutic effect of the Finsen rays should resolve itself merely into a question of determining lymph to the site of infection, it would be well in every case to preface it by inoculation procedures or, perhaps, even to use in association with these last some cheaper and less laborious therapeutic device. I would throw out merely as a suggestion that we have in the application of bags filled with hot sterilised sand[1] a very inexpensive and convenient method of determining a blood-stream to any region on the surface of the body.

Digression on the Results of Ordinary Surgical Methods as applied to the Treatment of strictly localised Tuberculosis.

Before saying what I have to say on the subject of the results obtained by treating strictly localised tubercular infections by the aid of therapeutic inoculations of a tubercle vaccine I will, if I may, say a preliminary word on the results as obtained by methods which are believed to be

[1] For the sterilisation of the sand I am accustomed to give the following instructions:

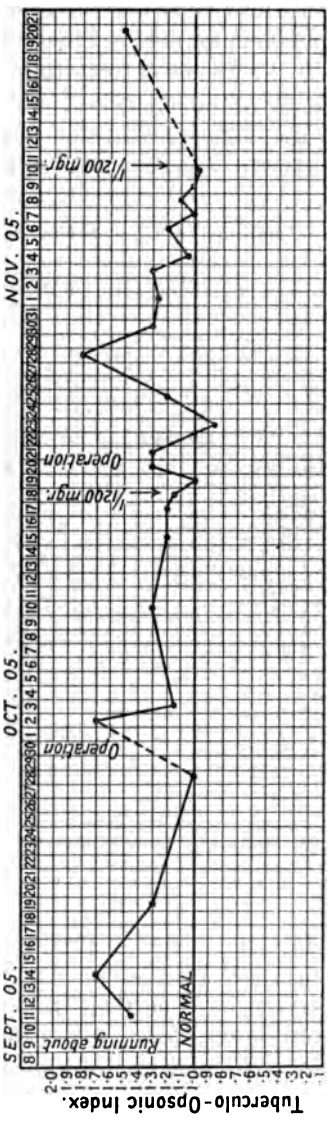
Place the sand in a saucepan over the fire, having previously stirred in a number of small pieces of white paper. Continue the stirring until, with the attainment of a temperature of 200° C., the pieces of paper have all turned brown.

purely surgical, leaving the discussion of the results obtained by the Finsen light treatment to be dealt with later in this discussion by Dr. Bulloch.

It is the belief of the surgeon—one, I take it, of his cherished beliefs—that it is possible to extirpate completely and effectively by the knife, in a large proportion of the cases which he undertakes, the invading micro-organisms. I for my part find it very difficult indeed to believe that this result can often be achieved even by the most radical operations. While I have great difficulty in believing that these means can be as effectual as they are claimed to be, I do not—though this may first fall upon your ears as a paradox — find any difficulty in believing that the good results which the surgeon claims are often achieved. But success is, as I gather, obtained in some cases where the operation leaves something to be desired from the point of view of completeness; and again, at other times, the efforts of the surgeon come to nought, in spite of the fact that the operation has been conducted with scrupulous care.

Even if we leave altogether out of account the possibility that the patients successfully operated upon may have been patients whose tuberculo-opsonic indices were previously to inoculation on the average higher than those of the patients unsuccessfully operated upon, the observations of my fellow-worker, Dr. J. Freeman, clearly show that there are other factors which may influence the result. There is in the first place the possibility that surgical interference with a tubercular focus may, as in the two scraping operations[1] which are in question in Curve IV, be followed by the whole train of events which we have learned to associate with the inoculation of a bacterial vaccine. Again, as in the initial rise of

[1] The same sequence of events has already been met with in connection with three other cases. One here referred to was a scraping operation undertaken upon tubercular glands, the other two were extirpating operations also undertaken in connection with tubercular glands. It would seem probable that similar results would be obtained also in connection with curetting operations undertaken upon the uterus in connection with bacterial infections.



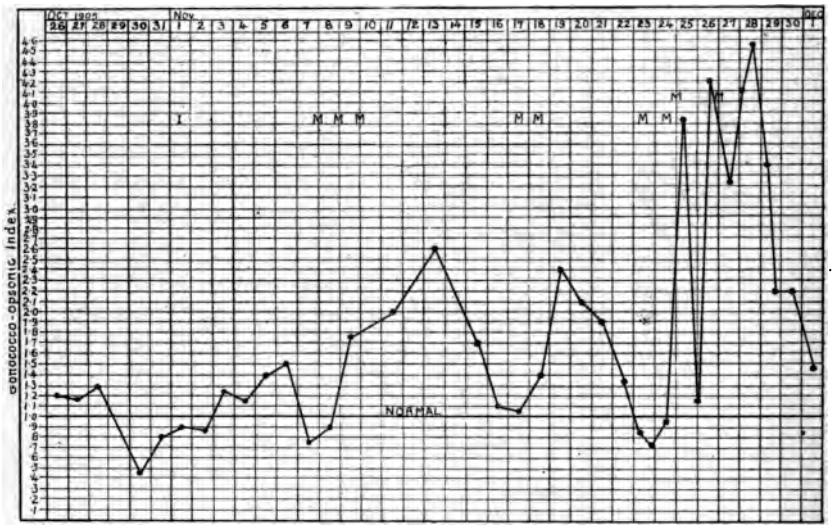
CURVE IV (obtained by Dr. J. Freeman).

Shows, in the case of a child suffering from tubercular caries of the fibula, that the tuberculo-opsonic power may be raised by active exercise and surgical procedures as well as by the incorporation of tubercular elements in the form of therapeutic inoculations of new tuberculin.

the tuberculo-opsonic power which is set forth in the same curve, physical exercise may be an active agent in connection with the production of immunity. Finally, as shown in Curve 5, massage of the focus of infection may produce effects similar to those of inoculation.

When we come to reflect upon the matter there is nothing in any of this to surprise us. A conveyance of

CURVE V (obtained by Dr. J. Freeman).



Shows the effect of massage upon the gonococco-opsonic power in the case of a man suffering from gonococcal arthritis. I, inoculation of a very small dose of gonococcus vaccine (50,000,000 gonococci). M, massage.

bacterial elements into the blood is precisely what might be expected from surgical procedures which open up the lymph spaces, or as the case may be from the activation of the lymph-stream by kneading operations or ordinary muscular movements. In view (*a*) of the observations of Meakin and Wheeler (to be referred to below, p. 39) on the effect of physical exercise upon the tuberculo-opsonic index in phthisis; (*b*) of the observations of Freeman, made

in my laboratory, on the effect of massage on the opsonic power in the case of a variety of bacterial infections; and (*c*) of the observations of Clarence Wright ('Archives of the Roentgen Ray,' December, 1905) on the effect of X-ray treatment on the tuberculo-opsonic power in the case of lupus patients, it suggests itself that it may prove possible to determine the nature of any localised bacterial infection by measuring the opsonic power of the blood with regard to the suspected micro-organism before and after massage, physical exercise, the application of X rays, or any other method which activates the local lymph-stream.

On the Results which have been obtained by the Treatment of localised tubercular Infections by the Aid of therapeutic Inoculations of a Tubercle Vaccine (Koch's New Tuberculin) controlled by Determinations of the Opsonic Index.

Returning from the above digression to take up again the main theme of this discourse, and coming to the question of the results which have been achieved by the therapeutic inoculation of Koch's new tuberculin safeguarded by systematic determinations of the opsonic index, I find myself face to face with the impossibility of conveying to you an adequate idea of the results which it is possible to achieve in the matter of the cure of localised tuberculosis. To convey to you such an adequate idea I should have to bring you face to face with the patients and to reproduce for you, in the case of those who were suffering from external lesions, their past by the aid of photographic records. In view of my having been prevented by external circumstances from securing photographs of the cases when they first presented themselves, and in view of the circumstance that the presence of the patients to-night would have broken in in an unwarrantable manner upon this discussion, I must do what I can by the bald method of narrative, inviting you hereafter to inspect the patients either at St. Mary's Hospital, or, if it shall be

signified that this is the wish of the Society,[1] here in this room before the close of this discussion.

Before entering into a recital of the cases I would point out that in each case a measurement of the tuberculo-opsonic power of the blood has (with only rare and isolated exceptions) been made in connection with each inoculation of tubercle vaccine. The burden of the very many thousands of hours of work which this has involved has been shared with me in the most devoted and self-sacrificing manner by my friends and fellow-workers, Captain Stewart R. Douglas, I.M.S., and Dr. J. Freeman. I would therefore have it borne in mind that the work which I shall here summarise is in very large part their work.

For the purpose of the summary I may classify the cases of localised tuberculosis which we have dealt with under the headings of *lupus, tubercular ulceration of the subcutaneous tissues and bone, tubercular glands, tubercular disease of the genito-urinary system, tubercular disease of joints, tubercular peritonitis,* and *apyrexial phthisis.*

While we have treated, or have under treatment at present at St. Mary's Hospital, examples of each and all of these classes of cases, we have, keeping in view the importance of testing the method of inoculation in the most rigorous manner, devoted our attention in particular to cases where definite objective evidence could be obtained of any alteration in the clinical condition, and by preference to cases where ordinary surgical methods had already been unsuccessfully exploited. In conformity with this I shall in the summary below consider in particular the results obtained in the treatment of the four first-mentioned categories of tubercular infection, and will pass over in silence the less convincing though equally satisfactory results which have been achieved by inoculation in the cases

[1] In conformity with the wish of the Society a number of the cases whose histories are chronicled below were exhibited at the meeting of the Society held on December 12th, 1905. The cases thus exhibited are in the records below distinguished by an asterisk *.

of tubercular peritonitis and joint-disease which we have had under treatment. I shall omit from consideration also the satisfactory results achieved in three out of the five cases of phthisis which we have treated by tuberculin inoculation. It is to be borne in mind in connection with this very small number of cases of phthisis treated that we have, except under very special circumstances, excluded this affection from treatment, because of the difficulty of eliminating in an Out-Patient Department that class of phthisical patients who, being already the subject of auto-inoculations, cannot, it seems to me, except under very special precautions, safely be treated by the method of inoculation.

Lupus.

If we except one of our very earliest cases—where the results of a few weeks' treatment were, probably owing to the administration of too large doses of the vaccine, such as to discourage the patient,[1] and to lead him to abandon the treatment—we may say that the inoculation treatment has, in all the cases of lupus we have dealt with, ameliorated, but so far only in one case[2] cured, the disease. Not infrequently we have seen certain of the patches completely cured, while the disease in other regions has remained refractory. These only partially successful results, which contrast in a striking manner with those obtained in connection with tubercular ulceration affecting the deeper tissues, depend, it seems to me, not so much upon a defective power of response to inoculations on the part of the lupus patient as upon the inadequate manner in which the antibacterial substances come into application upon the tubercle bacilli in the case where these are disposed in a skin which is but poorly supplied with blood. I do not doubt that if it were possible to superadd to the treatment by inoculation another form of treatment which achieves, as the Finsen light appears

[1] *Vide* Graham Little, 'British Journal of Dermatology,' September, 1904.

[2] This case was shown to the Society on December 12th, 1905.

to do, a sufficient transudation of lymph into the skin, the efficiency of the inoculation treatment as applied to lupus would be much greater than it has been in our hands.

Tubercular Ulceration of the Subcutaneous Tissues.

The clearest and most unfallacious evidence of the advantage which can be derived from the therapeutic inoculation of tubercle vaccine can be furnished in connection with tubercular ulceration of the subcutaneous tissues. It is not a question here of the achievement of success in a certain percentage of cases where ordinary surgical methods have failed. Up to the present, at any rate, it has been a question of *uniform* success. The following series of cases, all of which, except the last, are available for inspection, furnish evidence of what can be achieved by inoculation in cases which had defied all ordinary methods of treatment, and which might quite well have been reckoned desperate.

Case 1.*[1]—The patient, whose case I have already reported upon,[2] is a man of about thirty years of age. His history is as follows: In the autumn of 1902 he developed tubercular glands on the left side of the neck and a tubercular abscess on the point of the left shoulder of the same side. He was admitted to St. Mary's Hospital and was operated upon for the first time in January, 1903. The wound becoming invaded with tubercle and refusing to heal, further operative procedures were embarked upon. In all six successive scraping, extirpating, and skin-grafting operations were undertaken during the course of the year, the wound becoming in each case reinfected, and the area of ulceration being extended. In December, 1903, when the patient came up for treatment by inoculation, the whole area from the point of the left shoulder to the base of the ear formed a single deep eroded ulcer. The lobule of the ear was half eaten

[1] As explained, *supra* (p. 20), the patients who are distinguished with an asterisk * were exhibited to the Society on December 12th, 1905.

[2] 'Proceedings of the Royal Society,' vol. lxxiv, July, 1904, and 'Clinical Journal,' November 9th, 1904.

away and immediately underneath it a deep ulcerated crater had developed which looked as if it was going to break into the œsophagus. The adjacent side of the face was distorted by swelling, giving the patient the appearance which would go along with a one-sided attack of mumps. The axilla was occupied by a gland which was as large as a pigeon's egg, and the patient was haggard and very emaciated. After eight months' inoculation with new tuberculin, supplemented on several occasions by inoculations of a staphylococcus vaccine, and the local application of formalin gelatine,[1] I was able to report that steady improvement had been made under the treatment, that the swelling of the face had almost entirely disappeared, that the crater under the angle of the jaw had healed up from the bottom, that the gland in the axilla could no longer be felt, that the ulcerated wound had almost entirely closed over, and that the patient might now almost pass muster as a healthy man. After a further three months I reported that the wound was entirely closed and that there remained only an area of the size of a threepenny-piece which was still covered by scab. I also pointed out that the previous site of the ulcer was covered in, not by scar-tissue, but by a quite soft and elastic skin. Carrying on the history of the patient for another year, I have to report that after having got completely well, and after treatment had been discontinued for about six months, he presented himself again for treatment at the hospital. He had now, after alcoholic excesses and exhausting work as a barman, developed a very large, soft gland in the previously sound side of the neck, and another in the groin of the same side. His opsonic index was found to be very low. The glands in question rapidly broke down, leaving crateriform openings, which presented all the typical clinical appearances of syphilitic gummata. No improvement having manifested itself under a very thorough anti-syphilitic treatment carried out in the hospital, and the patient's tuberculo-opsonic index ranging always about 0·4, the tuberculin inoculations were recommenced, with the

[1] *Vide* author's paper, 'Lancet,' July 9th, 1904, p. 73.

result that he is now making a marvellously rapid recovery.

CASE 2.*—The patient, a woman, aged 31, has, like the last, been previously reported on.[1] Her history is as follows: She developed a tubercular infection of the glands of the neck at the age of fourteen years. Then suppuration supervened and the abscesses were opened, the wounds became infected, and other glands also became involved. Later, tubercular disease developed in the little finger of the right hand. The two terminal joints of that finger were removed fifteen years ago, when the patient was sixteen years old. About this time lupus broke out on her face and on her left arm and hand. At the age of nineteen years she underwent treatment with Koch's original tuberculin. She received from three to four inoculations a day (the total of her inoculations amounting to 150). This treatment resulted in violent inflammatory reaction in the patches of lupus, a piece of bone sloughed out of her left arm, and she remained in hospital seriously ill for thirteen weeks. She attributes, and no doubt rightly, the aggravation of symptoms and ultimate loss of her arm to these inoculations. We can now discern that there must have been produced a cumulative negative phase. After a respite vigorous treatment was resumed in another hospital. The lupus patches were then frequently scraped and many glands were extirpated from the neck. In 1900 the Finsen light treatment was resorted to and was persevered in for eighteen months. This effected superficial improvement in the condition of the face and neck, but the disease continued to spread in the deeper structures and in particular in the bones of the left arm. Finally, it became necessary to amputate this limb. The disease now re-invaded the stump and broke out in the point of the shoulder and in the front of the chest. Roentgen rays were now tried unavailingly. Finally, in December, 1903, the patient, who was then in a very reduced physical condition, was

[1] *Loc. cit.*

referred to me by Dr. E. G. Graham Little for treatment by tuberculin inoculations. I was able to report in November, 1904, that the patient had arrived at a tolerably satisfactory condition in the matter of her general health. Her body weight had gone up and had reached 141½ lb., as much as 5 lb. having on one occasion been gained in the interval between two successive inoculations. The discharge from the sinus over the sternum and from the sinus in the stump of the left arm had practically ceased. I am to-day able to state that the patient is in robust health, that the discharge from the sinuses has entirely ceased, and that she has been able for months to make use of an artificial limb. Except for some superficial patches of lupus on the face, she may be said to be perfectly well.

CASE 3.*—The patient is a female, aged 20. When she presented herself for treatment in December, 1903, she had the appearance of a child. Her bones protruded through the skin of her back somewhat after the fashion in which bones protrude in dried fish. The point of her nose was covered with a thick mass of scabs superposed upon a very angry-looking patch of lupus. The angle of the jaw and the front of the neck were occupied by patches of lupus in a similar condition. Both her feet and her hands were affected with lupus. Her hands in particular were a mere mass of ulceration, the bones of the hand being also affected in many places. The patient has made slow but steady progress under the inoculation treatment. The ulcers on her right hand are nearly healed, and those on her left hand considerably amended, and her general physique has improved. The patches of lupus on the front of her neck and under the angle of the jaw are now represented by perfectly sound cicatrices and the patch of lupus on the nose is improving.

CASE 4.*—The history of this patient, who has been under the care of Mr. H. Stansfield Collier, is as follows: In 1900, at the age of thirty, the right testicle and a gland in

the groin were removed on account of tubercular disease. Early in 1903 an abscess was opened some distance above the ankle on the outer side of the right leg. The wound did not heal. In December another abscess had formed over the external malleolus, and a considerable portion of the lower end of the fibula was gouged away. In July, 1904, another abscess developed in the lower third of the leg and was opened. Just before the patient was taken over for treatment by inoculation in January, 1905, the amputation of the foot was regarded as almost inevitable. The condition was as follows. A sinus wide enough to take a large drainage-tube led through the leg behind the ankle-joint. A deep ulcerated trench occupied the region of the extirpated fibula, and extended under the inner malleolus for a considerable distance. A gland the size of a bantam's egg occupied the right groin. Rapid improvement set in almost immediately after the inauguration of the inoculation treatment, the wound healing rapidly and the gland in the groin disappearing. The patient left hospital on the high road to recovery toward the end of June. With the continuation of the treatment the ulcer entirely healed, the whole affected area being occupied, as it is now, by very soft elastic skin which does not in any way interfere with the movements of the foot. Towards the end of September, 1905, a small swelling developed in connection with what had been the upper border of the ulcer. This was opened and scraped, and the patient is now practically well, except for the fact that the scar of the last incision is still covered with a very delicate scab.

CASE 5.*—The patient, a woman, aged 28, presented herself for treatment in October, 1904, with tubercular ulcers on her legs which dated back to her fourteenth year. These had been treated by antiseptics of various kinds for thirteen years and had been scraped and skin-grafted. On the right leg the ulcerated surface corresponded in its dimensions with a five-shilling piece. Around this was an extensive area of thin, glossy skin. The ulcer on the left side occupied an area which extended from a little below the

level of the ankle to nearly the middle of the leg. In this area the tendo-Achillis and the peronei tendons were laid bare, and the point of the foot was drawn down so that the toes alone came in contact with the ground. All round the ulcerated area the skin of the leg was thin and glossy. The patient's tuberculo-opsonic index worked out as 0·17. After admission to hospital the patient was treated with therapeutic inoculations of tuberculin, supplemented by occasional staphylococcus inoculations and the local application of formalin gelatine. After six months' treatment the ulcer on the right leg had completely healed, and that on the left leg had been reduced to comparatively small dimensions. The inoculation treatment, which had raised the tuberculo-opsonic index of the blood to 1·8 and which had maintained it generally well above 1, was now supplemented by skin-grafting, and the patient left hospital with the ulcers completely healed and looking a picture of health. This continued until some six weeks ago, when, in association with a sinking away of the tuberculo-opsonic index to 0·8, a small vesicle developed on the inner side of the leg at the border of the healed ulcer. This broke down into a superficial ulcer corresponding in dimensions to a lentil. In association with an improvement in the tuberculo-opsonic power obtained by minute attention to dosage and proper interspacing of the inoculations, extension of this small ulcer has been arrested.

Case 6.*—The patient is a man, aged 35. When he presented himself for treatment in July, 1904, he had been for two years the subject of an inflammatory knobby tumefaction of the subcutaneous tissues in the region of the jaw and over a considerable area of the throat. The case had been diagnosed as actinomycosis and had been treated without result by scraping and iodide of potassium. The patient's opsonic index with respect to the tubercle bacillus was 0·67. With respect to the staphylococcus it was 1. The patient is now, after fifteen months' inoculation with very small doses of tuberculin, nearly well.

Throughout the course of the treatment it has been brought out very clearly (*a*) that the clinical condition corresponds in a very accurate manner with the tuberculo-opsonic index and (*b*) that the patient's opsonic index can be maintained at a much higher level when doses in the neighbourhood of $\frac{1}{800}$ are inoculated than when larger doses are employed.

Case 7.*—The patient is a man, aged about 35, a furrier. When he presented himself last June for treatment the dorsum of his hand was occupied by a deep ulcer corresponding in dimensions with a full-sized watch and surrounded by a raised edge. The ulcer had been treated by scraping. The patient's tuberculo-opsonic index stood at 0·85. Rapid improvement both in the opsonic index and in the clinical condition followed upon the inoculation of tuberculin, supplemented when this appeared desirable by the inoculation of a staphylococcus vaccine. The ulcer has now entirely healed and the site of the ulcer is covered in with soft and elastic skin which does not in any way impede the movements of the fingers.

Tubercular Invasion of the Lymphatic Glands.

Next, perhaps, to tubercular ulceration of the subcutaneous tissue, tubercular affections of the lymphatic glands furnish the clearest evidence of the efficacy of therapeutic inoculation of tubercle vaccine. This result, as reflection will show, is in accordance with what might have been expected *à priori* in view of the fact that the tubercle bacilli are here disposed right in the path of the lymph-stream, which is passing back through the gland to the blood. I do not myself doubt from what I have seen of the effect of inoculation on tuberculous glands that the extirpation of these by surgical methods as well as the purely climatic treatment of this affection are destined to give place to the therapeutic exploitation of tuberculin inoculations controlled by the determination

of the opsonic index, and combined with hot sand poultices and rubefacients, or other measures which, like these, will produce an ampler lymph-flow in the whole territory —or may I call it "watershed" or "collecting basin"— whose lymph passes into the blood through the conduit of the infected gland.

CASE 1.—The patient was a young married woman who had undergone at the hands of two distinguished London surgeons three successive operations for the extirpation of glands. When she presented herself for treatment in January, 1904, three or four glands could be felt in the neck, the largest one being of about the size of a small walnut. After the diagnosis of tubercle had been confirmed by a test inoculation, undertaken with Koch's old tuberculin, the vaccinal treatment with the T.R. tuberculin was inaugurated. Three months later, after six inoculations, conducted with doses which were gradually increased from $\frac{1}{5000}$ milligramme to a maxium of $\frac{1}{500}$ milligramme, the glands could no longer be felt and the dragging pains in the neck had entirely disappeared. After the disappearance of the glands a few more reinforcing inoculations were given. In January, 1905, the patient presented herself again, with swelling in the glands that had been previously affected. This swelling was, as before, associated with dragging pains, and the patient was thinking of having recourse again to operative procedure. In lieu of this the tuberculin inoculations were resumed, with the result that after three inoculations, undertaken in the course of a month, the glands again completely disappeared. They have, so far as I can learn, given no further trouble.

CASE 2.—The patient was the wife of a medical man. She had suffered from childhood from swollen glands on one side of the neck. These had become the source of constant dragging pains, and the largest gland, situated under the angle of the jaw, was large enough to produce considerable disfigurement. After three months of the

inoculation treatment the glands had much diminished in size and no longer gave rise to any disfigurement or discomfort.

CASE 3.—The patient, who had been a nurse and who had already undergone two operations at the hands of a distinguished surgeon, was referred by him for treatment in April, 1904, with a recurrence of tubercular glands in the neck. After three months' inoculations the swelling in the glands had entirely subsided. In association with this there was a very marked improvement in the general health. By the desire of the patient the inoculations are still being continued as a precaution against further recurrence.

CASE 4.—The patient, a girl, aged 4, came under treatment in connection with a recurrence of glands very shortly after operation. Her tuberculo-opsonic index stood at 0·7. After a series of six or seven inoculations the swelling in the glands had entirely disappeared.

CASE 5.—The patient, aged 4, came under treatment at the end of June, 1905, in connection with a recurrence of tubercular glands after operation and continued discharge from a deep gaping wound in the submaxillary region. By the end of September, after a course of tuberculin inoculations, supplemented on one or two occasions by an inoculation of staphylococcus vaccine, the wound had completely healed over and the glands were notably diminished in size. By the end of October treatment was discontinued, the swelling in the region of the wound and in the glands having entirely disappeared, the child being in absolutely robust health.

Tubercular Disease of the Genito-Urinary System.

From some points of view more convincing, in others only less convincing, than the results obtained in connection with lesions which are directly accessible to sight and touch, are the results obtained in connection with tubercular dis-

ease of the genito-urinary system, in particular in the cases where these involve the bladder. We have in the fact that these cases are associated with distressing pain and frequency of micturition, and in the fact that the presence or absence of tubercle bacilli in the urine can here be determined by microscopic observation, the means of measuring success and failure.

CASE 1.—The patient, a man, aged 20, when first seen twelve months ago was suffering from extreme frequency, and looked worn with pain. He was only with difficulty able to draw himself upright, and could only with some distress climb upstairs. There were considerable swelling and tenderness in the prostate and back of the bladder, and the urine contained some blood and a large quantity of pus. Microscopical examination revealed tubercle bacilli in considerable numbers in the urine. Cultures showed that there was no other bacterial invasion. The patient had been previously treated with inoculations of new tuberculin, the doses having been increased by geometrical progression up to $\frac{1}{25}$ milligramme. After the inoculation of the larger doses the pain and frequency of micturition were greatly aggravated. After waiting till the immediate effects of the last inoculation had passed off, inoculation was recommenced with $\frac{1}{1000}$ milligramme of new tuberculin. The tuberculo-opsonic index of the blood now stood at 0·62. After repeating the inoculation with $\frac{1}{1000}$ milligramme at intervals of ten days, and then tentatively advancing to a dose of $\frac{1}{500}$ milligramme without achieving any sensible improvement in the opsonic index or clinical symptoms the dose was reduced to $\frac{1}{8000}$ milligramme. The inoculation of this dose at ten-day intervals was followed by steady and sustained improvement both in the opsonic power and clinical symptoms. There was also a marked diminution in the prostatic tumefaction. After the dose had been for a time increased to $\frac{1}{6000}$ milligramme it was again reduced to $\frac{1}{7000}$ milligramme. While the frequency of micturition and the prostatic swelling have been much abated, and

while the patient is practically free from pain, his urine still contains tubercle bacilli. His condition is, however, now such that he is able to hold his urine for two hours at a time and capable of undertaking without fatigue a long day's shooting.

CASE 2.—The patient is a young woman of very good physique. She came under treatment first in January, 1905, with a history of tubercular cystitis and tubercular disease of the kidney dating back two years. One of her kidneys had been removed and there was evidence of the involvement of the other kidney. The urine contained pus in considerable amount, and in association with this many tubercle bacilli and several varieties of contaminating bacteria, among others *proteus*. The patient's tuberculo-opsonic index was tested on two occasions before the inoculation treatment was initiated. On the first occasion it stood at 0·75, on the second occasion at 0·35. An improvement in the patient's symptoms set in practically immediately after the first inoculation undertaken with $\frac{1}{800}$ milligramme. The tuberculo-opsonic power rose on the day after inoculation to 1·7, and continued at this height or near this point for the next six days. An inoculation undertaken on this day with $\frac{1}{400}$ milligramme brought down the opsonic power of the blood. In association with this the patient complained of more pain. After the inoculations had been continued for about six months, when the tubercle bacilli had disappeared from the urine, and when, as a result of the inoculation of a proteus vaccine, the *proteus* also had disappeared, the patient felt so well that she mooted the question of engagement and marriage. Since then she has suffered a relapse, developing an acute cystitis. This attack, which was apparently associated with a reappearance of the *proteus* in the urine, is now subsiding.

CASE 3.—The patient, like the last, is a young woman of good physique who, after suffering from pleural effusion

and severe cramps in the loins, suddenly in December, 1904, developed severe cystitis and hæmaturia. Tubercle bacilli were now found in the urine. When she came under observation in September last she was suffering from great frequency of micturition (up to twenty-five times in the night) and pain. Tubercle bacilli were sparingly present in the urine, while a form of pneumococcus was abundant. Her tuberculo-opsonic index stood on the first examination at 0·85 and on two subsequent occasions at 0·9 and 0·93 respectively. Inoculation was begun with a dose of $\frac{1}{800}$ milligramme of tuberculin, but this dose appears to have been excessive, inasmuch as the patient spent after inoculation a week of misery, the frequency of micturition rising on one occasion to thirty-two times in the night. The dose employed in the next inoculation was $\frac{1}{2400}$ milligramme, and this dose has been employed since with very satisfactory results, pain being greatly diminished and frequency of micturition now averaging five times in the night, while an opsonic index of 1·6 has been achieved.

Case 4.—This case has already been reported on by me twelve months ago as follows[1]: The patient, a married woman, aged 43, was admitted to hospital under the care of Dr. D. B. Lees in the middle of March, 1903, complaining of frequency associated with severe local pain on micturition and dragging pains in the loins, in particular on the left side. The urine contained pus, epithelial casts, and tubercle bacilli in such numbers that they could be demonstrated in large clumps in every field of a microscope in preparations prepared from the urinary sediment. Examination of the bladder revealed the existence of a large ulcer. The kidneys were enlarged and tender; the left one in particular was affected and suspicious signs were detected in the apex of one lung. Tuberculin treatment was begun in the middle of April, 1903. The effect exerted upon the body weight during the period the patient was in hospital is exhibited in the figures below:

[1] 'Clinical Journal,' November 9th, 1904.

	Pounds.		Pounds.
April 20th	91	June 15th	103½
„ 28th	96	„ 22nd	105
May 11th	92½	„ 29th	107
„ 19th	93	July 6th	109¾
June 1st	96	„ 13th	107¼
„ 8th	101		

The drop of body weight which is recorded on May 11th coincided on the one hand with the development of increased local pain and symptoms of giddiness and flushing, and, on the other hand, with a rapid fall in the agglutinating power of the blood, which is displayed in Curve 1 (*supra*). These were all, I take it, symptoms of the supervention of a cumulative negative phase dependent upon a too hasty inoculation of progressively increasing doses of vaccine. After leaving the hospital in July, much alleviated in the matter of pain and frequency of micturition, the patient attended as an out-patient, and under the treatment her weight in September, 1903, reached 119 lb. The tuberculin inoculations were continued up to July, 1904. All this while the tubercle bacilli, which were examined for almost every ten days, became gradually less numerous. By May they had completely disappeared from the urine. The patient none the less still suffered from serious bladder trouble—due, as appeared on examination, to cicatrisation and great thickening of the bladder walls and possibly to some superadded ulceration referable to septic invasion by the *bacillus coli* and by a Gram-staining diplococcus—micro-organisms which have been throughout present in millions in her urine. Taking up her history from this point, I may add that shortly after the publication of the above report the patient came back with symptoms of a relapse, and tubercle bacilli were once more found in her urine. Under the influence of further inoculations of tuberculin these again disappeared from the urine, and she continues to be free from pain and is in very good health. She suffers, however, from incontinence.

CASE 5.—The patient is a man of some 45 years. His history is as follows: In 1904 the right testicle became swollen and an abscess formed which left behind a sinus in the posterior aspect of the scrotum. In July, 1905, when the patient came into hospital, the right testicle was found to be typically tuberculous and there was discovered also a small nodule in the left epididymis. The patient was unable to hold his urine for more than half an hour at a time night and day, and in association with this tubercle bacilli were found in the urine. He was now treated by inoculations of tuberculin and left hospital in September much improved. Since leaving hospital he has put on 14 lb. in weight, and the frequency of micturition has been reduced, averaging now only four times in the night.

Summary of the Results obtained by Therapeutic Inoculation in Cases of Localised Tuberculosis.

In view of the very favourable and, what is almost more important, uniformly successful results which can, as will have appeared, be obtained even in the most intractable cases of localised tubercular infection by the therapeutic inoculation of tuberculin carried out under the safeguards explained above, and in view of the fact that not less favourable results can be obtained by the aid of the corresponding bacterial vaccines in the treatment of localised infections by other micro-organisms, I do not hesitate to contend that we have, in the power of raising the antibacterial power of the blood with respect to any invading microbe, out of all comparison the most valuable asset in medicine. I would, in view of this new asset in medicine, fain induce the surgeon to abate something from his conviction that extirpation and the application of antiseptics offer in connection with bacterial infection the only possible means of cure; I would have the surgeon resort to extirpation only when the physician tells him that all other means have been exhausted; and I would have the physician assume everywhere the *rôle* of an immunisator; and I would have him defer handing over his patients to the surgeon before he

has tried in every case of localised bacterial infection which is unassociated with immediate risk to life the therapeutic inoculation of the appropriate bacterial vaccine.

PART III.

Treatment of Systemic Tubercular Infections by the Therapeutic Inoculation of a Tubercle Vaccine.

In connection with pyrexial phthisis and other forms of pyrexial tuberculosis we are face to face with a problem which confronts us also in connection with every other systemic infection—*i. e.* the problem as to whether, in view of the fact that the machinery of immunisation is already spontaneously called into action, any advantage can be looked for from the inoculation of bacterial vaccines. Before an answer can be given to the question, we must try to form to ourselves (*a*) some conceptions of the conditions with which we have to deal in ordinary systemic infections such as are represented by continued fevers, and again (*b*) some conception of the special conditions which we have to deal with in pyrexial phthisis and similar tubercular affections.

Conditions which we have to take into account in connection with ordinary continued Fevers.

In the case of continued fevers, such as typhoid fever and Malta fever in man and anthrax in animals, bacterial elements are passing more or less continuously into the blood from regions like the spleen, where the micro-organisms are cultivating themselves in close relation with the blood-vessels. These bacterial elements, the nature of which we need not pause to discuss, exert upon the organism not only toxic effects, but call forth also immunising responses, in all respects similar to those which are called forth by the inoculation of bacterial vaccines.

Where the influx of the bacterial elements which here come into consideration does not exceed a certain maximum, there can be registered, no doubt often after the intervention

of a negative phase, a definite increase in the antibacterial substances in the blood. Such an increase is registered, for instance, in connection with typhoid fever and Malta fever when, after the fever has persisted for some days, an agglutinative reaction greater than that which is obtainable with the normal blood is obtained. By the aid of the antibacterial elements (of which the agglutinins furnish only the most easily demonstrated and therefore the most familiar examples) the invasion of the blood-stream is checked. If now by the continued elaboration of the antibacterial elements the bacteriotropic pressure of the blood is brought up to, and is sustained at, a sufficiently high level, the antibacterial effect makes itself felt, not only in the actual blood-stream, but in the backwaters of the circulatory system, where the blood flows comparatively slowly, and in the end also in the tissues. The invading micro-organisms will be finally disposed of when a lymph, rich in antibacterial elements, floods through all the foci of lowered bacteriotropic pressure in which the bacteria are ensconced.

Alongside of the cases which run their course to this favourable conclusion there are other cases where the influx of bacterial elements into the blood is immoderate and uninterrupted. Here we may fear that, owing to a paralysis of the machinery of immunisation, the antibacterial power of the blood will not be sustained, and that the invading bacteria will establish themselves in the circulating blood. The possibility that, by the incorporation of a bacterial vaccine into the body of a patient who is already staggering under a severe bacterial intoxication, such a further quantum of poison might be added, as would just suffice to overtax his power of resistance, is a risk which has to be considered in connection with all therapeutic inoculations of bacterial vaccines, undertaken in connection with systemic infections. That risk may, according to circumstances, be very grave or insignificantly small. Let me take the extreme cases. When, as in a case of fulminating typhoid fever, the system is profoundly intoxicated, and when the absence of the

agglutination reaction and the diminished content of the blood in other antibacterial substances show that the patient's power of immunising response is probably already overtaxed, I presume that no one would like to take the responsibility of incorporating a further quantum of bacterial poison. In the contrary case of a comparatively light attack of Malta fever, where the fever is likely to run on for months without any serious intoxication of the system, and where the imperfect development of the agglutination reaction seems to indicate that the immunising impulses are making default, I have gladly taken upon myself, and have counselled others to take upon themselves, the responsibility of applying further immunising stimuli in the form of a carefully safeguarded series of inoculations. In each such case the event has justified the procedure.

The cases last considered have a direct application in connection with the question of undertaking inoculations of a tubercle vaccine in connection with pyrexial phthisis. I would point out in this connection that there is, as between inoculations of bacterial vaccines made into the subcutaneous tissue and the introduction of bacterial poisons directly into the blood-stream, a very important difference, which must be kept in view. If the vaccines were to be incorporated directly into the blood-stream, we should thereby contribute directly to the intoxication of the central nervous system and the heart; and we should, as the very disappointing results which are achieved in the immunisation of horses by the intravenous injection of diphtheria toxins clearly show, be advancing but little in the direction of immunisation. On the contrary, when bacterial vaccines are incorporated into the subcutaneous tissues and when they therefore come into application in a concentrated form upon these, and are held fast by these, we may quite well be effecting a great deal in the way of immunisation without contributing in any appreciable manner to the intoxication of the central nervous system and heart.

Special Conditions which we have to take into account in connection with pyrexial Phthisis and other localised tubercular Infections which are associated with Pyrexia.

In the case of localised tubercular infections which are associated with pyrexia, the conditions are different from those in the continued fevers which have been under discussion (*a*) in the respect that the influx of the bacterial elements into the blood takes place from regions which do not stand in immediate relation to the blood-stream, and (*b*) in the further respect that this influx is discontinuous and stands in definite relation (to an extent which does not hold good in the case of other continued fevers), with causes which are to a quite appreciable degree under control. The causes which come into consideration here are, in particular, physical exertion, and mental effort, or excitement. Under the influence of these causes there can be registered, not only a rise of temperature, but also a variation of the opsonic power similar to that which is encountered in connection with the inoculation of tubercle vaccine. I may give as instances of such variations the cases of two phthisical patients, who took part in a dance or other entertainment, with the result that they both became ill, and that their opsonic indices, which had never previously been found lower than 1, declined to 0·12 and 0·33 respectively; further, the case of another phthisical patient whose opsonic index fell in connection with overwork to 0·2 from a level of over 1. I may refer you also in this connection to a paper[1] by my friends Dr. H. Meakin and Dr. C. Wheeler, which records similar effects produced in the case of phthisical patients in connection with walking.

We have a very simple explanation of these facts if we suppose that, under the influence of the limb and chest movements, and the circulatory disturbance and increased lymph flow which are associated with excitement, physical exercise, or mental overwork, tuberculous poisons from the infected tissues are conveyed into the blood. Especially

[1] 'Brit. Med. Journ.,' November 25th, 1905.

may an influx of lymph, loaded with tuberculous poison, be expected in the case where the patient who is the subject of a tubercular infection of the leg undertakes walking. We have already in Curve 4, *supra*, seen in connection with a case of tuberculous disease of the leg a rise in the tubercle-opsonic index which was to all appearances the result of running about. I have also quite recently seen another case of a similar association in the case of a boy with tuberculous hip-disease who, after lying on his back for years with a normal temperature, developed pyrexia on beginning to walk. No doubt this boy conveyed into his blood as he walked a stream of lymph which had passed through his old tubercular focus. In connection with, and probably as a sequela to this, I registered a tuberculo-opsonic index of 1·4.

Possibility in connection with pyrexial Phthisis and other localised tubercular Infections which are associated with Pyrexia of quieting the Circulation and stanching the Lymph-Stream in such a way as to arrest the Auto-Inoculations, converting the systemic Infection in this manner into a purely localised Infection.

The fact that in pyrexial phthisis and other localised tubercular infections which are associated with pyrexia the bacterial poisons are not generated in direct relation with the circulatory system is, as reflection will show, a fact which is pregnant with all-important consequences in connection with the therapeutics of the systemic infections we have here in view. While it may be possible in the case of continued fevers like typhoid fever to effect something in the direction of reducing the severity of the intoxication and the dosage of the auto-inoculations by keeping the patient perfectly quiet, the abolition of the intoxication and the arrest of the auto-inoculations constitute in the case of phthisis not a remote ideal but an ideal which is every day realised. The complete rest in bed, which gradually reduces the temperature in the large majority of cases of tuberculous phthisis, as well as

in other localised forms of tubercular infection, is, I take it, to be regarded as a therapeutic measure for making an end to those auto-inoculations which follow upon every over-exertion, and which make the life of the phthisical patient, when abandoned to his own devices, what my fellow-worker, Dr. R. H. Urwick, has shown it to be,[1] to wit, a succession of negative and positive phases. I take it that the rest in bed might, with a view to further stanching the lymph flow, with advantage be supplemented in every case by the administration of therapeutic agents which will increase the coagulability and viscidity of the blood. I have no doubt that this object is already in many cases undesignedly and unwittingly attained by placing the patient on a dietary of milk.[2]

Consideration of the Question as to how far the Patient has been brought in the Direction of a Cure when his Pyrexia has been Abolished and his Auto-Inoculations have been arrested by Confinement to Bed.

We may usefully ask ourselves exactly how much will have been achieved in the case of a tubercular infection if, when the influx of tuberculous poison into the blood has been arrested and the pyrexia has been abolished, we stop at this point. The question is an all-important one in view of the years and years of complete inaction to which many patients are condemned on the theory that they are, while they continue to rest and wait, every day making progress in the direction of a cure. To anyone who has surveyed the tuberculous patients laid out on spinal chairs in our seaside health resorts—waiting, or the patients who are lying in bed or upon deck chairs in our open-air sanatoria—waiting, it is plain as demonstration can make it that there is gained for the patient, by the arrest of the influx of tuberculous poison into his blood, a power of assimilating his food and an appearance of vigorous health. If only to the appreciation

[1] 'Brit. Med. Journ.,' July 22nd, 1905.

[2] *Vide* author's paper on "Milk as a Medicinal Agent," Lancet,' Oct. 14th, 1905.

of this fact there could be added the belief that the cure of bacterial infections depends neither upon the storage of fat, nor upon the bronzing of the skin, nor yet upon the breathing of fresh air (sea-coast air, country air, pine-wood air, mountain air, or warm southern air), but only upon the destruction of the invading bacteria by the antibacterial substances of the blood (with or without the co-operation with the leucocytes), we should, I think, have come close to the truth.

It is, at any rate, my belief that with the cutting off of the auto-inoculations progress in the direction of immunisation is arrested, and that with that arrest the blood reverts in every case to the inferior level of antibacterial power at which the blood of the subjects of strictly localised tubercular infection normally stands. If this is so—and I infer from what I have gathered from Dr. Lawson and Dr. Bulloch that this is the condition of affairs in phthisis when it has by rest in bed been brought back into the condition of a strictly localised infection—it is eminently comprehensible that the patient is liable to relapse when on return to work he over-exerts himself in such a way as to convey into his blood—as happened in the case of the tuberculous disease of the hip before adverted to—tuberculous elements from foci in his tissues in which the tubercle bacillus has survived.

Programme of Treatment which would appear to be indicated in the Case of pyrexial Phthisis, or other localised tubercular Infection which may be associated with Pyrexia.

If the views which I have developed above are in harmony with the facts, the following programme would seem to be marked out for us in connection with every case of pyrexial phthisis: (1) Our first efforts ought to be directed to bringing back the infection to the condition of a purely localised infection. Rest in bed and the adoption of measures for increasing the coagulability of the blood would be the appropriate methods for the achievement of

this end. (2) As soon as this first object has been achieved it should be our aim to substitute for the inappropriately adjusted and inappropriately interspaced auto-inoculations which wore down the patient without achieving effective immunisation a system of appropriately adjusted and appropriately interspaced inoculations of a tubercle vaccine. (3) Finally, as soon as by the means just indicated a satisfactory anti-bacterial pressure has been achieved in the blood, it should be an object of endeavour, by the regulation of the patient's exercises and by attention to his blood-pressure and by taking steps where necessary to diminish the coagulability of his blood, to irrigate in a methodical manner all the foci of infection with a lymph rich in anti-bacterial substances.

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[1] The separate fasciculus of the 'Proceedings of the Royal Society' which contains this paper can, it is understood, be obtained from Harrison & Sons, St. Martin's Lane, London, W.C.

A STUDY OF SOME POINTS IN RELATION TO THE ADMINISTRATION OF TUBERCULIN T.R.

CONTROLLED BY OBSERVATION OF THE OPSONIC INDEX IN PULMONARY TUBERCULOSIS

BY

DAVID LAWSON, M.A.(St. And.), M.D.(Edin.), F.R.S.(Edin.)

SENIOR PHYSICIAN TO THE SANATORIUM AT BANCHORY, SCOTLAND

AND

IAN STRUTHERS STEWART, M.D.(Edin.)

CLINICAL PATHOLOGIST TO THE SANATORIUM AT BANCHORY, SCOTLAND

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The course of research which we have undertaken is one which cannot be completely carried out under a period of three years. It must therefore be understood that the present paper, covering as it does only a small area of the field to be explored, is of an essentially preliminary nature. In this communication we submit for your consideration certain questions which have suggested themselves to our minds, and the means which we have taken to elicit answers to these. The cases of pulmonary tuberculosis studied—with the exceptions named—were cases in which pyrexia at the time of making the observations was absent. They were for the most part cases of subacute or chronic disease, in which the temperature had subsided under sanatorial or climatic treatment.

Our method consisted in making *daily* examinations of the blood of each patient for a short term previous to the commencement of inoculations, and then daily after the

inoculation of tuberculin had been begun. This method possesses certain advantages over the less laborious method of estimating the opsonic index at the longer intervals usually followed by others. These advantages will become apparent as we proceed. The total number of blood estimations made during the period covered by this paper is 1750. As four-hourly temperature records, with clinical notes added from time to time, were kept throughout the period during which the patients were under observation, it has been possible, in some instances, to form an opinion as to the relationship existing between inoculations of tuberculin, variations in the opsonic index of the blood, and the more common clinical symptoms and signs usually observed in the course of the disease.

In considering how best to present the facts observed, the method of "question and answer" seemed to the writers to be superior to other forms, and, therefore, that mode has been adopted.

The questions which they have set themselves to answer in this paper are as follows:

Firstly.—Does any difference exist between the opsonic indices of the blood (*a*) in healthy persons, (*b*) in persons who have suffered from tuberculosis and are now cured, and (*c*) in persons who are suffering from pulmonary tuberculosis (not in an acute form)? If so, can the fact be turned to any practical account in the *diagnosis* of the disease?

Secondly.—Assuming that the above classes of persons have been inoculated with small doses of tuberculin, is such inoculation followed by a difference in the behaviour of the opsonic index in Classes *a* and *c*? If so, can this fact be utilised in connection with the *diagnosis* of the disease?

Thirdly.—Is there any other means by which the presence and duration of the *negative phase* of the blood can be reliably determined than by the laborious method of making daily observations of the opsonic index?

Fourthly.—To what practical use, if any, can the facts so far elicited be put in the *treatment* of pulmonary tuberculosis?

I.

The opsonic indices of the bloods of 25 healthy persons.

E. B.	...	1·4		
D. L.	...	1·2		
L. S.	...	1·2		
T. C. L.	...	1·2		
W. S.	...	1·2		
J. C.	...	1·2		
J. G.	...	1·1		
N. J.	...	1·1		
C. C.	...	1·1		
R. L.	...	1·1		
H. M.	...	1·1		
W. T.	...	1	...	·9 to 1·2 (country)
N. S.	...	1		Average 1·0
N. H.	...	1		
J. M.	...	1		
W. T.	...	1		
A. T.	...	1		
W. C.	...	1		
N. M.	...	·9		
G. C.	...	·9		
W. O.	...	·		
W. O. J.	...	·9		
R. J.	...	·9		
J. G.	...	9		
J. R.	...	9		

Dr. Bulloch's 66 cases . . .	·8 to 1·2 (town)
	Average ·95
Limits of sound health . .	·9 to 1·2

II.

The Opsonic Indices of the Blood of Thirty Cases of Pulmonary Tuberculosis cured in Sanatoria without Inoculation.

Case.	Interval elapsed since patient discharged from Sanatorium. Years.	Months.	Opsonic index.
1	3	6	·5
2	1	9	·5
3	3	2	·6
4	—	9	·7
5	2	2	·7
6	3	1	·7
7	—	8	·7
8	—	7	·7
9	2	6	·8
10	—	6	·8
11	4	3	·9
12	—	4	·9
13	4	4	·9
14	1	8	1·0
15	3	6	1·0
16	3	6	1·0
17	1	1	1·0
18	1	9	1·1
19	1	8	1·1
20	1	6	1·1
21	—	9	1·1
22	—	6	1·2
23	3	7	1·2
24	4	2	1·2
25	1	10	1·6
26	4	3	1·7
27	3	6	1·7
28	—	6	1·8
29	1	2	2·
30	1	2	2·1

Question 1.

We first proceed to consider the subject opened up by question number one, namely, "Does any difference exist between the opsonic indices of the blood in (*a*) healthy persons, (*b*) persons who have suffered from pulmonary tuberculosis and are now cured, and (*c*) persons who are suffering from pulmonary tuberculosis (not in an acute form)?"

In Table 1, through the kindness of Dr. Bulloch, we are able to present you with the result of the examinations of the blood of a large number of healthy persons in addition to those obtained by ourselves. Considering our own figures first, your attention is directed to the fact that whilst a marked degree of variation in the level of the opsonic indices recorded obtains, it is a variation within clearly defined limits, namely between 0·9 and 1·2. The result of Bulloch's observations on the same lines nearly coincides with ours. So that we may take it that, for all practical purposes, the opsonic index of a healthy person in relationship to the tubercle bacillus does not vary beyond the limits of 0·9 and 1·2.

Our next inquiry was made in connection with the blood of patients who at one time were known to be the subjects of tuberculous lung disease and who had apparently recovered. For this purpose we selected thirty persons who had passed through our hands as patients, and who, having fulfilled all the known tests of being cured, are now considered useful lives. Here we were at once struck by the fact that although to all outward appearance these persons were as healthy as those dealt with under the previous heading, their indices differed materially from those of the others. In Table II you will find that not one half of their number are to be found within the limits which we had set down as those of normal health. In ten cases the opsonic index stood below ·9, and in six cases above 1·2. In two instances it touched as high as 2. Notwithstanding their apparent good health, in the cases of one third of their number their bloods were shown to

be defective in the supply of protective substances in relation to the tubercle bacillus.

Continuing the line of inquiry, we next examined the blood of twenty-five persons undoubtedly suffering from pulmonary tuberculosis (other than acute forms), and at the time of examination undergoing sanatorium treatment. Here (Table III), in three instances, an index was present sufficiently high to bring it within the limits of normal health, but in the remainder of the cases the level of the index was lower than that associated with health.

We thus arrived at the conclusion that whilst there is little difference between the opsonic indices of persons under Classes 2 and 3, the difference between these and Class 1—the healthy persons—is definite and characteristic. They are invariably lower than those in health.

Wright has elsewhere suggested that the opsonic index may be used for the purpose of diagnosing the presence of tubercular disease, and the effect of this observation is to confirm the soundness of the view there expressed. In cases where there is doubt as to the diagnosis, an opsonic index beyond the limits of health—that is, either above 1·2 or below 0·9—may be regarded as highly suggestive of the presence of tubercular invasion.

A case of some interest is one in which there existed some doubt as to the diagnosis. There was a history of slight continued pyrexia which subsided two weeks after admission to the sanatorium. Only very occasional slight cough was present. No sputum was available for bacteriological examination, and the physical signs at the right apex were suggestive of early infiltration. Our suspicions as to the presence of the lesion were strengthened by the appearance seen on X-ray examination. It occurred to us that an examination of the blood might prove of assistance. This was made, and the abnormally high index of 1·5 was found to be present. The suspicion thus further increased was shown to be well founded when about a week afterwards expectoration appeared and bacilli were found in considerable numbers.

III.

Opsonic Indices of the Blood in Twenty-five Cases of Pulmonary Tuberculosis (Subacute or Chronic).

Case.	Sex.	Age.	Lobes.	Opsonic index.
1	M.	25	2	1·0
2	F.	22	2	·9
3	M.	28	3	·9
4	M.	28	4	·8
5	M.	52	4	·8
6	M.	27	3	·8
7	F.	26	2	·8
8	M.	28	1	·8
9	F.	26	4	·8
10	M.	—	3	·8
11	F.	26	3	·7
12	M.	29	3	·7
13	M.	52	3	·7
14	F	18	2	·7
*15	F.	34	Miliary	·7
16	M.	28	4	·7
17	M.	24	2	·7
18	M.	28	2	·7
19	M.	27	2	·7
20	M.	36	4	·7
21	M.	36	5	·6
22	F.	32	1	·6
23	F.	24	3	·6
24	M.	48	2	·5
*25	M.	27	Miliary	·5
		Average	. .	·72

* Terminal miliary.

IV.—*Table showing Twenty-five Consecutive Cases of Pulmonary Tuberculosis, in which Negative Phase followed the Inoculations of Small Doses of Tuberculin (T.R.).*

DAY.	A.	B.	C.	D.	E.	F.	G.	H.	I.	J.	K.	L.	M.	N.	O.	P.	Q.	R.	S.	T.	U.	V.	W.	X.	Y.
1	**·9**	**·7**	**·4**	**·8**	**·7**	**·8**	***1·2**	**·9**	**1·5**	**·8**	**1·**	***1·**	**·6**	***1·1**	**1·**	**2·1**	**1·3**	**1·3**	***1·2**	**·6**	**·5**	***1·1**	**1·**	**1·3**	·7
2	·8	·4	·2	·4	·4	·7	·9	·8	9	·6	—	—	·4	—	·4	—	·5	·5	1·2	·5	·3	·8	1·	·9	·6
3	·4	·8	·3	·8	·3	—	1·3	·8	·5	·6	·4	·6	·4	·6	1·	1·1	1·3	1·3	—	·4	·8	1·1	1·	1·2	·8
4	·5	·9	·9	·8	—	1·2	·4	—	1·	—	·4	·9	1·2	·9	·8	·7	1·4	1·3	1·1	·9	1·1	1·4	1·	·7	·6
5	·8	·8	·6	·9	—	·6	1·2	1·	·5	·5	1·	·9	1·2	1·	—	1·6	·7	—	1·	·9	—	1·	·8	1·2	1·
6	·8	·8	**·7**	·7	1·	·6	**1·2**	·6	·8	·6	1·	·7	—	·7	·9	1·6	1·5	1·	1·4	·9	1·	·7	1·4	1·2	·4
7	·8	·8	·4	1·1	1·7	1·4	1·2	—	—	·6	1·3	1·	·7	·7	1·5	1·3	1·2	·8	1·3	—	1·	1·	1·5	1·3	1·2
8	1·	1·	·6	·8	**·9**	1·	1·2	1·2	1·	1·	—	·9	**·7**	1·3	1·5	·7	—	1·5	1·3	·7	·5	1·	1·5	·8	**·9**
9	1·3	1·	·6	**·9**	·8	2·3	1·8	**1·1**	1·	·8	—	·8	·6	**1·3**	1·1	1·1	1·6	·8	1·6	1·2	1·2	1·3	1·5	**1·4**	·6
10	**1·**	·9	·5	·8	1·1	—	**1·3**	—	1·	**1·**	—	·7	·7	1·	1·5	1·4	1·2	1·	—	·5	—	1·4	1·5	·9	·9
11	·3	**·8**	·6	·8	·8	1·2	1·3	·9	1·1	·7	—	·8	1·2	·9	·9	1·8	·8	·9	1·4	—	—	1·5	1·8	1·2	1·4
12	1·3	—	·7	·7	·8	1·6	·5	·9	1·3	—	—	·8	—	1·	—	1·2	·9	—	1·3	—	—	**1·2**	1·4	1·2	·7
13	1·2	—	1·1	·3	·8	—	1·3	·8	1·1	·4	—	·5	—	1·7	**1·4**	—	1·2	1·	**1·7**	—	—	1·4	2·2	1·2	·9
14	1·2	—	**1·**	1·	·9	1·2	1·4	·6	1·2	·4	—	1·5	—	—	·6	1·4	1·	2·1	—	—	—	1·	**1·4**	1·1	·7

* Negative absent on first but present on second inoculation.
(The darker figures signify that the patient was inoculated at this point.)

Question 2.

The next part of our inquiry was directed towards discovering whether or not there exists any difference in the changes which take place in the opsonic index of the blood after inoculation of small doses of tuberculin in the first and third classes of persons as those already dealt with. In order to attain this end we wished to inoculate tuberculin (T.R.) in small amounts into healthy persons and to persons suffering from pulmonary tuberculosis respectively, but, for obvious reasons, a difficulty presented itself in the shape of securing an adequate supply of healthy subjects. In addition to the results of inoculating healthy subjects obtained in ourselves, we have succeeded in obtaining the results secured in two other cases of healthy members of the profession. In so far as the inoculations were not followed by any sign of lowering of the protective substances in our sera, we had no room for anxiety. Indeed, exactly the opposite phenomena ensued. Our indices in each case immediately rose, and from being 1 and 1·1 previous to inoculation, they speedily attained high levels—in one case reaching to 2·1. This feature, then, is common to the observations made on healthy subjects so far as we have been able to secure any—after tuberculin inoculation the level of the opsonic index does not fall, but, on the contrary, immediately rises.

In marked contrast to this stand the opsonic indices of twenty-five patients suffering from pulmonary tuberculosis, ascertained immediately after inoculation with small doses of tuberculin (T.R.). These cases (Table IV), with the exception of two, were at the time of inoculation all apyrexial. You will observe that in each instance—there is no exception—a distinct fall in the level of the opsonic index succeeded the inoculation. The period covered by this fall Wright first designated by the term "negative phase."

There seems, then, to be this distinction between the behaviour of the blood of healthy persons and that of

persons suffering from pulmonary tuberculosis, that, whilst in the case of the latter, inoculation of small amounts of tuberculin (T.R.) is at once followed by the establishment of a negative phase, no such phenomenon appears in the former.

Provided further observations determine the constancy of the presence of a negative phase after inoculation of small doses of tuberculin in other forms of tuberculosis, there seems to be a practical application of this observation in relation to diagnosis. The appearance of a negative phase after inoculation of a small quantity of tuberculin (T.R.) should enable one to distinguish between the blood of a subject of tubercular invasion and that of a person in sound health.

Question 3.

Assuming the correctness of the conclusions already arrived at, and the value of the indications given by the presence of the negative phase after inoculation of tuberculin, it seemed to us extremely desirable that a shorter and less laborious method of recognising the incidence and duration of the negative phase should become available than by routine blood examinations. In this connection we may say at once that observation of the behaviour of the respiration and pulse yielded us no light whatever. Others made upon the relationship existing between the negative phase and variations in the temperature, whilst they failed to secure the end in view, elicited some facts of sufficient importance to be worthy, as it seemed to us, of being placed on record.

With the object of ascertaining the *relative incidence of negative phase and temperature disturbance after inoculation had taken place*, to the end of assisting us in arriving at a diagnosis, we placed twenty-five cases of well-marked pulmonary tuberculosis under four-hourly temperature records, and inoculated them with a small dose of tuberculin.

The result of this inquiry is seen in Table V, where

VI.

Chart showing the Relationship of the Duration of the Temperature Disturb-

VII.

Table showing the Incidence and Duration of the Negative Phase produced by Inoculation of Small Doses of Tuberculin T.R. during Treatment of Pulmonary Tuberculosis (120 *instances*).

No negative phase	Persistent negative phase	Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
			14	12	10	5	7	4	10	4	4	3	4	1	1	5
15	21		84													

VIII.

Showing the Proportion of instances in which Inoculation made on various days would in the foregoing 84 *Cases have taken place during the Negative Phase.*

Inoculation on the		Negative phase.		Percentage.*
3rd day	...	46	...	55
7th day	...	20	...	24
10th day	...	9	...	11
13th day	...	5	...	6
After 14th day	...	4	...	5

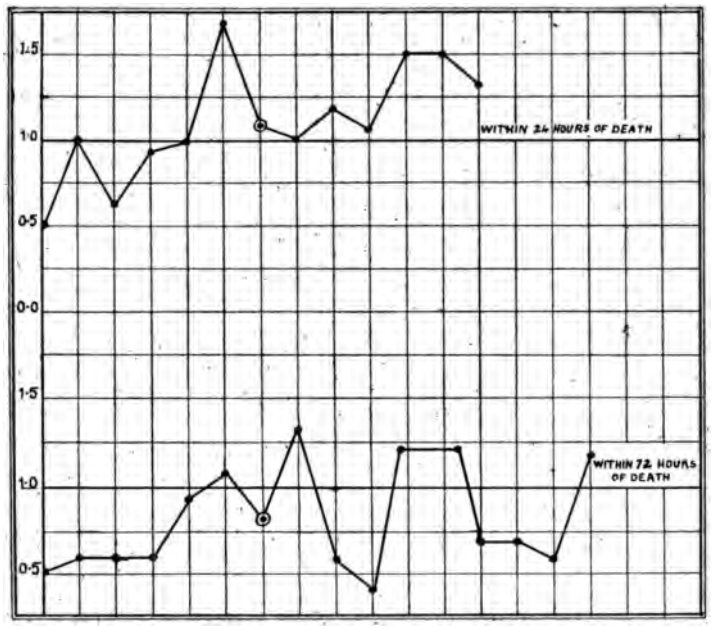
Thus, re-inoculation on the 8th day would have avoided the negative phase in 77 per cent. of instances, or in rather more than 3 out of 4 instances (modify).

Daily observation of the opsonic index of the blood, by enabling one to avoid inoculating during the negative phase, would have prevented harm being done in the remaining one fourth of the cases.

* Fractions ignored.

IX.

Opsonic Indices taken Daily during the Terminal Miliary Stage of Pulmonary Tuberculosis.



it is shown that whilst after inoculation a negative phase was obtained in eighteen cases, only in four instances did the temperature show any disturbance. On examining the results obtained by re-inoculating the remaining nine who had failed to respond, the comparison still favours the negative phase. If we use, as was done here, three inoculations, we discover that whilst temperature disturbance fails to be noted in only 47 per cent. of the cases, the negative phase is present in 100 per cent. When Koch's old tuberculin was introduced, we were told to base our conclusions as to the presence or absence of tuberculosis upon the temperature reaction which followed inoculation of that tuberculin. It is here shown there are many instances, in the cases dealt with amounting to over 50 per cent., where, although tuberculosis is undoubtedly present, the temperature reaction after inoculation with the T.R. preparation gives no indication of its presence whatever, negative phase being present in every instance. Temperature disturbance, therefore, is not to be relied upon. The establishment of a negative phase, on the other hand, as compared with temperature disturbance is a safe and reliable guide in the diagnosis of some types of pulmonary tuberculosis.

In course of our work we observed eleven instances in which establishment of a negative phase coincided with rise in temperature—we leave out of consideration those few instances in which it appeared to be accompanied by a fall in the temperature curve. We examined these minutely with a view to discovering whether it would have been possible, by *carefully watching this pyrexial manifestation, to have rightly gauged the duration of the negative phase.* In the figures, Table VI, shown there seems to be no harmony whatever. In two instances the duration of the negative phase and the pyrexial disturbance coincide; otherwise the duration of the temperature exceeds, and is exceeded by, that of the negative phase equally often. The temperature reaction when present, as shown, is slight, and in the majority of instances does not exceed three

days. We were, therefore, reluctantly forced to conclude that, alike as an indication of the incidence and of the duration of the negative phase, temperature disturbance is of no value whatever.

Question 4.

We come now to deal with the last question and what is, after all, the most important question which we have set ourselves to answer in this paper, viz. To what practical use can these facts be put in the treatment of pulmonary tuberculosis?

If the observation of the negative phase is important in relation to diagnosis, much more important is its relationship to treatment. Assuming the accuracy of the proposition, for which there are good grounds, that inoculation of tuberculin (T.R.) reinforces the negative phase when present at the time of inoculation, then it becomes a matter of paramount importance to ascertain exactly the state of the blood before we inject tuberculin. We have taken 120 cases of inoculation of patients under treatment in which daily observations of the state of the blood were made before and after inoculation had taken place. The result of an analysis of these is shown in Table VII. In fifteen instances no negative phase occurred. In 21 cases a persistent negative phase—that is, a negative phase extending beyond fourteen days—appeared, and the duration of the negative phase in the remaining 84 cases varied as shown in the diagram. A detailed consideration of those under columns 1 and 2 need not here detain us, but it is otherwise in regard to the remaining 84 cases. Taking these figures (VIII) as they stand, it may be profitable to consider what would have occurred had inoculation taken place by routine—say twice weekly. If all the patients had been reinoculated on the third day, in 46 instances, in so far as they would in that case have been reinoculated whilst the negative phase was still present, the inoculation, instead of doing good, would probably

X.

The Opsonic Indices of 25 *Cases of Pulmonary Tuberculosis after varying Terms of Treatment* (*without Tuberculin Inoculations*).

Name.	Duration of disease.		Duration of treatment.				Opsonic index.
			Climatic.		Sanatorium.		
	Years.	Months.	Years.	Months.	Years.	Months.	
M.	2	6	1	—	1	—	1·1
K.	1	2	—	—	1	2	1
L.	—	5	—	—	—	5	·9
H.	—	5	—	—	—	2	·9
McC.	4	3	—	—	1	7	·9
M.	1	—	—	—	—	2	·8
L.	4	6	4	—	—	—	·8
McD.	3	10	2	4	1	4	·8
F.	3	—	—	—	2	3	·8
W.	1	5	—	2	—	10	·8
G.	4	—	—	—	—	2	·8
T.	—	2	—	—	—	2	·8
P.	4	3	—	—	—	1	·7
McA.	4	1	2	6	1	1	·7
M.	7	—	1	—	1	2	·7
H.	8	—	6	—	—	6	·7
A.	1	2	—	—	—	9	·7
B.	1	9	—	—	—	10	·7
B.	2	—	—	3	1	4	·7
M.	1	—	—	—	—	4	·7
K.	—	4	—	—	—	4	·7
W.	3	—	—	—	1	4	·5
A.	3	6	—	—	2	2	·5
S.	1	5	—	1	1	—	·5
G.	2	4	—	—	1	10	·5

XI.

Comparison of the Opsonic Indices of the Bloods of Twenty-three Patients, taken after a term of Sanatorium Treatment only, with those taken after a short term of Sanatorium plus Tuberculin (T.R.) Inoculations Treatment.

Name.	O. I. before inoculation.	Doses given within a period of 5 weeks.	O. I. after inoculation.
S.	·5	4 of $\frac{1}{500}$	1·5
P.	·7	4 of $\frac{1}{500}$	1·3
McA.	·7	4 of $\frac{1}{500}$	1·1
McD.	·8	4 of $\frac{1}{500}$	1·
W.	·5	5 of $\frac{1}{500}$	1·1
A.*	·5	1 of $\frac{1}{500}$, 1 of $\frac{1}{1000}$	·8
M.	·7	3 of $\frac{1}{500}$	1·3
B.	·7	3 of $\frac{1}{1000}$	1·2
F.	·8	3 of $\frac{1}{500}$, 1 of $\frac{1}{250}$, 1 of $\frac{1}{500}$	1·3
A.	·7	3 of $\frac{1}{500}$	1·2
L.	·9	3 of $\frac{1}{1000}$	1·2
W.	·8	1 of $\frac{1}{1000}$	1·1
K.	1·	1 of $\frac{1}{1000}$	1·1
H.	·9	3 of $\frac{1}{1000}$	1·4
B.	·7	4 of $\frac{1}{500}$	1·3
M.	·7	1 of $\frac{1}{1000}$, 1 of $\frac{1}{2000}$, 1 of $\frac{1}{1000}$	1·5
G.	·5	4 of $\frac{1}{500}$, 1 of $\frac{1}{400}$	1·1
H.	·7	2 of $\frac{1}{1000}$	1·
G.	·8	3 of $\frac{1}{1000}$	1·
K.	·7	4 of $\frac{1}{1000}$	1·3
McC.	·9	3 of $\frac{1}{1000}$	1·4
T.	·8	2 of $\frac{1}{500}$	1·2
M.	·8	3 of $\frac{1}{500}$	

* Spinal complication. Index eventually

have done harm. Similarly, from re-inoculation performed on the seventh day, 20 would probably have derived harm, and so on as is shown in the table VIII. In direct proportion as we increase the period between the first and second injections up to the end of a fortnight, the risk is reduced from 55 per cent. at three days to 5 per cent. at the end of fourteen days.

We have, therefore, *in daily observations of the opsonic index* an invaluable guide which enables us to do what can be done by no other known means—namely, avoid re-inoculation at a time when, instead of exerting a beneficent action upon the course of the disease, it will promote the furtherance of toxic processes.

The next point which we submit for your consideration is the effect obtainable by inoculations of tuberculin by this method in cases which climatic and sanatorium treatment has hitherto, whilst benefiting, failed to cure. It is convenient to consider first two cases of miliary tuberculosis which did badly—indeed, both died. We may say that tuberculin inoculations were given at the urgent request of friends and with the full approval of consultants who saw both patients at a late stage of the disease. In neither case, although the record of the opsonic index (Table IX) brings us up to very nearly the time of death—in [illegible] case to within twenty-four hours and in the other [illegible] twenty-two hours—is it very low. Indeed, standing [illegible] higher than that of some cured patients, it [illegible] ly high. Reduced to chart form, both share [illegible] mon, that [illegible] large varia-tions, at [illegible] w normal [illegible] chart [illegible] ve wh [illegible] to [illegible]

to state the ultimate result obtained in those cases. Some of those patients had spent years abroad at health resorts of the highest repute, and had supplemented that course by undergoing terms of sanatorium treatment in this country. It was at the end of such treatment that the bloods were examined, and here (Table X) you observe that uniformly they showed low opsonic indices—indices well below normal in 20 out of 25 cases. These patients elected to have inoculations of tuberculin (T.R.) administered by this method, and on Table XI there is recorded the state of their opsonic indices after having undergone a period of not more than six weeks of such treatment. The chart also shows in each case the amount of tuberculin (T.R.) which they had received. These figures, we may say, were arrived at by taking an average of three consecutive readings, care being taken in making the estimation to avoid the negative phase. All other elements in the treatment having remained the same, the rise which had taken place in the supply of protective substances present in the serum which these higher indices point to can only be accounted for by the action of the tuberculin. It is therefore plain that in inoculations given in this way we have a valuable agent by means of which the resistance to, and therefore the power of combating the disease can be raised to a higher level than is in many instances obtainable by sanatorial and climatic treatment alone. Tables XII and XIII provide examples of cases treated in this way, in which recovery was eventually secured when the conditions had become to all appearances stationary after prolonged climatic and sanatorium treatment.

Consideration of the opsonic curve of the latter case reveals two points of interest. Firstly (Table XIV), it illustrates the method which is employed in order to gradually raise a patient's opsonic index. The period corresponding to the negative phase is jealously avoided, and a point slightly higher than the one at which inoculation last took place is successively selected for re-inoculations until a level is reached well above normal. Secondly, it illustrates the

XII.

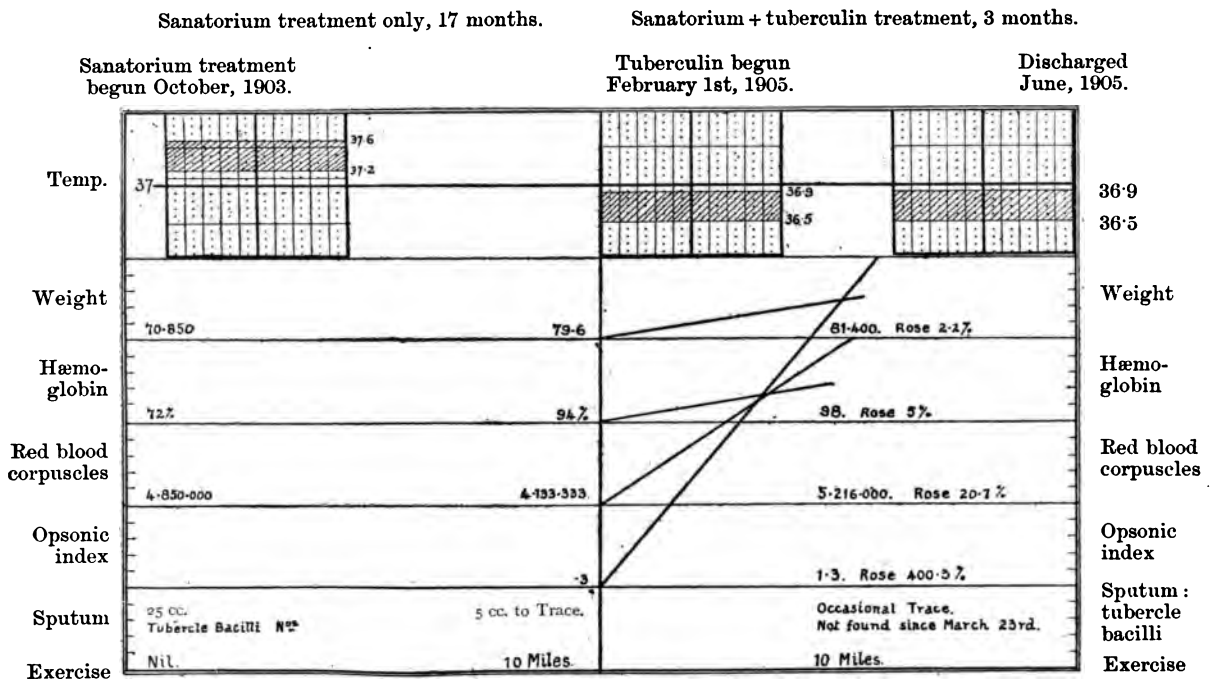
Male, æt. 26. Three-lobed lesions (bilateral).

TREATMENT.

	Sanatorium + 11 months. Climatic 3 years.	Sanatorium + inoculation 4 months.	
	March, 1904.	February 10th, 1905.	June 10th, 1905.
Temperature .	38 / 37 / 36		Percentage. 38 / 37 / 36
Weight . .	61.750 kilos.	65.800	68.800. 4·5 per cent.
Hb. . . .	78.		90. 100. 11·1 per cent.
R. B. C. . .	4,700,000.	4,100,000.	4,960,000. 20·9 per cent.
Opsonic index .		·86.	1·46. 6·9 per cent.
Sputum, amount	Trace.	Trace.	0. —
T. B. . . .	Present in fair nos.		0. —
Exercise . .	0.	6 miles.	10 miles. —
Physical signs .			Occasional post-tussive crep. remains in supra-clav. area. —

XIII.

Male, æt. 46. Pulmonary tuberculosis—Two-lobed lesion, right.



Result—An occasional crepitation is still noticeable in extreme apex. The patient appears to be in perfect health, and is believed to be cured.

condition compatible with recovery, namely not an index standing at a very high level, but one standing slightly higher than is found in normal health and, as is present in healthy persons, maintained steadily about that level. Eventually the oscillation has come to comparative rest. There is established a condition of equilibrium in the vicinity of normal. The analogy between the behaviour of temperature curves in pulmonary tuberculosis and the behaviour of opsonic curves is thus sufficiently striking; both are most unstable during active disease, and both alike return to a condition of stability with the falling away of the active signs.

Although the last table (No. XV) to which your attention is invited does not contain the record of work done by ourselves, the relationship between it and the subject with which we are concerned is so close that we feel no apology is necessary in using it.

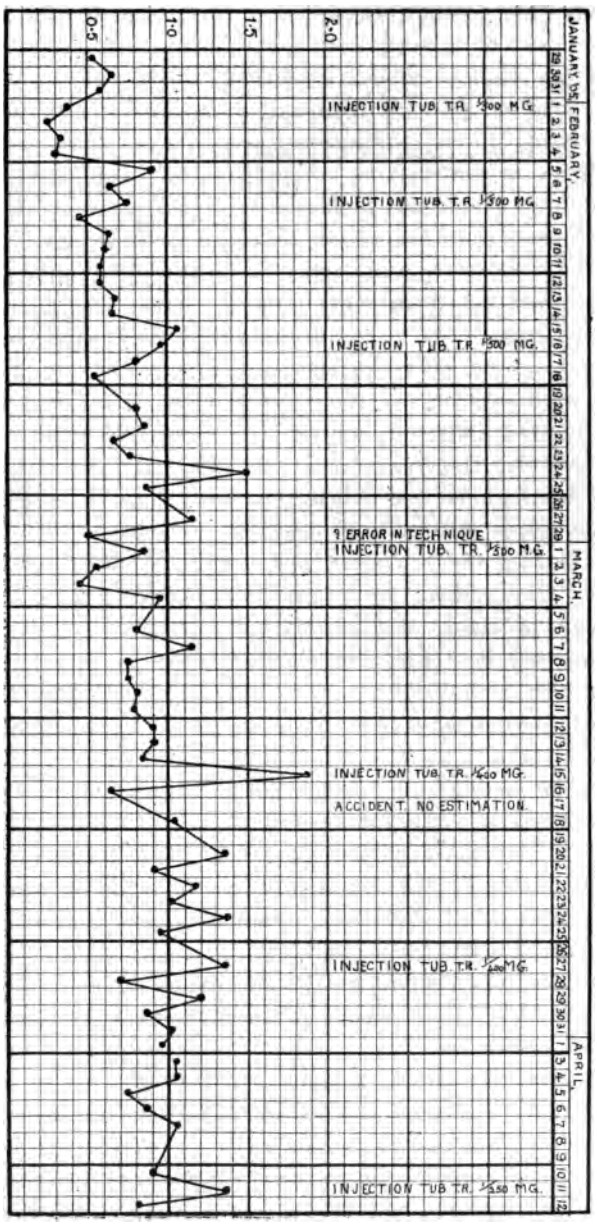
During the whole of the period extending from 1890 to 1901 Trudeau of America employed inoculation treatment in cases of pulmonary tuberculosis. In the brief summary here presented he compares the results obtained by pure sanatorial measures with those in which the sanatorium treatment was supplemented by inoculations of tuberculin in some form.

The deductions made from a body of work extending over twelve years, and coming from so weighty a source, merit the most careful perusal. The conclusion which this observer has arrived at is that the percentage of relapses in all classes of pulmonary tuberculosis in which tuberculin has been employed as a part of the treatment is very much smaller—for the exact figures we refer to Table XV—than where sanatorium measures alone have been relied on.

Assuming the correctness of the observations made by Trudeau, it seems that in those cases in which tuberculin was employed not only was the percentage of cures increased, but the liability to relapse was diminished. Is the explanation not to be found in the fact that, even

XIV.

G—, æt. 48. Pulmonary Tuberculosis.



V.

Table showing the Comparative Incidence of Negative Phase and Temperature Disturbance in Twenty-five Cases of Pulmonary Tuberculosis after Three Injections of Tuberculin (T.R.).

Negative phase.			Temperature.		
18	6	1	4	5	2
100 per cent.			47 per cent.		

Thus, whilst temperature disturbance—the guide recommended to us by Koch in using his old tuberculin—is in this instance absent in over 50 per cent. of cases of undoubted tuberculosis, the negative phase is present in every instance, namely, 100 per cent.

XV.

Trudeau's Results from 1890—1901.

A.

Cases treated (non-tuberculin).		Cases treated (tuberculin).		Advantage to tuberculin cases.
1367	...	143		
Alive.		Alive.		
38 per cent.	...	58 per cent.	...	20 per cent.
Dead.		Dead.		
39·6 per cent.	...	33 per cent.	...	Balance untraced.

B.

Incipient cases only.

Alive.		Alive.		
61 per cent.	...	76·7 per cent.	...	15·7 per cent.

handicapped as he was by the absence of any precise and scientific method to guide him in his work, such as is to be found in systematic observations of the opsonic index, he succeeded, by means of tuberculin inoculations, in raising the resistance of the cases so treated to a higher level than was reached in those cases in which he depended entirely upon sanatorial measures of treatment? If that is so, then there seems every likelihood of obtaining in the future, by means of this line of treatment, results which will prove superior to any which have been obtained in the past in the treatment of tubercular disease.

That a higher standard of protection can be obtained by the inoculation of tuberculin is claimed. How long the protection lasts we do not yet know. In patients who had been successfully treated by tuberculin inoculations whom we discharged six months ago, and whose blood was re-examined last week, we found no appreciable falling away.

In concluding the report on the result of these investigations, we gladly avail ourselves of the opportunity which the circumstance affords to gratefully acknowledge our sense of indebtedness to Dr. Wright for the privilege enjoyed of working for a time in St. Mary's Pathological Laboratory under his personal supervision, and for much valued guidance and help received at his hands from time to time in connection with our work.

THE TREATMENT OF TUBERCULOSIS BY TUBERCULIN

BY

WILLIAM BULLOCH, M.D.,

BACTERIOLOGIST TO THE LONDON HOSPITAL

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THE main currents of intellectual activity in the domain of pathology have flowed for the past thirty years towards the elucidation of the causes of disease. We have passed away from the earlier symptomatic and anatomical, and have arrived at ætiological concepts. A most important advance has been the demonstration that a number of diseases owe their origin to the invasion of the body by parasitic microbes. The doctrine that these microbes are specific has triumphed over other conceptions, and may be said to be a universal belief at the present time. The aim of this absorbing and intricate study has been the construction of a scientific theory of disease, and depending on this the elaboration of a rational therapy. But even this rational therapy is gradually narrowing itself down to a *specific* therapy. Remedies are being sought which lead to the exclusive destruction of the particular specific microbe which has been proved to be the cause of the given infection.

Following Edward Jenner, the pioneers of bacteriology,

notably Pasteur, sought to induce a prophylaxis by the inoculation, mostly in attenuated form of the ætiological agents themselves, or products derived from them. To Koch, however, belongs the credit of having been the first to attempt to *cure* an infection by a specific remedy, viz. tuberculin in tuberculosis.

When we reflect for a moment on the problem which confronted Koch it will be manifest that the results of such treatment cannot be compared with those in which a prophylaxis is induced against an infection like variola, where, in the natural course of events, an extraordinary degree of immunity is established for a number of years, or for the life of the individual.

The extensive study of tuberculosis has shown that man and beast are infected to an alarming extent. In man, at any rate, the observations of Naegeli and others lead one to assume that the disposition is almost universal. If exposed to tubercle bacilli for any prolonged period few escape without some lesion. By a long acclimatisation the tubercle bacillus has become extraordinarily parasitic and seemingly incapable of multiplying its numbers outside the living body. The parasitism is also evinced in the extreme chronicity of the tubercular processes, and the fact that the bacillus is not comparable in the intensity of its pathogenic effects with the rapidly fatal septicæmic blood infections. Recently, Theobald Smith has developed the idea, paradoxical as it may seem, that the more habituated a microbe becomes to subsisting in the living tissues, *i. e.* the more parasitic it becomes, the less actively aggressive it is and the more it endeavours by pure methods of defence to secure a nidus, wherein it may multiply undisturbed. The throwing up of cellular works in the shape of a specific granuloma by the host may thus be a disadvantage in so far that the bacillus is protected in an abode where it may sojourn until opportunity occurs for transmission to another host. It is, however, generally supposed, arguing from the analogy of lifeless *irritamenta*, that the enclosure of the alien substance by a wall of

granulation tissue is a sign that the organism is endeavouring to cope with the offensive agent by excluding it.

The most recent studies in immunity to tubercle lead us, however, to conclude that the enclosure of the tubercle bacillus by a wall of poorly vascularised granulation tissue is a drawback, as the anti-bacterial forces which we know to exist in the body humors are kept at bay, the parasite remaining locally, and being at long intervals discharged outward. In general, the defence offered by the bacillus is so powerful that only a relatively small degree of immunity is developed by the host. This statement rests on a large body of evidence, and it cannot be expected, even from a remedy like tuberculin, that a high degree of immunity can be attained in a short space of time, or that the curative effect of this remedy is comparable to its prophylactic effect. We cannot evade the conclusions reached by a generation of medical scientists, and it seems to me that this is all the more important at the present time, when the eyes of the civilised world scan the scientific horizon with anxiety for the long expected "cure for consumption."

The foundation of Koch's work—to my way of thinking his greatest work—was the observation that even small quantities of killed suspensions of tubercle bacilli can produce death in animals already tubercular. By reducing the dose to very minute proportions he found in a certain number of cases that the disease can be brought to a standstill. He found, however, that the dead bacilli which he had injected remain locally for long periods, and may ultimately give rise to abscesses. Whatever amelioration of the tubercular disease had taken place must have been due to substances which passed out of the bodies of the dead bacilli injected, and this gave the suggestion that such substances might be prepared artificially and injected in a form capable of rapid absorption. In this way originated tuberculin, now described as "old tuberculin" (T.O.), a concentrated glycerine extract of tubercle bacilli. When this extract was injected into

tubercular individuals the manifestations witnessed were pyrogenic and phlogogenic, the latter consisting of inflammation, leucocytic emigration, and necrosis of tubercular foci, which were visible to the eye. Koch regarded this local necrotising action as an essential element in the cure, and the explanation of the action accepted by him was that originated by Babes, and spoken of as the "addition theory," which assumed that the tubercle bacillus produces certain substances, some of which bring about a coagulation necrosis. This necrosis acts deleteriously on the bacillus and may cause its death. By the inoculation of tuberculin the necrotising effects are increased in intensity—a condition which seriously affects the vitality of the bacillus, so that ultimately a phase of tranquillity, or even cure, is established in the infected individual. The rise of temperature which accompanies the local reaction was looked upon as specific, in so far as it occurred only in tubercular individuals. In recent years it has been shown, especially by Preisich and Heim, that the tuberclin reaction is more complicated than was originally believed. They have proved that the presence of tubercular tissue is not necessary for the onset of the tuberculin febrile action. By transplanting collodion sacs containing the bacilli alone into the peritoneal cavity of guinea-pigs, followed by the inoculation of suitable doses of tuberculin, they have obtained typical tuberculin reactions. This reaction must be due either to substances which have diffused out of the collodion capsules, and which have united with the tuberculin to give rise to a substance which produces the reaction, or in virtue of the toxic action of the tuberculin a change is induced in the cells which renders them capable of manifesting the tubercular reaction. Preisich and Heim have in fact shown that there are substances in the serum of tubercular animals which, on admixture with tuberculin, are capable of setting up a typical reaction in normal animals. As they found, however, that such substances may be present in normal serum, they concluded that the rise of temperature follow-

ing an injection of tuberculin cannot be looked upon as specific of tuberculosis. The tuberculous reaction is, however, generally regarded as specific. Whatever may be the ultimate views held on the nature of this tuberculin reaction, there is no doubt that fifteen years ago Koch and other investigators considered that a local reaction is a necessary part of the curative action of tuberculin.

No remedy in therapeutics has suffered the fate of Koch's tuberculin. At first hailed with ecstasy as the long-sought panacea for tuberculosis, its short-lived glory was succeeded by a period of absolute rejection, and then one of indifference, so that to-day it may be regarded as having dropped out of the pharmacopœia of even the serious medical practitioner.

So convinced, however, was Koch of the virtues of tuberculin that he proceeded to perfect his discovery, and as he had observed that with the repeated inoculation of this substance a period of tolerance is established when the reaction, and with it, according to him, the curative properties come to an end, he strove to prolong the reaction period, and achieved this to a certain extent by tuberculin A, an extract of the tubercular cultures with $\frac{N}{10}$ sodium hydrate solution. The disadvantage of tuberculin A was, however, that abscesses were frequently produced, as the bacillus remained unabsorbed for long periods at the point where it had been inoculated. This led Koch to the idea that the difficulties of absorbability might be got over by the mechanical comminution of the bacillus. To this end highly virulent bacilli were dried in vacuo, and then comminuted by machinery. The dust was treated with distilled water, and the mixture was then placed in a centrifuge rotating 4000 turns per minute. In this way an opalescent fluid (T.O.) and a deposit were obtained. The deposit was then worked up with successive quantities of water, and was named T.R. This, under the name of tuberculin

T.R., or Koch's new tuberculin, is sold in commerce in bottles containing 10 mgr. solid substance per c.c. The opalescent fluid (T.O.) possesses properties analogous to the old tuberculin, whereas the T.R. as Koch himself recognised acts independent of a local reaction which, in fact, should be prevented at all costs. Koch, however, recommended forcing the inoculations as far as was compatible with the absorption of the tuberculin.

Following on the work of Koch other bacillary products have been recommended, such as tuberculoplasmin (Buchner), tuberculocidin and antiphthisin (Klebs), oxytuberculin (Hirschfelder), tuberculin (Denys), tuberkulol (Landmann), tuberculin (Beraneck). These remedies have been vaunted as superior, whereas few, if any, attain even the measure of success of Koch's tuberculin. Taking them as a group we may apply the term tuberculin as a collective name for soluble or emulsionised products prepared from the tubercle bacillus.

Between the years 1890 and 1897, while Koch was investigating the therapeutic value of his tuberculins, a remarkable event in medicine had interposed itself. I refer to Behring's discovery and application of serum therapy. At once it was thought that at last here was the line of real advance in the treatment of tuberculosis, but, despite the most strenuous effort, nothing even worthy of comment has been achieved by the various antitubercular sera which have been manufactured, and the attempts and methods have been so manifold that one is inclined to prophecy that the era of tubercular serotherapy is past.

What has been the result of eight years' experience with Koch's new tuberculin? Already, within a year of its introduction, a large number of authors here and abroad have written commentaries of disappointment. Others have condemned it as being contaminated or even infected with the tubercle bacillus itself. Others, again, who have given it a serious trial report that the results depend not so much in the remedy itself as in the

manner of its exhibition. Authorities like Turban, Goetsch, Petruschky, Spengler, and Moeller have pronounced in its favour, even in pulmonary tubercle. With few exceptions, dermatologists do not seem to have been convinced of its efficacy. The work of a man like Koch cannot be brushed aside as fanciful, and there is, I think, no doubt at all that tuberculin is a substance which possesses remarkable curative powers in tuberculosis. Recently in this country Wright has opened up the question of tuberculin therapy, and has achieved memorable results in the treatment of the localised forms of tubercle. He has shown that protective substances of opsonic nature exist in the normal serum, and that the opsonic content of the serum can be increased by the inoculation of tuberculin. It is manifest from his work that the chief defensive mechanism against tubercle exists in the serum, and not in the cells, as was believed, and the destruction of the bacilli by the cells must be preceded by the action of the serum. He has also elaborated a method by which it is possible to determine the opsonic content of the serum, and he has utilised this determination as a guide to the inoculation of the infected individual with tuberculin. An important outcome of his studies has been the demonstration that tuberculin is an extremely potent agent, and that its dosage hitherto has been excessive. I have worked a good deal with the methods invented by Wright, and propose to give some of the details of this work in connection with the treatment of tubercle, especially in its localised forms.

In his earlier work Wright noted that the opsonic index of individuals suffering from tubercle is lower than that of normal people. In order to determine whether this is constant I have examined first of all the indices of eighty-four healthy people, comprising forty-four medical students and forty hospital nurses. In all cases the serum was compared with my own, which was regarded as unity. The result was as follows:

Opsonic index of forty-four healthy medical students compared with the serum of the writer = 1·0.

1	case	= 1·2
15	cases	= 1·0
8	„	= 0·98
7	„	= 0·97
2	„	= 0·96
2	„	= 0·94
6	„	= 0·90
2	„	= 0·85
1	case	= 0·80
44	cases	average opsonic index = 0·96.

Opsonic index of forty healthy hospital nurses.

5	cases	= 1·1
13	„	= 1·0
5	„	= 0·98
4	„	= 0·97
2	„	= 0·95
6	„	= 0·90
2	„	= 0·85
3	„	= 0·80
40	„	average opsonic index = 0·96.

Taking the two series together we get an average index of 0·96 for the eighty-four people, the variations in health ranging from ·8 to 1·2.

Coming to cases of tuberculosis I have already published, in the 'Transactions' of the Pathological Society, the determination of the opsonic indices of 150 cases of lupus occurring in the Skin Department at the London Hospital. The great majority of these cases attended the Hospital for the purpose of X-ray or Finsen-light treatment.

Compared with the average opsonic index of 0·96 obtained in normal people the average for the 150 cases of lupus was 0·75, the cases being distributed as follows:

3	cases	Opsonic index =	·2— ·3
3	„	„ =	·3— ·4
21	„	„ =	·4— ·5
29	„	„ =	·5— ·6
33	„	„ =	·6— ·7
22	„	„ =	·7— ·8
18	„	„ =	·8— ·9
7	„	„ =	·9—1·10
14	„	„ =	1·0—1·4

75 per cent. of the lupus cases showed an opsonic index below the lowest normal limit of ·8.

Clinical data were available whereby the results obtained by Finsen therapy could be compared with the height of the opsonic index, and on analysing these data it was found in general that where the opsonic index is well below the lowest normal limit the results of Finsen therapy have been disappointing, whereas with indices in the normal limits or above them the clinical impression has been that the cases have done well. The mode of action of the exposure to light in Finsen's method has been the subject of much inquiry. It is admitted on all hands that under certain conditions of experiment light acts as a bactericidal agent. This, however, has not been proved in the case of Finsen light, where the rays have to traverse the skin. In all probability, and the above results lend support to this view, Finsen light acts mainly by producing a local inflammation with great vaso-dilatation, and a transudation of large quantities of plasma in the areas exposed to its action. If the serum is poor in antibodies the results of Finsen therapy are disappointing, and this suggests that its value might be enhanced if the antitropic content of the serum were increased by previous inoculations of tuberculin.

Eleven cases of surgical tubercle were examined with the following result:

1.	Tuberculosis of knee	Opsonic index =	·8
2.	„ knee and spine	„ =	·5

3.	Tubercular abscess of gluteal region; tubercular peritonitis	Opsonic index	= ·5
4.	Tubercle of bone for years (humerus, hip, peritoneum) .	,,	= ·7
5.	Tuberculosis of knee . .	,,	= ·75
6.	Tubercle of lymphatic glands .	,,	= ·3
7.	,, ,, .	,,	= ·6
8.	,, genito-urinary organs	,,	= ·6
9.	,, ,, ,,	,,	= ·6
10.	,, ,, ,,	,,	= ·7
11.	,, ,, ,,	,,	= ·6

Fourteen cases of so-called "sanatorium cures" or arrested cases of phthisis were examined, and the index was found depressed in all except one. These cases were all from the well-to-do classes, and in at least one of these cases, which was considered a perfect cure, the disease has relapsed within a year.

Case 1	.	Opsonic index	= ·7
,, 2	.	,,	= ·6
,, 3	.	,,	= ·7
,, 4	.	,,	= ·6
,, 5	.	,,	= ·5
,, 6	.	,,	= ·4
,, 7	.	,,	= ·6
,, 8	.	,,	= ·65
,, 9	.	,,	= ·75
,, 10	.	,,	= ·6
,, 11	.	,,	= ·5
,, 12	.	,,	= ·45
,, 13	.	,,	= ·6
,, 14	.	,,	= ·86

From these determinations in healthy and diseased people it would appear that an index below ·8 is abnormal. It is not possible to say when a low index is encountered whether the individual is already infected or is merely likely to be so. The very early diagnosis

of tubercle is difficult or impossible by ordinary clinical methods. Arguing from the case of staphylococcus lesions which are visible in the skin the probability is that a very low index indicates that infection has occurred. An abnormally high index is probably a sign of infection, but cannot be used as a prognostic, as it may occur in those cases which do well or in those which are quite hopeless. Repeated determinations of the fluctuations in the index are probably of more importance in forming an opinion on the future of the case.

The exact nature of the opsonic action has not yet been worked out. All investigators, however, are agreed that where different bloods are compared the variable factor is the serum and not the leucocytes. The existence of Metchnikoff's hypothetical "stimulins"—bodies which stimulate the leucocytes—still lacks demonstration. The relation of the leucocytosis, which accompanies most infections, to the opsonic content of the serum has not been made out. Bulloch and Ledingham in a large number of experiments failed to demonstrate that there is any close relationship between these factors. With certain drugs, such as sodium cinnamylicum ("Hetol") and tallianine, which produce marked leucocytosis, no increase in the quantity of the opsonin could be determined. Subcutaneous inoculations of a solution of nuclein from yeast had, however, a very marked effect in producing an opsonic increase although the leucocytosis was inconstant.

Specificity of opsonins.—This question has hitherto not been touched in the various memoirs which have appeared on opsonins. In conjunction with my assistant, Dr. Western, I have recently been able to demonstrate that a high degree of specificity exists. This has been shown in two classes of experiments. In the first the opsonic power of a serum was tested against both staphylococcus albus and tubercle bacillus. The serum was then mixed with one or other of these microbes, and after a sojourn in the incubator the mixture was subjected to

the prolonged action of the centrifuge, whereby the microbe was thrown down as a deposit, the supernatant liquid being then tested for both microbes. The result of experiments of this type is that the supernatant liquid is largely deprived of its opsonin for the particular microbe with which it has been in contact while it retains its opsonin for the microbe with which it has not been digested.

In the second class of experiment the serum of human beings was tested repeatedly, both against tubercle bacillus and against staphylococcus. Injections of tuberculin produced an increase in the tubercular opsonin while leaving the quantity of staphylococcic opsonin unaltered, and *vice versâ*. We may thus assume the demonstration of the specific nature of the opsonins in the serum.

Effects of the inoculation of tuberculin.—In almost every instance of scores of inoculations I have observed the occurrence of a negative phase. In the cases where this has been absent it has followed a very minute dose, or the same dose had been injected several times previously. The determination of opsonic curves also leads me to believe in the correctness of Wright's view that the negative phase is one of importance. It is extraordinarily variable, even where the same doses of tuberculin are given to different people. In some cases the descent is abrupt and steep, in other cases the negative phase persists over a number of days, and frequently the subjective symptoms of discomfort on the part of the patient are increased. I have on several occasions seen a definite exacerbation of the symptoms associated with a prolonged negative phase.

The maintenance of Wright's "high-tide" phase of the immunity curve is subject to great variations. In most cases, as far as my experience goes, the "high tide" is in the course of a few days succeeded by a fall again, although the fall is rarely as deep as that shown prior to the injection of tuberculin. In spite of this, the improvement may continue, a fact which leads me to assume that

there are other factors at work which at the present time cannot be measured.

The vaccine employed was Koch's new tuberculin, as manufactured by Meister, Lucius, and Brüning, at Höchst.

Cases.

All the cases which I have had to treat have been severe. The majority of them, in fact, had passed from the hands of physicians and surgeons, and were regarded as incurable. It is impossible to speak with certainty as to cure, because a great deal depends on what is meant by this term. In ordinary medical parlance there is a time element in the question, and one must distinguish between a temporary and a permanent cure. Thus one of the patients I have treated was a boy the subject of tubercular glands of the neck. An extensive operation was undertaken, and the diseased glands were removed from both sides of the neck. After a residence of some four weeks in the hospital he was dismissed "cured," although there was a slight discharge from one of the wounds. But this discharge never stopped, and six months later he was as bad as ever, with two sinuses leading down to softening glands. By the use of tuberculin alone these glands have disappeared and the wound is completely closed, so that there is a temporary cure; but no one can say that the cure is permanent until the individual has been a long time under observation.

I have treated two cases of genito-urinary tuberculosis, seven cases of lupus, and two cases of gland tubercle.

The results may be briefly stated as follows:

1. B—, by profession a surgeon. Suffered from genito-urinary tubercle, which had been operated on on several occasions. The disease recurred, and it was decided that further surgical interference was impossible. A prolonged course of tuberculin, with estimation of the opsonic

indices, has led to immense improvement, not only in the general health, but in the local area where the tubercular deposits have disappeared. This man is now in relatively good health.

2. E. C— (16), a girl weighing 3 st. 4 lbs., and the subject of extensive but quiescent tubercle of spine and genito-urinary tuberculosis. Four months' treatment has caused great amelioration in the distressing symptoms to which she had been subjected. The patient is still under treatment.

3. F. C— (23). Phthisis on maternal side. Patient had pleurisy at the age of ten. Lupus began in childhood, and extended over cheek and eyelid. Treated with X rays and 170 applications of Finsen light. Main area of disease healed up well, but fresh nodules frequently made their appearance. His opsonic index on two occasions was ·8. Four inoculations of tuberculin were given, viz. $\frac{1}{750}$, $\frac{1}{400}$, $\frac{1}{400}$, $\frac{1}{400}$ mgr. Patient discharged apparently cured.

4. F. T— (18), admitted 1901. History of lupus of three years' duration, disease affecting nose, cheek, mucous membrane of right nostril, soft palate, and uvula. Besides X rays, lactic acid, trichloracetic acid, and the Paquelin cautery, he had 225 applications of Finsen light. In August, 1905, there was still great thickening and œdema of lips; ulcerated patches on the lips and alæ nasi. Tuberculin injections $\frac{1}{500}$, $\frac{1}{500}$, $\frac{1}{400}$, $\frac{1}{400}$, $\frac{1}{400}$, $\frac{1}{500}$, $\frac{1}{400}$ mgr. Great improvement. October, œdema gone, ulcerated areas healing up. Improvement continued (January, 1906).

5. W. S— (23). Lupus twenty years. Extensive area on left cheek. Patient had 289 sittings of Finsen light, and was apparently cured in 1904; relapsed repeatedly. Tuberculin inoculations begun August, 1905— $\frac{1}{500}$, $\frac{1}{300}$, $\frac{1}{200}$, $\frac{1}{300}$ mgr. Discharged apparently cured, to be kept under observation. This patient returned in January, 1906, with two fresh nodules in the scar which otherwise is sound.

6. O. G— (14). Lupus dates from 1901. Neck, cheek, and nose affected. Treatment: X rays and 388 sittings of Finsen light. In July, 1905, several nodules still remaining. Tuberculin inoculated in doses of $\frac{1}{750}$, $\frac{1}{500}$, $\frac{1}{400}$, $\frac{1}{300}$, $\frac{1}{100}$, $\frac{1}{100}$ mgr.; apparently cured; discharged.

7. I. B— (22). Lupus seventeen years, very extensive. Treated with Finsen light (540 applications) off and on for five years. Tuberculin inoculations have been tolerated with difficulty, and lesions are slowly clearing up (January, 1906).

8. A. R— (26). Lupus of eleven years' standing. A most extensive case with great infiltration of the skin of cheeks, chin, neck, and chest. Treated by Finsen light 941 times. Excellent result achieved by this treatment, but disease relapsed. February 1905, numerous nodules. Treated with tuberculin—$\frac{1}{750}$, $\frac{1}{750}$, $\frac{1}{500}$, $\frac{1}{300}$, $\frac{1}{200}$, $\frac{1}{200}$. Apparently cured; discharged.

9. R. S—. Lupus for twenty years. By 1902 it had spread over whole face and on to neck. In 1890 she was treated with old tuberculin with benefit, but it is said to have upset her health. Prior to 1902 she was scraped thirty-nine times. Since 1902 has had 1466 applications of Finsen light. In 1904 a finger was amputated for dactylitis. In April the opsonic index was ·6. An inoculation of $\frac{1}{750}$ mgr. of tuberculin raised her index to normal, and it kept normal for three months. Since then she has had eight inoculations of $\frac{1}{500}$, $\frac{1}{400}$, $\frac{1}{400}$, $\frac{1}{300}$, $\frac{1}{300}$, $\frac{1}{300}$, $\frac{1}{200}$, $\frac{1}{200}$ mgr. Great improvement, although much scarred from scrapings.

10. J. W— (16). Tubercular glands of neck on both sides. Excision of glands February, 1905. Recurrence. Sinus formation and softening of glands. Tuberculin treatment for two months. Apparently cured.

11. W. E— (10). Abdominal tuberculosis. Weight 3 st. 2½ lbs. Treated with tuberculin without avail. Fæcal fistula for three weeks before death. P.M.—Lower

part of abdomen was a cavity containing fæces. Extensive tuberculosis with matting of intestines.

12. W. K—. Extensive lupus of back of hand and leg. Treated for four years with Finsen light, X rays, and scrapings. Admitted into London Hospital in the beginning of 1905. Received $\frac{1}{750}$ mgr. tuberculin in addition to continuous fomentations. Hand lesion commenced to clear up at once. The lesion in the leg broke down in June when it was scraped. This patient was shown at the Society in November when the lupus on his hand and leg was healed up. January, 1906.—Lesions still well. Opsonic index ·9. When first tested his index was ·3.

I am indebted to Dr. Western for the results on most of the above-mentioned lupus patients, and to Dr. Sequeira for permission to make use of these results.

THE TREATMENT OF TUBERCULOSIS OF THE URINARY SYSTEM BY TUBERCULIN (T.R.)

BY

JOHN PARDOE, M.B., F.R.C.S.

ASSISTANT SURGEON TO ST. PETER'S HOSPITAL, LONDON

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THE treatment of tuberculosis by tuberculin and anti-tuberculous serum has in the past been so discouraging that at present such methods are much at a discount. The calamitous results which in many instances attended the employment of Koch's old tuberculin in the early nineties led to an almost complete abandonment of all kinds of tuberculin, and it is but recently that interest has again begun to revive, owing largely to the work of Koch himself, and, amongst others, that of Arloing, Marmorek, and in this country Wright and Douglas.

My own attention has been called more particularly to this subject during the past seven or eight years by two observations—firstly, that tuberculosis of the urinary system, and, more particularly, primary tuberculosis of the bladder, is of far more frequent occurrence than is generally recognised, and, in the second place, the disappointing results of operative treatment of these conditions, including the use of bladder washes and instillations of all sorts.

It may be said that a surgeon dealing especially with

diseases of the urinary system will naturally meet with more cases of urinary tuberculosis than one working in a wider sphere, but the frequency with which cases of vesical tuberculosis, more especially in an early stage, have drifted, as cases of "obstinate cystitis," into the later stages before a definite diagnosis has been made, lends some support to my first observation. The extreme importance of early diagnosis will appear later on. The treatment of tuberculosis of the urinary tract, particularly the bladder, by operative measures is so disappointing in my experience that I have almost ceased to employ them, whilst tuberculosis of the kidneys is usually so far advanced, and so often accompanied by infection of other parts of the urinary tract when operations are resorted to, that permanent benefit seldom seems to result.

Although the question of tuberculosis of the kidneys and ureters must necessarily be mentioned in the course of these remarks, I wish more particularly to refer to primary tubercle of the bladder, or to those cases in which the condition of the bladder is the most important feature of the disease, and is, so far as can be judged, the primary infection in the urinary system.

Treatment by Operation and by Antiseptic Washes.

Operative treatment of vesical tuberculosis aims at the destruction of the foci of infection, either by a complete excision of the tuberculous area, or, when the infection is more diffuse, by scraping the infected regions and rubbing in such remedies as iodoform. In the early stages of invasion of the bladder by tubercle the deposits may be in either the superficial or deeper layers of the mucous membrane, or even in the submucous tissues. There is no ulceration, and accurate evidence of the extent of the disease can only be obtained by a careful cystoscopic examination. When the disease has progressed a little further, ulceration occurs, but not synchronously in every patch when the disease is diffuse. On examining such

cases with the cystoscope the process may be seen in every stage, necrotic ulcers co-existing with patches of inflamed and swollen mucous membrane, whilst it is reasonable to suppose that there are still more immature deposits which do not show at all.

The solitary tuberculous ulcer is, in my experience, exceedingly rare, unfortunately for the patients, for these are the only cases in which complete excision can be attempted. The nearest approach to this condition which I have seen was in case No. 2, where the ulcer appeared at first to be solitary, but more careful examination showed several minute unbroken deposits around it. Such being the characteristic distribution of tubercle in the bladder, it is obvious that such operations as excision and scraping must be limited to the narrow field presented by the true tuberculous ulcer. Even in these cases Hurry Fenwick recommends [1] the use of tuberculin to begin with, excision to be resorted to if the ulcer is seen with the cystoscope not to be healing. It is a very difficult thing to find small areas of disease in the mucous membrane of a bladder which has collapsed after being opened suprapubically, and the most one can hope for in a case of diffuse tuberculous cystitis is to be able to recognise the more obviously ulcerated patches, while the non-ulcerated deposits will almost certainly escape recognition.

Watson Cheyne [2] records five cases treated by simple supra-pubic drainage without any attempt at scraping or excision, and this course certainly seems to me wiser than indiscriminate attempts at either. The benefit which he observed from this practice he attributes to the rest given to the bladder and relief from painful and frequent micturition.

Perineal drainage has been advised for the same purpose, but should never be done. The drainage track

[1] 'Ulceration of the Bladder, Simple, Tuberculous, and Malignant,' E. Hurry Fenwick, 1900.

[2] 'On the Treatment of Tuberculous Diseases in their Surgical Aspects,' Watson Cheyne, 1900.

almost invariably becomes infected, and remains open as a fistula, with unhealthy, granulating walls,[1] and the drainage-tube often cannot be tolerated by the exceedingly sensitive bladder.

Injections of all kinds into the bladder are, in my opinion, injurious, for, as a rule, the symptoms are aggravated by them, and more harm than good is done. How can emulsions of iodoform and solutions of copper, mercury, or any other drug affect any but the ulcerated surfaces? The non-ulcerated deposits must be uninfluenced, and, owing to the great frequency of micturition usually present, the drugs are washed away within a very short time of their introduction. The less a tuberculous bladder is subjected to instrumentation the better for it, and when the use of an instrument is necessary, *i. e.* the cystoscope, the greatest pains should be taken to avoid the introduction of sepsis, for sepsis is to the tuberculous bladder as fire to tow. A consideration of the foregoing facts led me to try tuberculin injection, though without any very sanguine hope of much success.

Nature of the Remedy employed and of its Action.

A considerable number of tuberculines and anti-tuberculous sera have been employed since Koch published the details[2] of the preparation of his first tuberculin. Stated briefly, the various modifications introduced by Koch himself are as follows:—The first tuberculin (T.) was obtained by growing the bacilli for about two months on alkaline broth media, to which was added a small quantity of peptone and glycerin; the fluid thus obtained was passed through a porcelain filter, the bacilli being thus eliminated, and was evaporated to one tenth of its bulk, leaving a thick yellowish fluid, to which Koch gave the name of tuberculin (T.). The next tuberculin was prepared upon an entirely different principle. Dried cultures of bacilli were powdered

[1] See cases.

[2] 'Deut. Med. Woch.,' 1890.

in a mortar; the powder was mixed with distilled water and the mixture centrifugalised; the clear fluid thus obtained was called tuberculin oberstand (T.O.). The solid centrifugalate having been dried was mixed with distilled water and again centrifugalised; this process having been repeated several times the fluids obtained from each repetition were mixed together and 20 per cent. of glycerin added to the bulk; this Koch called tuberculin rükstand (T.R.), and this is the tuberculin which I have used in the series of cases here described.

Wright and Douglas,[1] however, cast doubts upon the sterility of this tuberculin, and having satisfied themselves by a series of observations that T.R. can be heated to 60° C. without injuriously affecting the activity of the solution, they subject the tuberculin to this heat, and also add to it 0·25 per cent. of lysol. The T.R. which I have used recently has been subjected to this heat for one hour, but I have not used the lysol. The importance of these extra precautions is also borne out by the fact that live bacilli have been found by Thellung in the new tuberculin,[2] and produced tuberculosis in rabbits and guinea-pigs.

Effects of Injection of T.R.

1. *At the site of injection.*—In the greater number of my cases very little local effect has been noted, a little swelling and hardness of a small space around the puncture persisting for from twenty-four to forty-eight hours in a few instances, but the majority of cases showed no reaction. In two cases, however, great reaction was noticed (Cases No. 17 and 14), the signs in each being identical. At the point of inoculation a considerable swelling formed, in one case (No. 17) the size of half a tangerine orange; the whole arm swelled to the finger tips; it was distinctly

[1] 'Proceedings of the Royal Society,' vol. lxxiv, No. 499.

[2] 'Deut. Med. Woch.,' 1901, No. 48. 'Centralbl. für Bakter.,' 1902, No. 1. Quoted by Bosanquet, "Serums, Vaccines, and Toxines," 1904 p. 245.

œdematous, and the axillary glands were slightly hard and tender. The swelling subsided in forty-eight hours, leaving a circular red and tender spot about a half inch in diameter at the point of puncture; this swelling had the appearance of being about to slough, but gradually subsided, leaving a depression resembling a smallpox mark. The injection which caused this result was half a milligram, and the same phenomena were seen on two subsequent occasions with the same dose, only to a much less degree; the dose was therefore reduced to one quarter milligram, and no further local trouble occurred. In the other case (No. 14) the symptoms were similar but not so severe, and no scarring remained at the needle puncture when the general swelling had subsided; in this case the symptoms followed injections of one milligram, and on decreasing the dose to a half milligram no further trouble was experienced. Both these cases occurred whilst I was using T.R., which had not been subjected to sterilisation by heat, and it is worthy of note that they only occurred with comparatively large doses of the remedy. I much regret that no bacteriological examination was made of the batch of T.R. from which these injections were taken.

2. *Effect upon the tuberculous deposits.*—The effects of the old tuberculin (T.) upon tuberculous deposits is well known from both clinical and experimental evidence in the human subject; it was most easily seen in cases of lupus, and by post-mortem examination of tuberculous rabbits and guinea-pigs after inoculations of tuberculin; in lupus a vigorous reaction is observed, the patches becoming swollen, red, and hot, these signs being followed by a necrosis and sloughing of the diseased area, after which healing commences in those cases which do well. In animals which have been killed by the injection of a large dose of tuberculin (T.) the greyish-yellow nodules of tubercle are seen to be surrounded by a zone of hyperæmia varying in intensity according to the rapidity of death; these results are said not to follow the employment of the new tuberculin (T.R.), but this is certainly

not the case in my experience of tuberculosis of the urinary bladder. In some of my cases very little change was noticed in the infected organs with the smaller doses of T.R., but when larger doses were employed increase of pain on micturition, increased frequency of micturition, and an increase of hæmaturia and pyuria appeared with general malaise, loss of weight, and sometimes sharp rises of temperature. These signs I consider showed that too large or too frequent injections of tuberculin were being used, and the doses were diminished in size and frequency; I think there can be no doubt that these phenomena were dependent upon active changes in the tuberculous patches induced by the action of tuberculin; confirmatory evidence upon this point was gained by a cystoscopy undertaken during one of these exacerbations (see Case 17), where the discrete tubercles previously observed were seen to be surrounded by a wider-spread zone of hyperæmia and congestion, the bladder capacity at the same time being reduced to about one half; this phase passed away on diminution of the dose and lengthening of the intervals between the injections.

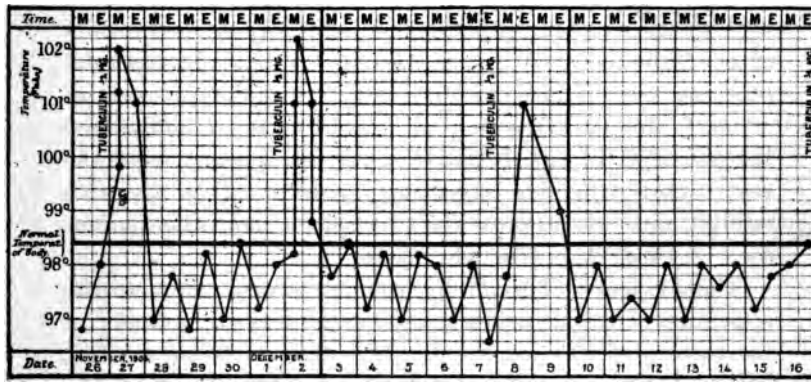
3. *Effect upon the system generally of T.R.*—Tuberculin (T.) was supposed to act, not by killing the tubercle bacilli, but by causing necrosis of the small cell infiltration induced by the bacilli, thus producing shedding of the bacilli from the infected areas. The action of T.R. is stated to be very different. Wright and Douglas [1] consider that the nature of a tubercle vaccine consists in the presence of, "a derivative of the protoplasm of the tubercle bacillus which is capable of producing an elaboration of tuberculotropic substances in the organism."

The now well-known researches of these authors have led them to formulate the theory that injections of T.R. in the human subject produce in the blood bodies to which they have applied the term opsonins, or elements in the blood fluids which modify the bacilli in such a way as to render them an easy prey to phagocytes. This

[1] "Proceedings of the Royal Society," vol. lxxiv, No. 499.

opsonic reaction or resistance is of a higher degree in healthy persons than in those infected with tubercle, and the opsonic power of the blood can be stated in the form of curves, which rise or fall with the increase or decrease of its protective and phagocytic power. Moreover, Wright and Douglas suggest, by a series of results, that the cumulative increase of the protective elements which is desired can be obtained only by the proper regulation and interspacing of the successive doses of vaccine, and not only is it necessary to ascertain by the rise of the curve to its maximum that the highest point of protection is obtained, but that by too frequent or too large doses the opsonic reaction is diminished, as is shown by the fall of the curve. If it can be confirmed that only by a study of these curves the doses of tuberculin can be accurately measured, it is a most important consideration for those who, like myself, have relied on clinical evidence for this purpose, for, unfortunately, the estimation of opsonic curves is not only a matter for a skilled bacteriologist, but is a proceeding which consumes an immense amount of time. For these reasons it is, so far as I can see at present, quite unsuited to the exigencies of daily practice. It therefore remains to be asked, can the doses be regulated sufficiently well by clinical signs to ensure a good result? I think the answer to this question is, that it is usually obvious from the patient's condition and symptoms when the maximum dose to be used with advantage has been reached, for I have already indicated some of the symptoms which show themselves in cases of tuberculous cystitis. That I have over-dosed my patients on some occasions I feel certain, but by following the method of a gradual increase until that dose is arrived at which causes some reaction and malaise, and then diminishing it to a dose which falls short of these effects, a fairly good result is usually obtained. I began tuberculin injections a considerable time before Wright and Douglas's work was published, and therefore knew nothing about opsonic curves, the only laboratory method of checking results

which was at my disposal being the method of estimating the agglutinating properties of the blood serum upon tubercle bacilli, which was not then and is not now considered to be in any way a reliable test. I therefore based the size and interspacing of the doses upon the clinical evidence already indicated, and this must be borne in mind in considering the results in the cases mentioned. A comparison of the results in this series of cases and a series treated by opsonically graduated doses would, I think, be of great interest. The symptoms of over-dose which I have noted have always been of short duration,



and invariably accompanied a fairly large dose of the vaccine; I have never seen these effects produced by less than one two-hundredth of a milligram. This temperature chart shows the effects of inoculations of T.R. of too great a size.[1]

The Diagnosis of Suitable and Unsuitable Cases for Treatment.

It is important to recognise that all cases of urinary tuberculosis are not suitable for treatment by T.R.; this

[1] I must emphasise the fact that I am here speaking of tuberculosis of the urinary system only, the symptoms of which I consider a very delicate test for regulation of doses. In such conditions as tuberculous adenitis opsonin indices may be absolutely essential.

depends upon the fact which I have already stated, that local reaction does undoubtedly occur. I believe that Hurry Fenwick was the first to call attention to the danger of using T.R. where both ureters are affected or where there is strong presumptive evidence that this is the case; this evidence can only be obtained by a careful cystoscopic examination conducted with the utmost gentleness and with a scrupulous regard for asepsis; it should therefore be a rule never to commence the use of T.R. until after a careful cystoscopy. A glance at this specimen[1] will reveal the necessity for this precaution; the bladder is not very markedly infected, but both ureters are studded with tubercle, and any acute swelling of the infected area in this case would have caused total blocking of the ureters and resulted in suppression of urine. This occurred in Case No. 15, where I deprecated the use of T.R., but this advice was disregarded, with the result that after five injections of from $\frac{1}{1000}$ to $\frac{1}{500}$ of a milligram total suppression took place, and the patient died in three days from the onset.

The evidence afforded by the cystoscope refers to the appearance of the ureteric orifices and the character of the urinary efflux from them. If both orifices are swollen, inflamed, and in some cases surrounded by ulceration, the probability is that the ureters are also infected, whilst it is often possible to observe a flaky or even distinctly purulent efflux from one or both sides before changes have taken place in the orifices. T.R. should never be given unless there is a clear orifice and a clear discharge on one side at all events.

That this cystoscopic evidence is open to fallacy I am well aware; for instance, a ureter badly infected with miliary tubercle may conceivably discharge a nearly clear urine. Such a case I had the opportunity of seeing recently where the cystoscope showed a clear stream issuing from a ureter which subsequent operation proved to be

[1] See plates I and II.

studded with minute tubercles with primary disease in the corresponding kidney; the orifice in this instance being neither swollen nor ulcerated. On the other hand, tuberculosis of the bladder may cause swelling and ulceration of the mucous membrane around the ureteric orifices although the ureteric mucous membrane is not as yet affected. But such cases are rare, and certainly do not outweigh the valuable evidence to be obtained in the majority of instances from a cystoscopic examination.

In cases where the cystoscope shows a bladder free from or but slightly infected with tubercle with strong evidence of a unilateral infection of one kidney and ureter, i. e. a clear and normal efflux from one side with a purulent efflux and an infected orifice on the other side, nephrectomy and ureterectomy followed by the use of T.R. are indicated.

Method of employment.—The T.R. is given hypodermically with a sterilised syringe. Wherever possible I keep the patient in bed or, at all events, in the house for the initial stages of the treatment, the temperature and general symptoms being carefully noted. I now commence with a dose of one five-hundredth of a milligram, and give increasing doses every other day until a definite reaction is obtained, usually marked by a rise of temperature of two degrees or so, some malaise, and a slight increase of pain and frequency of micturition. The dose is then reduced to that quantity which apparently causes no reaction, and is given steadily once a week for long periods; should a definite reaction again occur, the dose is once more diminished and given at longer intervals. My experience of T.R. in the treatment of tuberculosis is limited to the urinary system, and here I consider the clinical evidence is a sufficiently delicate indication. Over-dosing causes such definite symptoms of loss of ground, evidenced by increased pain, hæmaturia and frequency of micturition, with a heightened temperature and loss of body-weight, that they cannot be overlooked; they correspond with Wright's negative phase of the opsonic curve, and I feel

content that, by a careful watch upon these symptoms, the dosage can be sufficiently accurately regulated.

During the progress of treatment the patient's weight and temperature should be carefully noted, together with the subsidence or progress of the symptoms particularly applicable to the organs affected, and it is perhaps hardly necessary to add that all hygienic and dietetic treatment found beneficial in tuberculosis generally should be followed. In those cases which show favourable progress, the numbers of tubercle bacilli found in the urine steadily decrease.

A cystoscopic examination from time to time conducted with the precautions to which I have alluded will show the extent of healing which has taken place.

Results.

I have included in this paper no cases which have not been under observation for more than one year, but even so I feel that it is impossible to speak with any certainty as to the results obtained in those few cases which have apparently regained perfect health. Tuberculosis of the urinary system has such long periods of latency, that he would be bold indeed who prophesied a permanent cure in patients apparently well for a year or more. This is evidenced by a case (No. 19) of this series who has suffered from tuberculosis of the bladder for at least seventeen years, during which time he has had periods of a year and more with almost entire absence of symptoms; but the renewed interest taken in tuberculin renders any record of results, whether good or bad, of sufficient importance to warrant their publication.

In the twenty-one cases the details of which will be found in full at the end of this paper, I have been able to obtain information of all up to within a few weeks, with one exception. I have not included a considerable number of patients who have disappeared during the course of their treatment and whose movements I have

been unable to trace, although many of them were in a very encouraging condition when lost sight of.

Of these twenty-one cases five appear to be cured. Bearing in mind, however, the great tendency to relapse shown by tuberculosis of the urinary system, I prefer to call them only apparent cures.

Four cases show a very marked improvement, evidenced by absence of pain, diminution of the frequency of micturition, absence of hæmaturia, and cystoscopic evidence of the amount of cure obtained.

Six cases show no improvement. In some of these I consider that T.R. has not had a fair trial, particularly in Case No. 14. This woman was subject to outbreaks of drinking lasting sometimes for two or three weeks on end, during which she would consume from one to three bottles of whisky a day. The injections had to be stopped during these drinking bouts, and for some time after.

In one or two other cases also the injections were not continued regularly, owing to the patients feeling so much better that they stopped away, only returning when their symptoms began to reappear.

Six cases died. In one of these I have no doubt T.R. was the direct cause of death (case No. 15). T.R. should not have been given in this case at all, and it was only at the patient's urgent request that I gave him five injections. He had a very severe reaction with one-fiftieth milligram, and as I was certain that both ureters were infected, I refused to give more. He insisted on having further injections on returning home to the country, and died very rapidly with complete suppression of urine.

In all the fatal cases it will be noticed that the infection was somewhat extensive. I append here, in tabulated form, the results I have obtained up to date, from which easy reference can be made to cases detailed at the end of this paper.

Died.	*No improvement.*	*Much improved.*	*Apparently cured.*
Case	Case	Case	Case
No. 1	No. 9	No. 3	No. 2
7	13	6	4
11	14	8	5
15	16	12	10
20	17	—	18
21	19	—	—

Conclusions.

My experience with other methods of treatment has been disappointing in the extreme, for I cannot call to mind any case of apparent cure of vesical tuberculosis by operative measures, and the published records of such cases are indeed few. I therefore think that, so far as these series of cases goes it is not unduly optimistic to claim that the results gained by injections of T.R. are at least as good as those by any other method.

It will be noted that the earlier the case is brought under treatment, or, to put it in another way, the more circumscribed is the infection, the better are the results. In not one case where the cystoscope showed diffuse infection has very much benefit been noted. The cases of apparent cure occurred where only a small amount of bladder surface appeared to be involved.

I do not think that in T.R. we have a perfect remedy for tuberculosis of the urinary system, but for vesical tuberculosis it seems to me the best remedy at our disposal. Before I used it I felt little or no hope of effecting much improvement; but I now feel that in some cases there is hope of a cure, and in a larger proportion of cases of at all events great improvement.

I shall venture to ask permission of the Fellows of this Society to bring before them the later histories of these

cases, together with those of patients whose treatment has been too recently commenced to be mentioned to-day, unless the onward march of science, in the meantime, brings to us most happily a more perfect and hopeful method.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
1	M., 36	Feb., 1902.—Symptoms of pain and hæmaturia for 2 years. Frequency of micturition: day, hourly; night hourly. Pain in penis after each act of micturition. A little bright red blood seen at the close of micturition several times every day. Urine contains blood, mucopus, and many tubercle bacilli. Stream spasmodic and irregular. Neither kidney palpable; no deposits in epididymes, vasa, prostate, or seminal vesicles. Family history very bad; strong history of tubercle; brother, sister, uncle, and aunt died of phthisis	Very wide-spread tuberculous cystitis. Several shallow and sloughy ulcers on base, and many congested patches on fundus and lateral walls. Right ureteric orifice swollen and ulcerated. Discharge of flaky urine at long intervals. Left ureteric orifice normal, with a clear rapid efflux	Much bladder washing had been tried during the preceding 2 years. Injections of T.R. were commenced with a dose of $\frac{1}{500}$ milligramme, and increased to $\frac{1}{10}$ milligramme. This dose caused a sharp reaction. Temperature 103°; much malaise and a rigor. Dose dropped to $\frac{1}{50}$ milligramme, and given weekly for 3 months. No improvement noted. In April, 1903, pain and tenderness appeared in right loin, followed by a swelling; this increased rapidly. I cut down upon it and evacuated 4 pints of inodorous flaky pus from the right kidney. Frequency of micturition and pain had gradually increased. The patient died one month later.
2	M., 35	March 11, 1902.—Commenced symptoms with hæmaturia, at first appearing after cycling 6 months ago; bright red, mixed with urine, never clots. Has recurred frequently since. Pain: aching in lumbar regions, worse on exertion; no penile pain. Frequency: day, 7 to 8 times; night, once. This was increased a month ago, but relieved by rest. Stream: good.	1. March 12, 1902.—Single ulcer in bladder, below and inside left ureteric orifice, ? tubercular. 2. March 28.—Ulcer same; some splashes found around left ureteric orifice. 3. July 28.—Ulcer healing and covered with sago-like granulations; left ureteric orifice rather thick-lipped. 4. Jan. 18, 1903.—No sign of old	March 13, 1902.—Instillation of iodoform emulsion. April 18.—Tuberculin $\frac{1}{2500}$ mg. April 22.—Tuberculin $\frac{1}{500}$ mg. Continued with doses weekly up to $\frac{1}{10}$ mg. until August. Sept. 1.—Resumed injections of tuberculin as an O.P. Had some aching in left renal area. Ceased injections Oct. 27. Dec. 29.—Injection $\frac{1}{4}$ mg.; suspicion of hæmaturia. Jan. 5, 12, 19, 1903.—Injection $\frac{1}{4}$ mg. Jan. 26.—No injection; passed a small uric acid stone after left renal colic. June 22.—Frequency: day, 3 hours; night, 0. Slight occasional hæmaturia. July 20.—Urine turbid. Aug. 24.—Still some hæmaturia. Jan. 11, 1904.—Pain in left loin and groin; not losing weight. Feb. 1.—Frequency:

			no stoppage. Urine: 1020, acid, albumen, trace of blood present; no tubercle bacilli were found. Neither kidney felt. Prostate normal. Family history: father died of scrofula. June 16, 1902.—Tubercle bacilli found in urine for the first time; frequently found during 1902	ulcer; some submucous tubercle on trigone, just below left ureteric orifice; orifice circular and pit-like. 5. Dec. 15.—Cocaine, 5 oz. distension. Left side generally congested. Clear urine from right orifice, none seen from left. No ulcer nor submucous tubercles seen. 6. April 10, 1904.—Cocaine 8 oz., distension. Bladder perfectly normal, with exception of scarring at site of old ulcer. Clear and regular efflux from both ureters. 7. July, 1905.—Cocaine 8 oz., distension. Bladder perfectly normal	day, 2 to 3 hours; night, 4 hours. Weight, 10 st. March 28.—Frequency: day, 5 times; night, 0. April 11.—Urine acid, but turbid; no hæmaturia; no lumbar pain now. June 6.—Left renal aching again. Weight, 9 st. 11 lb. July 18.—Frequency: day, 3 hours; night, 0. Still pain. Dec. 12.—Thick viscid sediment in urine for last 8 weeks, with left renal pain. April 10, 1905.—Urine bright and clear; no symptoms. July.—No symptoms. Has gained one stone in weight—11 st.
3	M., 57	Jan. 7, 1903.—Length of illness 9 months. Pain: urethral; throbbing and eased by micturition; recently suprapubic pain. Frequency: day, hourly; night, ½ hour to 2 hours. Hæmaturia: none. Urine: turbid, sp. gr. 1010, acid; trace of albumen; no blood; losing flesh latterly. Discharging sinus in connection with left epididymis, which is enlarged, hard, and nodular; sinus present for 2 weeks. Prostate: small; no backache. Family history: one sister died of phthisis; his wife died of phthisis; 3 children died of phthisis; patient said to be consumptive when younger; no sign of phthisis on examination now; many tubercle bacilli in the urine	Jan. 14, 1903.—Ragged, crateriform ulcer close to orifice of left ureter (definitely tuberculous)	Jan. 24, 1903.—Tuberculin $\frac{1}{10}$ mg. Feb. 8.—Tuberculin continued, and now having mg. $\frac{1}{5}$; to continue treatment at home; pain much diminished. Frequency: day, 2 hours; night, 3 hours; letter from patient, Jan. 11, 1905 (two years' interval).—Pain: penile during and after micturition. Frequency: day, ½ to 1 hour; night, 2 hourly. Hæmaturia: occasionally. Urine contains pus and mucus. Weight: lost considerably. Patient continued the tuberculin injection for a few weeks after leaving hospital in Feb., 1903, but then omitted them as they caused headache and malaise. Sept., 1905.—Getting worse; probably will not live long. Total period of T.R. injections was 3 months. No improvement was noticed whilst treatment was conducted at home. Improvement whilst in hospital was marked.

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2	M., 35	March 11, 1902.—Commenced symptoms with hæmaturia, at first appearing after cycling 6 months ago; bright red, mixed with urine, never clots. Has recurred frequently since. Pain: aching in lumbar regions, worse on exertion; no penile pain. Frequency: day, 7 to 8 times; night, once. This was increased a month ago, but relieved by rest. Stream: good,	1. March 12, 1902.—Single ulcer in bladder, below and inside left ureteric orifice, ? tubercular. 2. March 28.—Ulcer same; some splashes found around left ureteric orifice. 3. July 28.—Ulcer healing and covered with sago-like granulations; left ureteric orifice rather thick-lipped. 4. Jan. 18, 1903.—No sign of old	March 13, 1902.—Instillation of iodoform emulsion. April 18.—Tuberculin $\frac{1}{2500}$ mg. April 22.—Tuberculin $\frac{1}{2000}$ mg. Continued with doses weekly up to $\frac{1}{10}$ mg. until August. Sept. 1.—Resumed injections of tuberculin as an O.P. Had some aching in left renal area. Ceased injections Oct. 27. Dec. 29.—Injection $\frac{1}{2}$ mg.; suspicion of hæmaturia. Jan. 5, 12, 19, 1903.—Injection $\frac{1}{2}$ mg. Jan. 26.—No injection; passed a small uric acid stone after left renal colic. June 22.—Frequency: day, 3 hours; night, 0. Slight occasional hæmaturia. July 20.—Urine turbid. Aug. 24.—Still some hæmaturia. Jan. 11, 1904.—Pain in left loin and groin; not losing weight. Feb. 1.—Frequency:

		no stoppage. Urine: 1020, acid, albumen, trace of blood present; no tubercle bacilli were found. Neither kidney felt. Prostate normal. Family history: father died of scrofula. June 16, 1902.—Tubercle bacilli found in urine for the first time; frequently found during 1902	ulcer; some submucous tubercle on trigone, just below left ureteric orifice; orifice circular and pit-like. 5. Dec. 15.—Cocaine, 5 oz. distension. Left side generally congested. Clear urine from right orifice, none seen from left. No ulcer nor submucous tubercles seen. 6. April 10, 1904.—Cocaine 8 oz., distension. Bladder perfectly normal, with exception of scarring at site of old ulcer. Clear and regular efflux from both ureters. 7. July, 1905.—Cocaine 8 oz., distension. Bladder perfectly normal	day, 2 to 3 hours; night, 4 hours. Weight, 10 st. March 28.—Frequency: day, 5 times; night, 0. April 11.—Urine acid, but turbid; no hæmaturia; no lumbar pain now. June 6.—Left renal aching again. Weight, 9 st. 11 lb. July 18.—Frequency: day, 3 hours; night, 0. Still pain. Dec. 12.—Thick viscid sediment in urine for last 8 weeks, with left renal pain. April 10, 1905.—Urine bright and clear; no symptoms. July.—No symptoms. Has gained one stone in weight—11 st.
3	M., 57	Jan. 7, 1903.—Length of illness 9 months. Pain: urethral; throbbing and eased by micturition; recently suprapubic pain. Frequency: day, hourly; night, ½ hour to 2 hours. Hæmaturia: none. Urine: turbid, sp. gr. 1010, acid; trace of albumen; no blood; losing flesh latterly. Discharging sinus in connection with left epididymis, which is enlarged, hard, and nodular; sinus present for 2 weeks. Prostate: small; no backache. Family history: one sister died of phthisis; his wife died of phthisis; 3 children died of phthisis; patient said to be consumptive when younger; no sign of phthisis on examination now; many tubercle bacilli in the urine	Jan. 14, 1903.—Ragged, crateriform ulcer close to orifice of left ureter (definitely tuberculous)	Jan. 24, 1903.—Tuberculin $\frac{1}{1\frac{1}{2}0}$ mg. Feb. 8.—Tuberculin continued, and now having mg. $\frac{1}{10}$; to continue treatment at home; pain much diminished. Frequency: day, 2 hours; night, 3 hours; letter from patient, Jan. 11, 1905 (two years' interval).—Pain: penile during and after micturition. Frequency: day, ½ to 1 hour; night, 2 hourly. Hæmaturia: occasionally. Urine contains pus and mucus. Weight: lost considerably. Patient continued the tuberculin injection for a few weeks after leaving hospital in Feb., 1903, but then omitted them as they caused headache and malaise. Sept., 1905.—Getting worse; probably will not live long. Total period of T.R. injections was 3 months. No improvement was noticed whilst treatment was conducted at home. Improvement whilst in hospital was marked.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
Case 7 (*cont.*)		Tubercle bacilli found (Aug. 6)		quency: day, 6 times; night, once. Dec. 10.—Frequency increased: day, hourly; night, 3 to 4 times. Perineal pain. Blood present. Dec. 17.—Frequency: day, 1½ hours; night, 3 to 4 times. Weight, 9 st. 8 lb. Dec. 24.—Weight, 9 st. 7¾ lb. Jan. 14, 1904.—Weight, 9 st. 11 lb.; 21, weight, 9 st. 11½ lb. Feb. 4.—Frequency: day, 1½ hours; night, 3 times. Weight, 9 st. 12 lb. Feb. 11.—Perineal pain still. Feb. 18.—Weight, 9 st. 13 lb. March 10.—Frequency: day, 1½ hours; night, 5 to 6 times. March 31.—Again hæmaturia. Weight, 9 st. 13 lb. March 31.—Bleeding occasional. Weight, 10 st. Frequency: day, 1½ hours; night, 3 times. April 14.—Frequency: day, 1½ hours; night, 3 times. Weight, 9 st. 11¾ lb. Oct. 28.—Frequency: same. Small clots for 3 days. May 12.—Weight, 9 st. 9 lb. May 26.—Frequency: day, hourly; night, 3 times. Urine turbid. Penile pain during micturition. June 9.—Weight, 9 st. 2 lb. June 16.—Frequency: day, 1½ hours; night, 4 times. Went to the seaside and there resumed T.R. injections, starting with $\frac{1}{2000}$ mg., and working up to ½ mg. with no great reaction. Continued for 3 months, then stopped injections. Some benefit noted. Frequency and pain less. Died in Nov., 1904, after 5 days' illness, from acute pulmonary tuberculosis.
8	M., 41	July, 1903.—Frequency: gradually increasing for 3 years; now amounting to: day, ½ hourly; night ½ hourly. Pain in glans penis. Hæmaturia continuous. Occasional severe pain in the lumbar region, last-	July 20, 1903. — Both ureters discharging clear urine; great congestion of bladder neck. Aug. 26.—Patch of congestion seen (probably tubercle). Feb. 25.—Cocaine 10 per cent. To right of blad-	August 28, 1903.—Inj. tuberculin $\frac{1}{2000}$ mg.; 30, $\frac{1}{1500}$ mg. Discharged from hospital. Sept. 14.—Tuberculin $\frac{1}{2500}$ mg. Oct. 5, $\frac{1}{2000}$ mg.; 12, $\frac{1}{1500}$ mg.; 19, $\frac{1}{1500}$ mg. Frequency: day, 1 to 1½ hours; night, 3 times. Urine clear; no blood. Oct. 26.—Tuberculin $\frac{1}{25}$ mg. Nov. 9.—Tuberculin ¼ mg. Frequency: day, 8 times; night, 3 times. Nov. 16.—Tuberculin ¼ mg. Frequency: day, 2 hours; night, 3 times. Nov. 23.—Tuberculin ¼ mg.; 30,

ing an hour, and causing retching. Oct. 5.—Tubercle bacilli found in centrifuged specimen of urine	der apex three raised tubercles, with central, yellow, breaking-down patch in one. Just below these is a brownish healed ulcer, showing scarring and commencing contraction around, with raised radiating bands. Left orifice normal; clear urine; right orifice surrounded by congested tubercular patch. June 16, 1904.—Cocaine 10 per cent. Distension ʒvij. Same scarred ulcer at fundus with radiating bands, but tubercles around it are not so marked. To left of fundus a recent small ragged ulcer on congested base. On the whole better. Oct. 27, 1904. Cocaine 10 per cent. Distension? Ulcer previously noted is healed. One patch of submucous tubercle to	½ mg. Dec. 7.—Tuberculin ½ mg.; 14, injections omitted. Frequency: day, 1 to 1½ hours; night, 3 times. Jan. 11, 1904.—Frequency: day 1½ to 2 hours; night, 3 to 4 times. Jan. 25.—Complains of severe aching; no hæmaturia. Feb. 22.—Frequency: day, 1½ hours; night, 3 times. March 7.—No tubercle bacilli can be found in urine. March 28.—Frequency: day, 2 hours; night, 3 hrs. Is better whilst taking capsules Ol. santal. May 9.—Frequency: day, 2 hours; night, 3 times (at best). Pain is decidedly less. June 13.—Pain was only slight; no hæmaturia. Frequency: same. July 18.—Still slight penile pain. August 8.—No hæmaturia for about 12 months. August 29.—Frequency; day, 2 hours; night, 4 times. Oct. 3.—Feeling better; no low pain. Oct. 27.—Frequency: day, 1½ hours; night, 1½ hours. Tuberculin $\frac{1}{100}$ mg. See cystoscopy. Nov. 14.—Frequency: day, ½ hour; night, ½ hour. Penile pain after micturition. Dec. 12.—Frequency: day, 1½ to 2 hours; night, 3 times. Pain: occasionally penile after micturition: none inside. To recommence tuberculin. Jan., 1905.—Commenced a fresh series of T.R. injections $\frac{1}{1000}$ mg. weekly. April.—Steady improvement with T.R.; now getting $\frac{1}{100}$ mg. weekly. Frequency: day, 2 to 3 hours; night, once (always better in warm weather). No blood seen, and urine fairly clear as a rule. July.—No T.R. for one month; condition very good; no pain; frequency as at last note; urine clear.

left of trigone at base; one to right of fundus; general improvement. Dec. 15.—Cocaine 10 per cent. Distension ʒviij. Ulcer healed on anterior wall. Contraction bands around it marked. Some recent (mostly submucous) tubercles around ulcer on anterior wall of bladder. Leash of vessels around both orifices. April, 1905.—Distension ʒx. No ulceration; some radiating bands of scar tissue on anterior wall; no tubercles seen; suspicious patch between ureters on posterior wall; congested, but not ulcerated.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
Case 7 (*cont.*)		Tubercle bacilli found (Aug. 6)		quency: day, 6 times; night, once. Dec. 10.—Frequency increased: day, hourly; night, 3 to 4 times. Perineal pain. Blood present. Dec. 17.—Frequency: day, 1½ hours; night, 3 to 4 times. Weight, 9 st. 8 lb. Dec. 24.—Weight, 9 st. 7⅞ lb. Jan. 14, 1904.—Weight, 9 st. 11 lb.; 21, weight, 9 st. 11½ lb. Feb. 4.—Frequency: day, 1½ hours; night, 3 times. Weight, 9 st. 12 lb. Feb. 11.—Perineal pain still. Feb. 18.—Weight, 9 st. 13 lb. March 10.—Frequency: day, 1½ hours; night, 5 to 6 times. March 31.—Again hæmaturia. Weight, 9 st. 13 lb. March 31.—Bleeding occasional. Weight, 10 st. Frequency: day, 1½ hours; night, 3 times. April 14.—Frequency: day, 1½ hours; night, 3 times. Weight, 9 st. 11¾ lb. Oct. 28.—Frequency: same. Small clots for 3 days. May 12.—Weight, 9 st. 9 lb. May 26.—Frequency: day, hourly; night, 3 times. Urine turbid. Penile pain during micturition. June 9.—Weight, 9 st. 2 lb. June 16.—Frequency: day, 1½ hours; night, 4 times. Went to the seaside and there resumed T.R. injections, starting with $\frac{1}{200}$ mg., and working up to ¼ mg. with no great reaction. Continued for 3 months, then stopped injections. Some benefit noted. Frequency and pain less. Died in Nov., 1904, after 5 days' illness, from acute pulmonary tuberculosis.
8	M., 41	July, 1903.—Frequency: gradually increasing for 3 years; now amounting to: day, ½ hourly; night ½ hourly. Pain in glans penis. Hæmaturia continuous. Occasional severe pain in the lumbar region, last-	July 20, 1903. — Both ureters discharging clear urine; great congestion of bladder neck. Aug. 26.—Patch of congestion seen (probably tubercle). Feb. 25.—Cocaine 10 per cent. To right of blad-	August 28, 1903.—Inj. tuberculin $\frac{1}{250}$ mg.; 30, $\frac{1}{150}$ mg. Discharged from hospital. Sept. 14.—Tuberculin $\frac{1}{250}$ mg. Oct. 5, $\frac{1}{200}$ mg.; 12, $\frac{1}{150}$ mg.; 19, $\frac{1}{150}$ mg. Frequency: day, 1 to 1½ hours; night, 3 times. Urine clear; no blood. Oct. 26.—Tuberculin $\frac{1}{25}$ mg. Nov. 9.—Tuberculin ½ mg. Frequency: day, 8 times; night, 3 times. Nov. 16.—Tuberculin ½ mg. Frequency: day, 2 hours; night, 3 times. Nov. 23.—Tuberculin ½ mg.; 30,

ing an hour, and causing retching. Oct. 5.—Tubercle bacilli found in centrifuged specimen of urine	der apex three raised tubercles, with central, yellow, breaking-down patch in one. Just below these is a brownish healed ulcer, showing scarring and commencing contraction around, with raised radiating bands. Left orifice normal; clear urine; right orifice surrounded by congested tubercular patch. June 16, 1904.—Cocaine 10 per cent. Distension ʒvij. Same scarred ulcer at fundus with radiating bands, but tubercles around it are not so marked. To left of fundus a recent small ragged ulcer on congested base. On the whole better. Oct. 27, 1904. Cocaine 10 per cent. Distension? Ulcer previously noted is healed. One patch of submucous tubercle to left of trigone at base; one to right of fundus; general improvement. Dec. 15.—Cocaine 10 per cent. Distension ʒviij. Ulcer healed on anterior wall. Contraction bands around it marked. Some recent (mostly submucous) tubercles around ulcer on anterior wall of bladder. Leash of vessels around both orifices. April, 1905.—Distension ʒx. No ulceration; some radiating bands of scar tissue on anterior wall; no tubercles seen; suspicious patch between ureters on posterior wall; congested, but not ulcerated.	½ mg. Dec. 7.—Tuberculin ½ mg.; 14, injections omitted. Frequency: day, 1 to 1½ hours; night, 3 times. Jan. 11, 1904.—Frequency: day 1½ to 2 hours; night, 3 to 4 times. Jan. 25.—Complains of severe aching; no hæmaturia. Feb. 22.—Frequency: day, 1½ hours; night, 3 times. March 7.—No tubercle bacilli can be found in urine. March 28.—Frequency: day, 2 hours; night, 3 hrs. Is better whilst taking capsules Ol. santal. May 9.—Frequency: day, 2 hours; night, 3 times (at best). Pain is decidedly less. June 13.—Pain was only slight; no hæmaturia. Frequency: same. July 18.—Still slight penile pain. August 8.—No hæmaturia for about 12 months. August 29.—Frequency; day, 2 hours; night, 4 times. Oct. 3.—Feeling better; no low pain. Oct. 27.—Frequency: day, 1½ hours; night, 1½ hours. Tuberculin $\frac{1}{1000}$ mg. See cystoscopy. Nov. 14.—Frequency: day, ½ hour; night, ½ hour. Penile pain after micturition. Dec. 12.—Frequency: day, 1½ to 2 hours; night, 3 times. Pain: occasionally penile after micturition: none inside. To recommence tuberculin. Jan., 1905.—Commenced a fresh series of T.R. injections $\frac{1}{1000}$ mg. weekly. April.—Steady improvement with T.R.; now getting $\frac{1}{1000}$ mg. weekly. Frequency: day, 2 to 3 hours; night, once (always better in warm weather). No blood seen, and urine fairly clear as a rule. July.—No T.R. for one month; condition very good; no pain; frequency as at last note; urine clear.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
9	M., 20	Oct. 11, 1903.—Five months ago first noticed urine turbid. Slight pain at end of micturition in glans penis. During last month had noticed that last few drops of urine had been tinged with blood. Frequency: day, 6 times; night, once. No lumbar pain. Urine pale, slightly turbid; reaction acid; sp. gr. 1018; pus and albumen present; blood absent; centrifuged deposit contained tubercle bacilli. Weight, 8 st. 10 lb., losing. Right testis: lower pole of epididymis contains three distinct hard nodules, and there is a small sinus in scrotal skin leading from there; have been noticed 4 years. Left testis normal. Prostate and vesicles normal. No tubercular history in family	Oct. 14, 1903.—Ether. Distension 10 oz. was allowed easily. Tuberculous ulcers seen, largest about ¾ in. diameter, and covered with greyish slough; numerous smaller ulcers seen, some covered with blood-clot; remaining mucous membrane congested, with numerous raised tubercles. Right ureteric orifice normal. Left orifice blurred and indistinct. Sept. 29.—Cocaine 10 per cent., distension 7 oz. Tubercles less widely distributed, mostly on posterior wall, and almost entirely submucous; two small patches breaking down. A good deal of scarring on right side. Both orifices healthy. Oct., 1905.—Cocaine 5 per cent., distension 8 oz. General congestion of bladder base. Right side as at last note. No ulcerated surface, but especially deep congestion,	Oct. 15.—Inj. tuberculin $\frac{1}{250}$ mg.; 17, $\frac{1}{200}$ mg. Still hæmaturia. Oct. 19.—Inj. tuberculin $\frac{1}{150}$ mg.; 21, $\frac{1}{100}$ mg.; 23, $\frac{1}{50}$ mg. Urine free from blood, symptoms otherwise unchanged. Oct. 25.—Inj. tuberculin $\frac{1}{25}$ mg.; 27, ¼ mg. No reaction produced by series. Out-patient: Nov. 12, 1903.—Inj. tuberculin ¼ mg.; 19, ½ mg. Frequency: day, 5 to 6 times; night, once. No blood. Oct. 26.—Inj. tuberculin ¼ mg. Urine turbid, acid, no blood, albumen present. Dec. 3rd.—Injection ½ mg.; 10, ½ mg. Frequency: day, 3 to 4 times; night, once. No pain. Lapse of 3 months. March 10, 1904.—Pain after micturition. Hæmaturia again after 6 months' freedom. Frequency: day, 2 hours; night, 3 times. Tuberculin $\frac{1}{100}$ mg. March 17.—More pain since injection; none to-day. March 24.—Tuberculin $\frac{1}{50}$ mg. Frequency: day, 2 hours; night, 2 hours. March 31.—Tuberculin ¼ mg. Feeling better. April 7.—Tuberculin ½ mg.; 14, ½ mg.; 21, ¼ mg. April 28.—I stop injections. Slight hæmaturia in evenings. Frequency: day, 2 hours; night, once. May 12.—Bleeding ceased; right epididymis broken down and discharging. Frequency: day, hourly; night, 3-hourly. Tuberculin $\frac{1}{100}$ mg. May 26.—Tuberculin $\frac{1}{50}$ mg. Losing weight (8 st. 2 lbs); occasional hæmaturia. June 2.—Tuberculin $\frac{1}{25}$ mg.; 13, ¼ mg. June 16.—Thick hæmaturia last night; none to-day. Frequency: day, hourly; night, 3 to 4 times. Complains of perineal "irritation." Injections omitted. July 7.—Usually, last urine at night tinged with blood. July 14.—Weight 8 st. 4 lb. July 21.—Still slight bleeding. Frequency: day, 3 hours; night, once. Aug.—Condition remains same. Sept. 1.—Still slight bleeding. Frequency: day, 2-

			with two or three points of blood extravasation on posterior wall, immediately above inter-ureteric wall	hourly; night, 3 times. Sept. 8.—Frequency: day, 3-hourly; night, once. Weight 8 st. 5 lb. Sept. 29.—Weight 8 st. 4 lb. Oct. 6.—Tuberculin $\frac{1}{10}$ mg.; 13, $\frac{1}{10}$ mg. Oct. 20.—Tuberculin $\frac{1}{100}$ mg. Frequency: day, 1½ hours; night, once. Blood again at end of micturition. No attendance until Dec. 29.—No blood since seen last, but urine, usually turbid, now acid; albumen and pus present. Pain at tip of penis after micturition; smarting, when bladder full, in suprapubic area. No lumbar aching. Frequency: day, 2 to 2½ hours; night, once. Weight 8 st. 5 lb. Tuberculin $\frac{1}{150}$ mg. May 18, 1905.—Continued series of T.R. weekly until this date reaching maximum of $\frac{1}{10}$ mg. Condition unaltered, except weight, which has increased to 8 st. 11 lb. Oct. 26.—No T.R. since last note. Condition unchanged.
10	M., 43	Jan. 7, 1904.—No family history of tubercle. Gradually increasing frequency of micturition for last nine months, now amounting to—day, ¼ hourly; night, ½ to 1 hourly. Pain: urethral after micturition. Hæmaturia: only during last 3 days. Faint tinge of blood at end of micturition. Stream: dribbling after flow. Left lumbar: aching for a few days. Urine: 1028, acid, pus and albumen present in small amount. Testes and epididymis normal. Prostate: tuberculous nodules in upper part of each lobe, larger on the right side. Tubercle bacilli present in the urine	Jan. 12, 1904.—Both ureteric orifices normal. To inner side of right orifice is a raised congested patch with small submucous hæmorrhages. Above trigone is a raised area covered with greyish-white sloughy material—edges ragged and uneven. No other tuberculous lesion found. Jan. 5, 1905.—Cocaine, Dist. ℥x. Two or three very small ? nodules on interureteric bar. Leash of vessels to inner side right orifice and scar contraction at site of old slough. June, 1905.—Dist. ℥x cocaine. Bladder appears perfectly healthy	Jan. 17.—Inj. tuberculin $\frac{1}{1000}$ mg.; 20, $\frac{1}{150}$ mg.; 22, $\frac{1}{100}$ mg.; 24, $\frac{1}{50}$ mg.; 26, $\frac{1}{25}$ mg.; 28, ¼ mg. Reaction 18 hours after injection of ¼ mg., headache, sickness, and temp. 101·6°. Injections were then stopped. Feb. 3rd.—Frequency: day, 4 to 5 times; night, once or twice. Pain: practically absent. Blood: none. Discharged. Seen on Dec. 29, 1904. Went to Brighton Convalescent Home for 3 weeks, and resumed duty as policeman in March, 1904, and had no pain and no frequency. In Oct., 1904, found occasionally frequency. Now—Frequency: day, 4 to 5 hours; night, 0. Blood *nil*. Urine clear. No albumen. Prostate: nodules in upper part of each lobe and in vesicles. Testes normal. Gaining weight. June, 1905.—Perfectly well.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
11	M., 32	Jan. 8, 1904.—Patient is one of a family of thirteen, one of whom died in Brompton Hospital, cause unknown. Frequency: commenced 18 months ago and gradually got worse, and now amounts to — day, ½-hour; night, ¾-hour. Pain: commenced 6 months ago. Supra-pubic before micturition, in glans penis after. Hæmaturia: occasionally at finish of micturition. Urine: turbid for 3 months; pale, sp. gr. 1018, reaction acid. Albumen pus present. Prostate: small nodule on right side. Testes and vesicles normal. Tubercle bacilli in urine	Feb. 12, 1904.—Distension ʒiv under $CHCl_3$. Left orifice: large, surrounded by submucous tubercles. Right orifice: on large œdematous papilla and surrounded by polypoid œdematous prominences. Base: very congested; numerous submucous tubercle. Above base on left side was an ulcerated surface covered by blood clot and a smaller submucous hæmorrhage in right lateral wall	Feb. 13.—Tuberculin $\frac{1}{1000}$ mg.; 15, $\frac{1}{500}$ mg.; 17, $\frac{1}{100}$ mg.; 19, $\frac{1}{100}$ mg.; 21, $\frac{1}{10}$ mg.; 23, $\frac{1}{10}$. Patient had improved under treatment up to 22nd, and was allowed up on a couch. Frequency diminished to—day: 2 hours; night, 1½ hours. Pain: less. Hæmaturia: none. After injection of $\frac{1}{10}$ mg. the pain and frequency returned. No rise of temperature, no diarrhœa and no malaise. Injections were omitted, and patient soon regained condition on Feb. 21. March 4 and 7.—Tuberculin $\frac{1}{10}$ mg.; 9, 12, $\frac{1}{10}$ mg.; 14, ½ mg.; 16, ½ mg. No further improvement since above, on discharge. Died July 15, 1904.
12	F., 16	March 15, 1904.—Two years' history of increased frequency of micturition, with several slight attacks of hæmaturia. Now has pain at neck of bladder after micturition lasting some minutes. No supra-pubic or lumbar pain. Frequency: day, 2-hourly; night, 2-hourly; unaffected by rest or exercise.	Ethyl chloride and ether. Distension 8 oz. Small ulcer involving outer side of right ureteric meatus, the latter larger and thickened; a little flaky material in the efflux from it. A large patch of infiltration extending outwards from this, surface intact.	Commenced treatment with $\frac{1}{100}$ mg. tuberculin injections twice weekly, and increased to 1 mg. Sharp reaction with ½ mg., temperature rising to 103°. Continued treatment steadily. Sept., 1904.—Very slight reaction with ¾ mg. twice a week. General condition much improved. No tubercle bacilli found in urine after repeated search. No blood and no pus. Dec., 1904.—1 mg. of T.R. has been given steadily twice a week. Little or no reaction. Temperature rises to 100° in 8 hours, but reaches normal in 36 hours. Very little pain after micturition; sometimes none

		Hæmaturia every few days, slight, but bright red, with occasionally a few small clots. Urine: turbid, blood, pus, and epithelial *débris*; many tubercle bacilli present. Neither kidney palpable nor tender	Clear flow from healthy left ureter. Dec., 1904.—Cocaine Distension 8 oz. Scarring at site of old ulcer. Clean efflux from both ureters. Right ureter distorted by scar contraction. Some patches of congestion, but no ulceration present	for a week. Urine clear; faint cloud of albumen; no blood or pus; no tubercle bacilli. Oct., 1905.—Reports practically free from symptoms. Nov., 1905.—Tubercle bacilli found in very small number again. Has also seen a little blood. General condition excellent.
13	M., 34	March 30, 1904.—Six months' history of pain after micturition, and several slight attacks of hæmaturia. Now pain: penile, lasting four or five minutes after micturition. Frequency: day, hourly; night, twice. Hæmaturia: generally a little blood in the urine; occasionally a few clots. Urine: pale, thick, flocculent with muco-pus, neutral, slightly offensive; many tubercle bacilli present. Neither kidney palpable or tender. Nothing in epididymes, vasa, vesiculæ, or prostate	April 5, 1904.—Cocaine, 5 per cent. Distension 8 oz. Several patches of reddened and swollen mucous membrane on left side of base and at left of fundus. One patch of submucous tubercle. The right ureteric orifice is occupied by a small mass of swollen mucous membrane, almost polypoid in appearance, moving with the efflux. Left orifice normal. Clear discharge from both sides. Oct. 19, 1905.—Distension 8 oz. Right ureteric orifice clear. Much scar contraction at site of patch of submucous tubercle. Still many patches of swollen and reddened mucous membrane. Clear efflux from both sides	April 5, 1904.—Commenced with $\frac{1}{1000}$ mg. tuberculin, increased to $\frac{1}{250}$ mg. weekly doses for 3 months. For 2 months $\frac{1}{1000}$ mg. For 2 months $\frac{1}{100}$ mg. For 3 months $\frac{1}{100}$ mg. For 2 months $\frac{1}{50}$ mg. May, 1905.—No reaction with any dose. Weight slightly increased. No hæmaturia for 6 months. Pain varies, sometimes more acute, sometimes absent. Tubercle bacilli still present. Oct., 1905.—No injections since May. Condition unaltered. Frequency: day, hourly; night, twice. On the whole is in much the same condition as when he first attended. Tubercle bacilli present.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
14	F., 37	March 31, 1904.—Intense urethral pain during and after micturition. Urethra dilated and bladder scraped and iodoform rubbed in in Nov., 1903. Much worse after this. Now—Frequency: day, 20 to 30 minutes; night, hourly. Hæmaturia: none. Pain: after every micturition, sometimes does not cease until next act. Urine: acid, 1015, pus, mucus. Much epithelium, a little blood in microscopic amount. Many tubercle bacilli. Neither kidney felt. Very heavy drinker at intervals. Sometimes only one or two drinking bouts in 6 months, but these bouts last two or three weeks	Ethyl chloride - ether. Distension only ℥v maximum. Much irregular ulceration on anterior wall and fundus. Some congestion at the base. Both orifices healthy and discharging clear urine	Started with $\frac{1}{250}$ mg. of T.R. and gradually worked up to $\frac{1}{2}$ mg. With this dose had severe reaction both local and general. Arm swelled to finger tips and took 3 or 4 days to subside. Great increase of local pain, and the frequency, which had much diminished, again increased. Went back to $\frac{1}{25}$ mg. Treatment was continued for 4 months. Then severe drinking bout interfered. Attempts have been made to continue treatment, and whilst receiving T.R. some improvement is noted, but the drinking interferes with any steady progress. October, 1905.—In much the same condition. Sometimes can hold urine for 2 hours and has less pain, but repeated attacks of drinking check all real progress.
15	M., 40	May 14, 1904.—Four years ago pain in right lumbar region referred to groin. Came on in moderately severe attacks about once in two weeks, and lasted 3 months. Similar pain 9 months ago. Hæmaturia: only noticed once when small amount of blood was passed 6 months ago; none since. Frequency: increasing for 6 months;	May 16, 1904.—℥vj distension: much superficial ulceration of the entire base extending up on posterior wall; both ureteric orifices hidden by swelling, but efflux was very cloudy	May 20.—Tuberculin $\frac{1}{2500}$ mg.; 22, $\frac{1}{2000}$ mg.; 24, $\frac{1}{1500}$ mg.; 26, $\frac{1}{1000}$ mg.; 28, $\frac{1}{500}$ mg. Temperature rose to 101·2° with headache; no sickness nor diarrhœa. Frequency: day, 1½ hourly; night, 2½ hourly; painless. May 30.—Temp. 99°. May 31.—Tuberculin $\frac{1}{25}$ mg. June 2.—$\frac{1}{6}$ mg. No further reaction. June 3.—Left hospital. Recommended not to pursue T.R. treatment any further. Had five injections of $\frac{1}{10}$ mg. Within a few hours of the last injection the temperature ran up to 103·5°; total suppression of urine followed, and the patient died in 3 days.

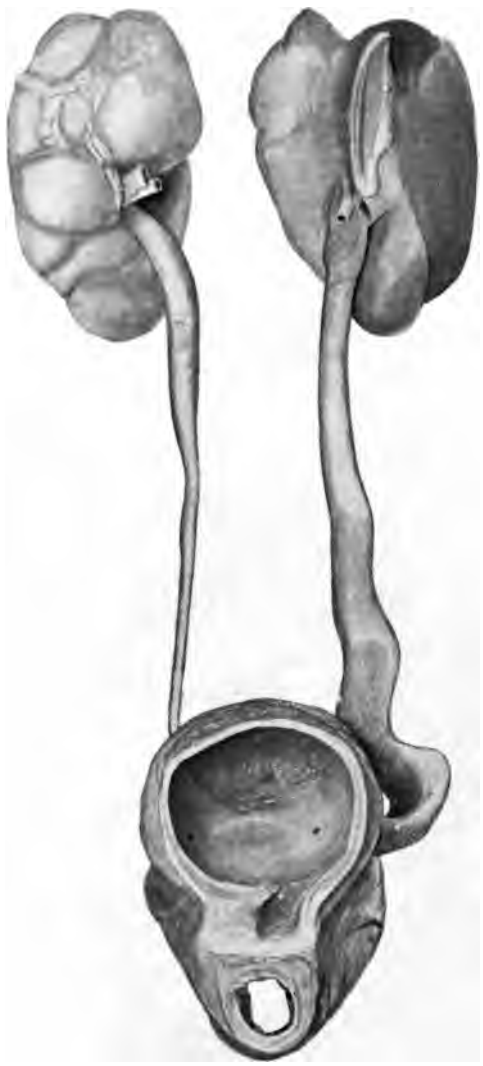
		now: day, 1½ hourly; night, 1½ hourly. Pain: in glans penis after micturition; supra-pubic pain before micturition. Losing weight rapidly. Signs of phthisis at right pulmonary apex. Urine: turbid, and contains numerous tubercle bacilli. Kidneys: not palpable; testes and prostate normal		
16	M., 24	No family history of tubercle. Symptoms for 3 months, commencing with hæmaturia, slight for 10 days and mixed with urine. Frequency quickly increased to—day, hourly; night, 0. Pain: none. No backache. After being free from hæmaturia for 2½ months it recurred 10 days ago as a few drops at end of micturition, with pricking pain at glans penis at finish of act. Supra-pubic pain relieved by micturition. Frequency: June 28, 1904—day, 8 times; night, 0. No nodules in testes or prostate. Urine: pale, turbid. Faintly alkaline, sp. gr. 1012. Albumen: small amount. Phosphates in excess. Blood and pus present. Tubercle bacilli present in large numbers.	June 16, 1904.—Cocaine 10 per cent. Dist. ℥x. Right orifice: large, and placed on raised, thick mucous membrane, and surrounded by ring of submucous tubercles, one of which below the orifice had broken down into a small ulcer. Above and to right of orifice another patch of tubercle surrounding a ragged ulcer. Left ureter normal and clear urine from each. Sept. 1st.—Two small patches of submucous tubercle. Ulcers healed. Oct. 17.—Cocaine. Dist. ℥vij. Much improved. All ulcers healed. Right ureteric orifice better; tubercles not so widespread. Jan. 5, 1905.—Cocaine. Dist. ℥vj. Patch close to right orifice, rough surface. Congested. No open ulcer. No tubercles seen. Definite submucous tubercles in lower end of patch above left orifice	In hospital. June 30.—Tuberculin $\frac{1}{3\,\frac{1}{0}0}$ mg. July 2.—Tuberculin $\frac{1}{3\,\frac{1}{0}0}$ mg.; 4, $\frac{1}{1\,\frac{1}{0}0}$ mg.; 6, $\frac{1}{1\,0\,0}$ mg.; 8, $\frac{1}{5\,0}$ mg.; 10, $\frac{1}{2\,5}$ mg.; 12, $\frac{1}{4}$ mg.; 14, $\frac{1}{3}$ mg. No reaction produced by series. Left for Weston-super-Mare for 3 weeks. July 25.—Tuberculin ½ mg., temp. rose to 103° next day. July 29.—Tuberculin ¼ mg., temp. rose to 100° next day. Aug. 1.—Tuberculin ⅓ mg., temp. rose to 100° next day. Aug. 4.—Tuberculin ½ mg., temp. rose to 100° next day. Aug. 8.—Tuberculin ⅔ mg., temp. rose to 102·8 next day. Aug. 12.—Tuberculin ⅔ mg., no rise. Omitted tuberculin as apparently quite well until Oct. 15.—Recurrence of bleeding with penile pain and frequency: day, hourly; night, 6 times. Oct. 18.—Tuberculin $\frac{1}{1\,0\,0}$ mg.; 20, $\frac{1}{5\,0}$ mg.; 22, $\frac{1}{2\,5}$ mg.; 24, ¼ mg.; 26, ⅓ mg., no reaction. Oct. 29.—Tuberculin ⅓ mg., no reaction. Nov. 3.—Tuberculin ½ mg., temp. 102·2° next day, then normal. Nov. 8.—Tuberculin ⅔ mg., temp. 103° next day, then normal. Nov. 14.—Tuberculin ½ mg., temp. 101° next day, then normal. Nov. 21.—Tuberculin ⅔ mg., no reaction. Weight, 9 st. 5 lb. Nov. 26.—Tuberculin ½ mg., temp. 102° next day, then normal. Dec. 1.—Tuberculin ⅔ mg., temp. 102° next day, then normal. Dec. 8.—Tuberculin ¼ mg., temp. 101° next day, then normal. Dec. 16.—Tuberculin ⅓ mg., temp. 100° next day, then normal. Dec. 28.—Tuberculin ⅔ mg., temp. 101°. Frequency: day, hourly; night, 3 times. Blood: very occasionally small clots. No penile pain. Slight right lumbar aching. Weight, 9 st. 5 lb. Continued with doses of $\frac{1}{2\,5}$ mg. weekly (these gave no reactions) for 6 months. July, 1905.—Frequency: day, 1½ hours; night, twice. Pain and symptoms much the same.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
19	M., 34	Aug. 4, 1904.—Commenced with increased frequency 16 years ago; gradually increasing to ¼-hourly day and night in 18 months, when the urine was pale and turbid, and occasionally blood-stained. He was operated on by perineal cystotomy in Leipsic, a fistula remaining open for 18 months, through which part of urine was passed during micturition. He never became quite well; occasionally passing blood; frequency remaining 2-hourly by day and night. Pain in glans penis after micturition; no relation to exercise. Backache: nil. Hæmaturia: as recently as 2 days ago. Urine: pale, turbid; reaction acid; sp. gr. 1020; albumen, pus, and blood present; tubercle bacilli found after centrifuging. Four years ago inoculation experiments with urine into guinea-pig gave a positive result of tubercle. Prostate: nodule in left lobe *per rectum*. Testes and epididymes normal. No history of tubercle	Aug. 5, 1904.—$CH.Cl_3$. Absolute distension 5 oz. Several small tuberculous ulcers about fundus and in trigonal area, which is much congested. No submucous tubercle seen. Clear urine from each ureteric orifice. Nov. 24.—Cocaine 10 per cent. Distension 5 oz. On the whole better. Less congestion. No ulceration seen, but diffuse tubercles with surrounding inflammatory zone. Both ureteric orifices large, with open œdematous lips, but clear urine from each; right orifice drawn up by old cicatrisation. Oct. 19, 1905.—Cocaine 5 per cent. Distension 4 oz. Intense general congestion of the whole base of bladder. One large ragged ulcer seen on anterior wall towards fundus. Both ureteric orifices hidden by swelling of mucous membrane	C.O.S.F., t. d. s. Aug. 6.—Inj. tuberculin $\frac{1}{2\,5\,0}$ mg. Left hospital at own wish to attend O.P. Aug. 11.—Inj. tuberculin $\frac{1}{2\,0\,0}$ mg. Aug. 15.—Inj. tuberculin $\frac{1}{1\,5\,0}$ mg. Small clots in urine. Frequency: day, 2 to 3 hours; night, 2 to 3 hours. Aug. 18.—Inj. tuberculin $\frac{1}{1\,0\,0}$ mg. Weight 9 st. 13 lb. Aug. 21.—Some malaise after last injection. More pain. Frequency: day, hourly; night, hourly. No injection. Aug. 25.—Tuberculin $\frac{1}{1\,0\,0}$ mg.; 29, $\frac{1}{5\,0}$ mg. Sept. 1.—Tuberculin $\frac{1}{2\,5}$ mg. No reaction; pain less. Frequency: day, 1½ hours; night, 1½ hours. Sept. 5.—Tuberculin ½ mg. Sept. 8.—Tuberculin ½ mg. Frequency: day, ½ to 1 hour; night, ½ to 1 hour. Sept. 12.—Slight malaise. Omit injection. Weight 9 st. 12 lb. Sept. 15.—Better. Frequency: day, 1 to 1½ hours; night, sans. Tuberculin $\frac{1}{2\,5}$ mg. Sept. 22.—Tuberculin ½ mg. Blood once during week. Sept. 29.—Tuberculin ½ mg. Oct. 6.—Tuberculin ½ mg. Less pain. Weight 9 st. 13 lb. Oct. 13.—Tuberculin ½ mg. Still a little blood. Oct. 20.—Tuberculin ½ mg. No blood. Frequency: day, 1 to 1½ hours; night, 1 to 1½ hours. Oct. 27.—No injection this week. Nov. 3.—Tuberculin ½ mg. Pain certainly less since commencing treatment. No blood for 3 weeks. Nov. 10.—Tuberculin ½ mg. Nov. 17.—Tuberculin ½ mg. Blood during the week twice. Nov. 24.—Frequency increased to ¾ hours for 3 days after last injection. Tuberculin $\frac{1}{2\,5}$ mg. Dec. 1.—Frequency varies from: day, 3 hours to 1½ hours; night, 3 hours to 1½ hours. Tuberculin $\frac{1}{2\,5}$ mg. Weight 9 st. 12 lb. Dec. 8.—Better; pain "practically nil." Frequency: day, 2½ hours; night, 2½ hours. Tuberculin $\frac{1}{2\,5}$ mg. Dec. 15.—Tuberculin $\frac{1}{2\,5}$ mg. Tinge of blood yesterday. Weight 9 st. 13 lb. Jan. 20, 1905.—Continues with $\frac{1}{2\,5}$ mg. June.—Has

		in family. Weight: lost 2 st. in 2 years		continued steadily with $\frac{1}{15}$ mg. every fortnight. Frequency: day, 2 hours; night, 3 hours. Pain is almost absent, and there has been no hæmaturia since early in April. Oct. 19.—Has had no injections since last note. Not nearly so well. Frequency: day, hourly; night, 1½ hours. Pain very severe at close of micturition. Generally sees a little blood once or twice a week. Urine thick with muco-pus.
20	M., 39	Aug. 8, 1904.—Two years ago first noticed slight supra-pubic pain and found that he passed some faintly blood-tinged mucus in his urine. Later had aching in testes and in supra-pubic area, worse after micturition. A year ago he passed some blood clots in the urine and on one occasion noticed that urination was followed by dribbling of blood from the urethra. Since this time he has gradually got worse, pain in testes, penis, and supra-pubic region, and more severe and accompanied by pain in right inguinal region. Frequency—increased for a year and now amounts to: day, ¼ hour; night, ½ hour. Hæmaturia: none for 6 months. Never passed stone or gravel. Urine: pale, sp. gr. 1007. Faintly acid reaction. Albumen present. Pus and few blood discs present, but no tubercle bacilli were found. Family history: No history of tuberculosis	Aug. 10, 1904.—Chloroform. Distension ℥iv (absolute). Widespread deposit of tubercle, chiefly about the base, where there were numerous submucous hæmorrhages. No actual ulceration was seen, possibly owing to small distension. Clear urine from either ureter	Aug. 11.—Inj. tuberculin $\frac{1}{250}$ mg.; 13, $\frac{1}{200}$ mg.; 15, $\frac{1}{150}$ mg.; 17, $\frac{1}{100}$ mg. Pain much less marked. Frequency diminished to: day, hourly; night, hourly. No rise of temperature. Aug. 19.—Inj. tuberculin $\frac{1}{50}$ mg.; 21, $\frac{1}{25}$ mg.; 23, ¼ mg. Frequency: day, hourly; night, 1½ to 2 hours. Pain diminished again. Discharged to out-patients. Aug. 29.—Tuberculin ½ mg. Weight, 8 st. 10 lb. Sept. 5.—Tuberculin ½ mg. Frequency: day, ½ to ¾ hour; night, hourly, at best. Sept. 12.—Tuberculin ½ mg.; 19, ½ mg., pain less. Frequency sometimes as long as 1½ hours. Sept. 26.—Tuberculin ½ mg. Weight, 8 st. 10 lb. Oct. 3.—Tuberculin ½ mg. Frequency: day, hourly; night, ½ hourly. Oct. 17.—Tuberculin ½ mg. Frequency: day, ½ to 1½ hours; night, 2 hours. Weight, 8 st. 12 lb. Oct. 24.—Tuberculin ½ mg.; 30, ½ mg. Nov. 7.—No injection to-day. Frequency: day, ½ to 1 hour; night, hourly. Not so well. Nov. 21.—Tuberculin ½ mg. Less pain. Weight, 8 st. 11 lb. Dec. 5.—Tuberculin ½ mg. Frequency: day, ½ to 1 hour; night, 2 hours. Weight, 8 st. 12½ lb. Blood: only faint trace once. Dec. 12.—Tuberculin ½ mg. Still improving. Jan. 20, 1905.—Tuberculin ½ mg. Not so well. More frequency and pain. Has lost 4 lb. in weight. April, 1905.—Has not attended since last note. Writes that he is steadily getting worse. Has had no T.R. for 3 months. June, 1905.—Died after 3 days of complete suppression of urine 5 months after the last dose of T.R.

No. of case.	Age and sex.	History.	Cystoscopic examination.	Treatment and result.
21	M., 27	Sept. 24, 1904.—Trouble with micturition since 12 years old. Intermittent hæmaturia during this time. Slight aching pain in left ileo-costal space posteriorly, fixed, only very occasionally present. No pain on micturition. Frequency: day, 3 hours; night, once. Hæmaturia: clots daily. Urine: acid, 1022. Blood, pus and albumen present. Kidneys not palpable	Sept. 26, 1903.—Ragged ulceration of bladder and mucous membrane. Bleeding very easily set up	Oct. 8.—Tuberculin $\frac{1}{250}$ mg.; 10, $\frac{1}{300}$ mg.; 12, $\frac{1}{150}$ mg.; 14, $\frac{1}{100}$ mg.; 16, $\frac{1}{50}$ mg. No reaction. Increasing weight. Oct. 18.—Tuberculin $\frac{1}{25}$ mg.; 21, $\frac{1}{4}$ mg. Urine contains a little pus. Frequency: day, 4 to 5 times; night, twice. Out-patient. Oct. 28, 1903.—Tuberculin $\frac{1}{4}$ mg. Nov. 4.—Tuberculin $\frac{1}{4}$ mg.; 11, $\frac{1}{4}$ mg.; 18, $\frac{1}{4}$ mg. Frequency: day, 5 to 6 hours; night, once. Nov. 25.—Tuberculin $\frac{1}{4}$ mg. Dec. 16.—Tuberculin $\frac{1}{4}$ mg.; 23, $\frac{1}{4}$ mg.; 30, $\frac{1}{4}$ mg. Jan. 6, 1904.—Tuberculin $\frac{1}{4}$ mg.; 13, $\frac{1}{4}$ mg.; 20, $\frac{1}{4}$ mg.; 27, $\frac{1}{4}$ mg. Feb. 3.—Injections cause headache so omitted. March 9.—Frequency: day, 5 to 6 hours; night, once. No further attendance. Jan. 7, 1905.—Died from general tuberculosis (Dr. McFarlane).

Pardoe: Treatment of Tuberculosis of Urinary System. Plate I.



Bladder, ureters, and kidneys extensively infected with tubercle. The right ureter is, in its lower third, a fibrous cord. The left ureter is enormous. The ureteric orifices, however, show no sign of tuberculous infection; the chief area of ulceration in the bladder is towards the fundus.

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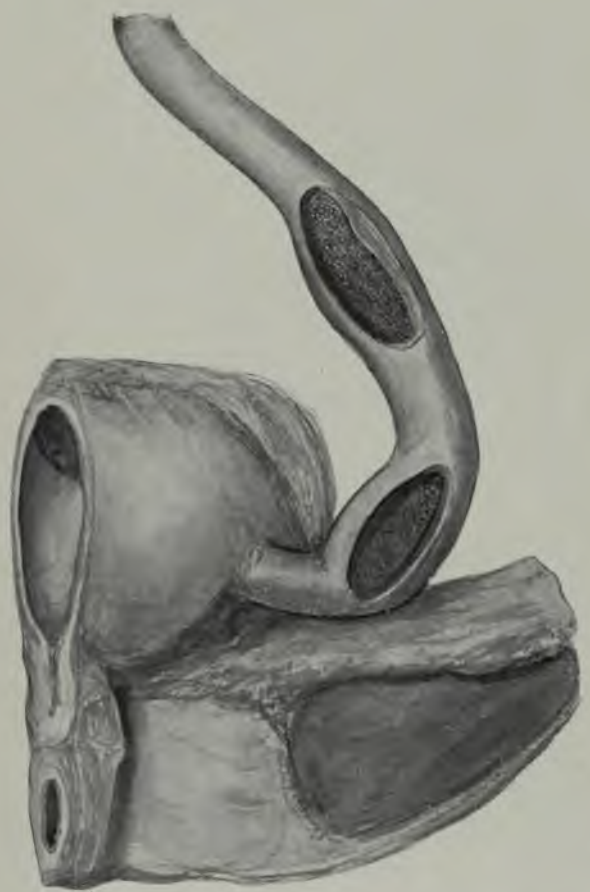
Pardoe: Treatment of Tuberculosis of Urinary System. Plate II.



Side view of left ureter seen in the other plate. The ureter has been opened in two places to show the extensive deposit of tubercle.

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DISCUSSION.

The PRESIDENT thought that the mechanism of immunity to bacterial poisons had never been so clearly enunciated as in Dr. Wright's paper; its applications as to explanation of the phases of the natural history of tubercle, and the adaptability of the principle to treatment had also been clearly laid down. It was of interest that there might be several opsonins in the blood, side by side, although the opsonic material had not been separated. The comparison between the auto-intoxication of tuberculous patients and the result of injections of tuberculin was illuminating, as also was the explanation of the effect of exercise in flushing centres of tubercular change through the generally increased blood-pressure. From the small number of cases occurring in his experience, the point that seemed to him of primary importance was that the disease should be fairly localised and quiescent before tuberculin treatment was commenced. It suggested that in the stormy cases sanatorium treatment should precede the tuberculin injections. It would be of interest to know whether such sanatorium treatment had an influence on the opsonic index. The determination of the opsonic index had an important bearing on the question of whether exercise should or should not be prescribed. Reference was made to the deliberate and temperate fashion in which the results and suggestions of the papers had been advanced. There was ground for hope that a clinical index would shortly be arrived at, and a routine of treatment laid down (and that with a minimum of test observations), which would be generally applicable, for it was evident that at this stage opsonic observation could only be made in a few instances of tuberculous disease.

Dr. G. W. Ross said he had had the privilege of learning the methods of blood examination devised by Dr. Wright and Captain Douglas in Dr. Wright's laboratory. For the past nine months he had applied those methods at the Victoria Park Chest Hospital: so that he might, perhaps, best contribute to that interesting discussion by briefly relating his experience in the practical application of the principles enunciated by Dr. Wright in the every-day work of a hospital largely devoted to the treatment of pulmonary tuberculosis. He must first of all acknowledge his great indebtedness to Dr. Wright for his unfailing kindness and assistance throughout that investigation, and also to the honorary and resident staff of the Victoria Park Hospital, who had also offered him every assistance. Before proceeding to employ Dr. Wright's methods in the diagnosis and treatment of pulmonary tuberculosis, it was essential to determine the characters of the opsonic index in the patients in the wards of the hospital. Attention should be drawn to the fact that the

great majority of these patients were more or less advanced in the disease. Very few were early cases. He had estimated the content of the blood in anti-bacterial substances in one hundred cases taken indiscriminately from the wards; of these 51 per cent. showed, on the initial examination, an opsonic index above 1·2—*i. e.* above normal; 38 per cent. showed an opsonic index between 1·2 and 0·8—*i. e.* within the normal limits assigned by Dr. Bulloch; 11 per cent. showed an opsonic index below 0·8—*i. e.* below normal. Of these eleven cases four were early, five advanced, and two tuberculo-fibrotic. All but three were apyrexial. Furthermore, in conjunction with Dr. F. Heygate Ellis, he had observed the variations in the opsonic index of thirty ward patients (mostly advanced cases) over periods of from several weeks to several months. The blood in each case was examined at intervals of about ten days, and in all 155 observations were made. He did not propose to analyse these cases further than to record several observations emanating from a study of them. (1) Of the thirty cases, twenty-seven showed an opsonic index above normal—(*i. e.* 1·2) during some period of their stay. (2) Of the thirty cases, twenty-five showed a fluctuation of at least 0·3 in their opsonic indices during some period. Of the remaining five cases, three showed a high opsonic index at some period. (3) Of the thirty cases, twenty-seven, on the initial examination, were within or above the normal limits, and in most of these there was observed a definite tendency towards a lower or low opsonic index after rest in bed. This downward tendency was as a rule arrested and the opsonic index distinctly elevated with exercise. (4) No concurrence in point of time was found between the fluctuation of the temperature and the fluctuation of the tuberculo-opsonic index. In general, however, the subjects of a continuous pyrexia, medium or high, showed an increased or a high opsonic index. He next applied these observations to the *diagnosis* of pulmonary tuberculosis from various other conditions, and he found the following considerations of value in enabling him to arrive at an accurate diagnosis in doubtful cases. (1) The observation of a tuberculo-opsonic index of 1·3 or higher was, in his experience, highly significant of an active tuberculous infection. He had not yet recorded a tuberculo-opsonic index as high as 1·3 in any case that was not definitely the subject of a tuberculous infection. *Illustrative case*: Phyllis K—, aged 6, showed certain indefinite signs of pulmonary tuberculosis. The tuberculo-opsonic index was 1·4. Subsequently, after many examinations, tubercle bacilli were found. (2) If in the absence of a high index on the initial or subsequent examinations, several observations of the tuberculo-opsonic index showed a fluctuation of four decimal points, it was in his opinion distinctly in favour of the presence of a tuberculous infection. (3) The determination of

an opsonic index of 0·6 or less upon several occasions probably meant a tuberculous infection, but the evidence upon this point was as yet insufficient. He had some observations which supported the probability that the so-called "hereditary predisposition" was based on a deficiency of the anti-bacterial substances of the blood. If this were so, it would obviously be difficult to determine whether a low opsonic index meant an infection or only a predisposition. He felt confident, however, that the determination of the presence or the absence of a fluctuating opsonic index would help them materially to overcome this difficulty. Moreover, he believed that a low tuberculo-opsonic index might occur in patients the subject of a serious illness other than tuberculosis. He had observed a tuberculo-opsonic index of 0·6 upon two occasions in such a case several days before death. The autopsy showed an entire absence of any tuberculous infection. (4) The non-occurrence of a high or of a fluctuating tuberculo-opsonic index in patients acutely ill is very strong evidence against the infection being tuberculous. He had five cases supporting this statement, and in all of these the question of an acute tuberculous infection had to be, and was, seriously considered. In all of these cases acute tuberculosis was eliminated by means of the tuberculo-opsonic reaction, and the correct diagnosis greatly facilitated. Of these five cases one was a case of malignant disease of the lung—proved on autopsy. One case had, since the tuberculo-opsonic observation, developed definite signs of multiple sarcoma. Two cases were ulcerative endocarditis, both proved on autopsy. One was a case of enteric fever and pneumonia, proved on autopsy. Furthermore, the application of the above principles is of considerable assistance in determining the presence of, or in eliminating a tubercular process in, the following conditions: (1) Bronchiectasis, (2) fibroid phthisis, (3) bronchitis and emphysema, and (4) simple debility. He had cases illustrating all of these classes in which a diagnosis was satisfactorily reached. In connection with Dr. Lawson and Dr. Stewart's suggestion concerning the significance of a negative phase following upon the inoculation of a small dose of tuberculin, he had the following observations to record: *Firstly*, in his own case he obtained no negative phase after the inoculation of $\frac{1}{2\,5\,0}$ mgr. of tuberculin; *Secondly*, in only two out of six cases which were definitely pulmonary tuberculosis was there a negative phase after the first inoculation, but in the remaining four cases a negative phase occurred after the second inoculation, so that these few observations were quite in accord with those of Dr. Lawson and Dr. Stewart. The great practical value of Dr. Wright's methods in diagnosis was strikingly illustrated in a case that had been sent to him a few days previously for investigation in which acute tuberculosis was seriously considered. Briefly, the patient, a young man, suffered from fleeting pains and inter-

mittent rigors. He looked ill, and had a temperature of 102° F., but presented no physical signs. He gave a history that pointed to the probability of gonorrhœa. Determination of his tuberculo-opsonic index showed this to be normal, but his opsonic index to the gonococcus was twice normal—a fact which, to his mind, was very strong evidence of a systemic gonococcal infection. *Treatment*—He had treated six cases of pulmonary tuberculosis with tuberculin (T. R.) controlled and safeguarded by careful observations of the tuberculo-opsonic index. Exigencies of time prevented him from presenting them more than a brief summary of his results. He might preface a general consideration of the cases by outlining the principles that guided him in their selection and treatment. He had considered that a tuberculo-opsonic index at or below 1·0 should be the criterion of the suitability of the case for inoculation, for it had seemed to him that for those patients showing an opsonic index of, say, 1·4 or more, Nature was doing her utmost. Further, he had determined to begin with a small dose and to increase it at appropriate intervals (as shown by examination of the blood) in the hope of obtaining a cumulative action. It was expedient to divide these six cases which were inoculated into two classes—(*a*) the more or less advanced, four cases; (*b*) the less advanced or early cases, two cases. In class (*a*), two were discharged "much improved," and two simply "improved." He was perfectly aware that such a result was not unusual in patients undergoing the ordinary routine treatment without tuberculin; but it should be noted that these four patients were only under inoculation treatment for the very short period of two months or at the most three months. Nevertheless, although his mind was quite open to conviction, he could not but help feeling that the success of inoculation with tuberculin was highly problematical when applied to advanced cases. As concerned the moderately advanced or early cases, he was distinctly of the opposite opinion, and the two cases in class (*b*) above, in addition to a theoretical consideration of the whole subject, strengthened him in this belief. *Case* 1—A youth, aged 20, under the care of Dr. Heron. Duration of the disease at least seven months; upper and lower lobes of the right lung were slightly involved in a catarrhal tuberculosis. Tubercle bacilli present. Opsonic index 1·0 before inoculation; six inoculations of tuberculin (T. R.) were given in seven weeks in doses of from $\frac{1}{8\,0\,0}$ mgr. to $\frac{1}{2\,0\,0}$ mgr. There was no constitutional or temperature disturbance from the inoculations. The level of opsonic power was considerably raised, and except for occasional fluctuations was maintained at a fairly high level. The patient gained 8 lb., and the cough and expectoration ceased. The physical signs were unaltered. *Case* 2—Female, aged 17, under the case of Dr. Lyon. Duration of the disease about seven months, and the upper lobe of

the right lung alone was involved. Tubercle bacilli present. The opsonic index was 1·0 before inoculation; seven inoculations were given in nine weeks, in doses of from $\frac{1}{800}$ mgr. to $\frac{1}{200}$ mgr. After the first inoculation there was slight shivering for two nights, but no rise of the temperature. Subsequent inoculations produced no constitutional disturbance. The level of the opsonic power was distinctly raised, and although during the six weeks preceding inoculation this patient had remained *in statu quo*, she rapidly improved under inoculation, so that ten weeks later the cough and expectoration had ceased and the pain had disappeared. He did not for a moment contend that the disease was arrested in these two favourable cases, but he did feel that the results obtained were distinctly encouraging; and had not the patients left the hospital, and so prevented his continuing the inoculations, he believed that the diseased process would ultimately have been controlled. He wished to draw attention to several points of practical importance emanating from a study of these cases. (1) There was no reaction at the site of inoculation except a slight thickening in one instance; (2) the only constitutional disturbance observed was a slight shivering for two nights following upon the first inoculation—this occurred in two cases; (3) there was no disturbance of the temperature consequent upon inoculation; (4) the patients frequently complained of depression during the period in which he knew, by examination of the blood, that the negative phase was existent and, on the contrary, of exhilaration during the period of exaltation of the opsonic power; (5) the occurrence of a "negative phase" was the rule, although occasionally it made default; (6) in all cases the level of opsonic power was definitely raised, and he was able by appropriate inoculation to maintain a much higher level than existed before inoculation; (7) he failed to obtain an accumulation of the opsonic power, which he had attempted to do by an increase of dosage, and his practice now was to begin with not more than $\frac{1}{1000}$ mgr. of tuberculin and not to increase this dosage so long as he obtained a satisfactory immunising response. Further, he did not now inoculate until he had determined by blood examination that the positive phase was passing off. That was to say, he was quite satisfied if he could maintain a moderate increase of the anti-bacterial substances and the good progress of the patient continued. In addition to pulmonary tuberculosis he had inoculated the following cases of localised tuberculosis: (1) A case of tuberculous adenitis and tuberculous ulceration of the skin. The enlarged glands disappeared and the tuberculide cicatrised. (2) A case of tuberculous cystitis. All symptoms, as well as tubercle bacilli in the urine, had disappeared, and the patient said that he felt in normal health. Both these patients were under the care of Dr. Hadley, to whom he was indebted for permission to record them. He had now under inoculation a case of inoperable tuberculous adenitis

and a severe case of tuberculous iritis. Both of these patients were making excellent progress. From actual experience in the every-day work of a hospital which had largely to do with pulmonary tuberculosis, he felt convinced of the accuracy of Dr. Wright's belief that they had in these two new forms of treatment the most valuable asset in medicine, not only in diagnosis but in treatment; and further, as concerned pulmonary tuberculosis he believed that a new era in treatment had arrived which was fraught with the most encouraging prospects if only due care and persistence were exercised in the application of Dr. Wright's brilliant discoveries.

Dr. A. WHITFIELD had been working with Dr. Wright's method for about a year. The time required to make the examinations hardly seemed to him to be so great as to take the method out of the hands of at any rate the younger clinicians. Tubercle of the skin was specially resistant to treatment, and out of many cases he had seen only one get well, and no case of lupus vulgaris had been cured by him. A rapidly increasing case of lupus under tuberculin treatment was slightly better, improvement occurring from the centre towards the periphery. One case of scrofulodermia had done well, and two of erythema induratum had been brought under control. The low opsonic index in tuberculous cases he believed to be not a congenital thing, but in some obscure way associated with the tuberculous infection. The difficulty of getting the charged serum to the lupus tissue was great; he had injected with thiosinamine in one case for the purpose of producing a reaction. In one or two cases he had used the old tuberculin (T.O.) in minute doses ($\frac{1}{1000}$ or $\frac{1}{2000}$ c.c.). It caused no constitutional reaction as a rule, but a slight hyperæmia of the local lesion, and it seemed to be efficient in raising the opsonic index. One great advantage of Wright's method was, he thought, that it abolished the so-called "unsuitable" case, which was in reality one calling for extremely minute adjustment of the dose.

Dr. W. D'ESTE EMERY said that the opsonic index was not necessarily proportionate to the amount of opsonin in the blood, and that on progressive dilution of a specimen of normal blood with normal saline solution the index fell off slowly at first, then for a short time roughly proportionately to the degree of dilution, and lastly, more rapidly than the dilution; a curve showing the decrease in the opsonic index with progressive dilution was roughly of the nature of a parabola. Thus, in a particular case, taken as an example of a number of experiments, each leucocyte had taken up an average of 25 organisms when the serum was undiluted; with 4 parts of serum and 1 of normal saline each had ingested 23 instead of 20, as would have been the case if the number were proportionate to the dilution; with 3 of serum and 2 of saline the number was 20 instead of 15; with 2 of

serum and 3 of saline 16 instead of 10; with 1 of serum and 4 of saline 10 instead of 5; and without serum, but an equivalent volume of saline, 2 were taken up by each leucocyte. A suggested explanation was that in any culture there were organisms which differed amongst themselves in the ease with which they were ingested by leucocytes, a few being taken up in the absence of any opsonin, whilst others required large doses before they were edible. It followed from these results that the serum of a patient with an opsonic index of 0·5 contained only a quarter or a third as much opsonin as that of a normal person, and hence that he was presumably not so well protected as the index seemed to show. Conversely, a patient in whom the index had been raised to 2 was much more than twice as well protected as a normal person. The blood in this case must contain a very large amount of opsonin, and this led him to the hope that it might in the future be found possible to prepare a potent opsonic serum for the production of passive immunity by the injection of animals conducted on Wright's principles. With regard to the practical application of the method of vaccination as applied to tubercle, his experience was limited to surgical cases of the disease, in which he had obtained good results and was especially struck by the benefit to the general health that was obtained in almost all cases, even before the local lesion showed signs of improvement. He suggested that vaccination of a patient was indicated before surgical operations for tubercle, since if the latter were undertaken when the patient was in the positive phase the danger of dissemination should be greatly diminished. The relation of the opsonic index to inherited predisposition to tubercle needed further investigation. He quoted a case of a patient with a bad family history of tubercle who was in robust health and lived in ideal surroundings; he had been operated on two years previously for tuberculous glands and there was no sign of recurrence or of disease elsewhere, yet his index was persistently 0·6. This seemed to show that a low index might show congenital predisposition to the disease as well as an actual infection.

Dr. Butler Harris emphasised the necessity for using extremely small doses of tuberculin; the system of progressively increasing the doses meant a long negative phase and deterioration in the clinical state. A dose of $\frac{1}{200}$ mgr. produced long negative phases, with the attendant lassitude and depression. He believed that doses of $\frac{1}{1000}$ mgr. produced more rapid progress, and to the patient appeared to act as a tonic. He insisted on the importance of the opsonic method in diagnosis, maintaining that it was applicable even in general practice. He referred to two young men in whom, without definite signs of tuberculous disease of the lung, there was ill-health with a variable or low opsonic index. Both these cases improved after

tuberculin injection. In another case the presence of a normal opsonic reaction had been of value as indicating that the case was not tuberculous, although the physical signs in the chest pointed to its being so. The case proved to be one of pneumococcus infection. With regard to Mr. Pardoe's paper, he considered his doses of tuberculin far too large. A case of tuberculosis of the bladder, in which the opsonic index was 0·3, made rapid improvement after injections of minimal doses of $\frac{1}{1000}$ to $\frac{1}{500}$ mgr. In a case of lupus, which had existed for fifty-one years, the opsonic reaction was at one time as high as 1·5, owing probably to auto-inoculations from an infected ankle-joint. By rest in bed this dropped to below normal when the tuberculin injections were begun, and the lupus nodules gradually cleared up. Other favourable cases were quoted.

Dr. A. E. WRIGHT, in reply, referred to the question of isolation of opsonins. It was a convenient phrase for a property of the serum, but it did not, he thought, represent bodies that could be isolated.

Dr. BULLOCH, in reply, alluded to the question of suitable and unsuitable cases; such a distinction was not possible. The chief point was that with small doses the most severe lesions might be treated with absolute safety as far as the patient's life was concerned.

Dr. LAWSON, in reply, said that, in regard to the indices of patients discharged from sanatoria, in many the index was below normal, and among these relapse had been met with in two cases, but in none of those with high index was relapse observed. The view that the resistance of the patient to the disease varied in direct arithmetical proportion to the opsonic index needed more evidence in its favour before acceptance. He considered that patients with a low opsonic index should not be discharged from sanatorium treatment until the index had been raised.

Mr. PARDOE, in reply, thought the method could not become one for general practice, as the technique was beyond the scope of most general practitioners. The results obtained by doses measured by opsonin indices reported during this discussion were, however, so remarkable that he, for his part, felt bound to revise his dosage by this method, and compare the results so obtained with the results he had placed before them that evening.

PRIMARY MALIGNANT DISEASE OF THE VERMIFORM APPENDIX

BY

H. D. ROLLESTON, M.D.,

PHYSICIAN TO ST. GEORGE'S HOSPITAL AND TO THE VICTORIA HOSPITAL FOR CHILDREN;

AND

LAWRENCE JONES, M.S.,

ASSISTANT SURGEON TO ST. GEORGE'S HOSPITAL.

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PRIMARY malignant disease of the vermiform appendix has long been recognized, but the earlier reports of its occurrence are not sufficiently conclusive to warrant their acceptance as genuine, either from a lack of any histological confirmation or from absence of anatomical proof that the growth in the appendix was not secondary.

In reviewing the literature we have considered all cases of primary malignant disease of the vermiform appendix, whether described as carcinoma, endothelioma, or sarcoma.

HISTORICAL.

The earliest report of a case was Merling's (1) in 1838, in which an appendix found at an autopsy was thickened

and firm, with several small, hard tumours in its walls and a perforation near the base. He concluded that it was affected with primary malignant disease; but since microscopical evidence was, of necessity, wanting the case must remain doubtful. Twenty-seven years later, in 1865, Prus (2) described an appendix almost identical with that found by Merling, with the addition of a soft, sessile, hæmorrhagic tumour about the perforation, but this case, again, cannot rank owing to absence of any histological examination. For the same reason the four cases published by Rokitansky (3) in 1867 as instances of primary carcinoma must be excluded. These four patients died from other causes, and at the autopsies the appendix, in every case, was transformed into a cyst-like swelling, with fibrous walls and gelatinous contents, traversed by a delicate fibrous network. These were assumed to be examples of a stenosing colloid carcinoma, but, as suggested by Elling (4) and others, their characters are quite compatible with the view that the condition was one of cystic dilatation or mucocele of the vermiform appendix. A similar reticulated condition of the walls was met with in an appendix described by Latham (5) in which there was no suspicion of new growth. An interesting feature of these four cases is that the ages of the patients averaged 65, an age, as will be seen, that is more than double the average in the accepted cases (*vide* p. 8). The next reputed instance of primary carcinoma is Kolaczek's (6) in 1875, in which an abscess was opened in the right iliac fossa and never healed. At the autopsy there was carcinoma of the cæcum communicating with the fistula; the base of the appendix opened at the site of the ulcerated cæcum. There is thus no reason for the assumption that the carcinoma was other than primary in the cæcum. Leichenstein (7) in 1876, among 154 cases of primary carcinoma of the intestine, excluding those of the rectum, mentioned three involving the vermiform appendix, but, as he states that it is "a collection of published cases together with the records of pathological institutes and hospitals,"

there is no proof that they are original, and, furthermore, no details are given of their microscopical appearances. In 1880 Bierhoff (8) reported a case of carcinoma of the uterus, ovary, and rectum, with metastases in the liver and spleen and also a small nodule of new growth in the wall of the appendix, obstructing its lumen and producing a distal mucoid dilatation. There is no reason for supposing the change in the vermiform appendix to be other than secondary.

Up to this time, then, no reliable proof had been forthcoming as to the existence of primary carcinoma of the vermiform appendix, but in 1882 Beger (9) brought forward the first incontestable example in a man aged 47 years, who for three and a half years had suffered from a fistula in the right iliac fossa, dating from an abscess in that situation. At an operation the fistula was found to lead directly into the appendix, which was infiltrated throughout by carcinoma, the growth projecting into the cavity of the cæcum but not actually involving its walls. The patient died thirty-six hours after the operation, and post mortem the retroperitoneal glands were found to have become implicated, but there was no suggestion that the growth was other than primary.

Maydl (10) in 1883 mentions, without giving details, 1 case among 20,480 autopsies at Vienna; this is the same case as those sometimes attributed to Nothnagel (11) and Ziemann (12); so that these three reputed instances should, therefore, only rank as one case.

In the next case, reported in 1884 (13) by Draper, the ileo-cæcal valve was constricted and the gut above distended with fæces, the cæcum was thickened and red, while the appendix at one point was dilated and its walls showed the appearances characteristic of colloid carcinoma. Though this is possibly a genuine example of the disease under consideration, the change noted at the ileo-cæcal valve might be the primary growth, and the starting-point is not sufficiently certain to warrant admission to the list of cases.

In 1893 Hastings Gilford (14) reported a case of sarcoma of the appendix, basing his diagnosis upon the microscopical changes present; these, however, so closely resemble those of inflammation as to make the real nature of the disease still in doubt. Until this time, then, out of 14 reputed cases, all, with the exception of Beger's, are of too doubtful a character to be accepted.

From the year 1895, the date of Glazebrook's report of a case of endothelial sarcoma (15), verified by the microscope, and of Lockwood and Kanthack's psammoma, which is not included, as no details appear to have been published (16), we have reference to 48 reported examples of primary malignant disease, 5 of which cannot, for various reasons, be accepted, and 2 of which are the same as Maydl's case, already mentioned above (Ziemann, Nothnagel).

In the following year, 1896, Stimson (17) operated upon a patient the subject of a primary malignant growth, and in 1897 4 cases were reported, 1 by Mossé and Daunic (18), 2 among the 12 examples of obliterating appendicitis described by Letulle and Weinberg (19), and 1 by Ruyter (20), which must be referred to in some detail. The patient was operated upon for recurrent appendicitis; there were many adhesions around the appendix, which contained a concretion and was surrounded by numerous abscesses. Recovery after a protracted convalescence finally appeared to be complete, but six years later, when the man died from other causes, a small cystic tumour was found in the stump of the appendix, and proved microscopically to be carcinomatous. If the appendix was completely removed at the operation, any subsequent growth should be regarded as cæcal rather than appendicular in origin. Of course, if part of the adherent appendix was left behind as a stump, the growth may have been primary there, but in the absence of any statement to this effect it is unsafe to include the case in our present list.

The first recorded case of round-celled sarcoma was Warren's (21), in 1898, in which year J. H. Wright (22)

reported an instance of carcinoma. Monks (23), in 1899, published an example of a carcinoma involving the cæcum, in the centre of which was a slough, thought to be the remains of the vermiform appendix. Elting states that this case has sometimes been regarded as a primary growth of the appendix; this is certainly an erroneous view, and does not appear to have been held by Monks.

From 1900 reports of primary malignant disease become much more frequent, and nearly all can be accepted without question. In this year 2 more examples were brought forward by Letulle and Weinberg (24), another by Rolleston (25), a fourth by Giscard (26), a fifth by Hurdon (27), and 4 by A. O. J. Kelly (28), 1 of Kelly's being an endothelioma. In 1900 alone 9 genuine examples of primary malignant disease of the appendix were recorded, or as many as the total number of accepted cases before this year.

In Whipham's (29) case, published in 1901, a small growth of spheroidal-celled carcinoma was found post mortem in the vermiform appendix. This case, however, is excluded by several authors on the ground that there were growths also in the glands, liver, and the left ovary, which last they regard as the primary seat of the disease. It is, however, accepted by Moschcowitz (30), who agrees with Whipham that the origin in the mucous coat of the appendix shows that the growth was primary there, a view which we also take (*vide* p. 12). In this year a case of carcinoma was reported by McBurney (31), who mentioned another case of Lartigan's (the pathological nature of both having been recognised by Hodenpyl), and a fourth case was put on record by Goffe (32).

Jessup (33) in 1902 recorded one, and Harte and Willson (34) two other cases of undoubted primary carcinoma.

In the 'Annals of Surgery' for 1903 there were articles by Elting (4) and by Moschowitz (30), who discussed the subject at far greater length than had been attempted hitherto, and added 3 fresh cases each. We are indebted to these authors for the details of several cases which are not available in the originals.

In St. Bartholomew's Hospital 'Reports' for 1903 (35) one case of columnar-celled carcinoma of the vermiform appendix is mentioned without much detail; in the same year Weir (36) and Norris (37) each furnished a case, and Paterson (38) reported another example of sarcoma.

In 1904 there were 2 more examples of carcinoma recorded by Burnam (39), and by Fiske-Jones and Simmonds (40).

In 1905 1 case of carcinoma was recorded by Battle (41), and 1 of endothelioma by Sargent (42); and in their work on diseases of the vermiform appendix, Kelly and Hurdon (43) bring forward 3 fresh cases of carcinoma, and mention one of sarcoma by Bernays. This last, however, was sufficiently extensive to involve the apex of the cæcum, necessitating removal of that viscus, so that a cæcal origin for the growth is not outside the range of possibility.

This brings the literature on the subject up to the present date, and it will be seen that, after critically reviewing the reports of all the published cases, the number of satisfactory instances dwindles considerably.

Altogether, including a fresh one of our own, which we are reporting by the kind permission of Mr. H. S. Pendlebury, under whose care it was, there are 62 cases, which have, from time to time, been taken to be examples of primary malignant disease of the vermiform appendix, but out of these it is hardly fair, in the absence of microscopical evidence, to accept those of Merling, Prus, Rokitansky, and Maydl, and, by subtracting these 7 cases, the number is reduced to 55. The exclusion of Leichenstein's 3 cases, and of those attributed to Nothnagel and Ziemann, brings the number down to 50. Further, the cases of Kolaczek, Bierhoff, Draper, and Monks were probably primary in the cæcum, and in two others—Ruyter's and Bernay's—the growth was so situated as to involve the apex of the cæcum and to make that viscus appear to be the probable origin of the disease. Gilford's case and that recorded by Kanthack and Lockwood are not included for

reasons already given. Thus the total number of cases of primary malignant disease of the vermiform appendix which are available for analysis is reduced to 42.

Of these, 37 have been recorded as instances of carcinoma in one form or another by the following authors: Beger 1, Stimson 1, Letulle and Weinberg 4, Rolleston 1, Giscard 1, A. O. J. Kelly 3, Hurdon 1, McBurney 1, Lartigan 1, Mossé and Daunic 1, Wright 1, Whipham 1, Goffe 1, Jessup 1, Harte and Willson 2, Elting 3, Moschcowitz 3, Walsham 1, Weir 1, Fiske-Jones and Simmonds 1, Battle 1, Kelly, H., and Hurdon 3, Burnam 1, Norris 1, Rolleston and Jones 1; 3 have been reported as endothelioma—Kelly, A. O. J. 1, Sargent 1, Glazebrook 1; and 2 as sarcoma—Warren 1, Paterson 1.

It is interesting to note that out of our list of 42 cases no less than 28 are reported by American authors; of the remainder 7 are English, 6 French, and 1 German.

In most of these the condition was found during operation, but 8 of the carcinomas were found either at autopsies or as the result of routine examination of the appendix afterwards, and 1 endothelial sarcoma was so discovered. Such were the cases of Whipham, Letulle, and Weinberg (Cases 5, 6, 9, *vide* list of cases, p. 20), Mossé, and Daunic, Elting (Case 28), Wright, Lartigan, and Glazebrook.

There are, therefore, 33 instances in which primary malignant disease was found in appendices removed during life, but the true nature of the disease was not suspected in any case before operation.

As to the frequency of malignant disease in this situation, that it is a rarity no one would venture to deny, but now with the routine microscopic examination of appendices in cases of supposed appendicitis the number of instances of the disease will, no doubt, continue to increase. The fact that its malignancy is so much less than that of most carcinomas suggests that it may often have been overlooked. And again, the growth, especially if superadded to an already existing stenosis, has frequently, as in the

cases of Letulle and Weinberg, been so small as only to be recognized by the microscope. Out of the available 42 cases, 41 have been placed on record during the past ten years, a striking proof of the value of a routine examination of all appendices removed during life, or found post mortem to present the slightest suspicious pathological change. At St. George's Hospital alone, 2 appendices during the last five years, which had been excised for supposed simple inflammation, presented this change, and another was found at an autopsy. For these reasons, and from the ability of some authors to report 2, 3, or even 4 examples occurring in their own experience, it is fair to conclude that the rarity of the condition, though undoubted, has been exaggerated.

Etiology.

The *age* is given in 36 cases out of the 42 cases of primary malignant disease; the youngest patients[1] were those of Sargent, and of Letulle and Weinberg (Case 10), aged 12, and there were others aged 14 and 15; at the other extreme was a man aged 81 (Elting, Case 28), and it is interesting to note that both in this and the next eldest (A. O. J. Kelly, Case 16, aged 63) the growth was columnar celled, an unusual type in the vermiform appendix (see histology, page 135).

The average age is found to be 30·6, 30·3, and 39 years in the carcinomas, endotheliomas, and sarcomas respectively, or, taking all three classes together 30·8. If the two oldest patients mentioned above are excluded, the average is reduced to 27·8 years.

It is interesting to compare the age-incidence of primary carcinoma in other parts of the intestine. In 41 cases of primary carcinoma of the duodenum the average age was 52 years (44); in 9 cases of primary carcinoma of the jejunum and ileum that we have collected it was 47·2 years, in 30

[1] In a paper recording three fresh cases Baldauf ('Albany Medical Annals,' December, 1905) describes primary carcinoma of the appendix in a girl aged 8 years.

cases of primary carcinoma of the cæcum 47·8 years, and in 100 cases of primary carcinoma of the remainder of the large intestine 49·34 years (45). It therefore appears that the average age-incidence of primary carcinoma of the vermiform appendix is seventeen years lower than in other parts of the intestine.

Further, the age-incidence varies in the different kinds of carcinoma of the vermiform appendix, being 52 years in the columnar-celled, 32 in the transitional forms, 24 in the spheroidal-celled, and 25·5 in those merely described as "carcinoma."

The early occurrence of carcinoma is well seen when the ages are arranged in decades, as in the subjoined table:

Years.	Carcinoma.	Sarcoma.	Endothelioma.
1—10	—	—	—
10—20	6	—	1
20—30	12	—	1
30—40	7	—	—
40—50	4	1	—
50—60	1	—	1
60—70	1	—	—
70—80	—	—	—
80—90	1	—	—

27 out of 36, or 75 per cent., occurring before 40.

Sex.—In the 36 cases in which the sex of the patient is mentioned the difference is not sufficiently marked in the two sexes to draw the conclusion that the disease is commoner among women, as it appeared to be at the time of Moschcowitz's paper in 1903; 16 have been found in men and 20 in women (both the sarcomas were in men); 2 endotheliomas were found in women and 1 in a man, and 18 out of 31 carcinomas were in women.

Associated Conditions.

Only an incomplete summary of the morbid conditions found in the appendix in the published cases of primary new growth is possible, as, in many cases, the observer's

attention has evidently been focussed on the existence of the growth to the exclusion of any other less striking or less important feature.

Acute inflammation was found in 13 cases.

Obliterating appendicitis was mentioned in 11, in 3 of which the growth was described as arising at the stricture, but it is possible that the stricture in some of the other 8 cases was due entirely to the growth, as it was stated to be in Giscard's case (26), in which there was pus in the distal portion of the appendix and an abscess in the right iliac fossa.

Catarrhal appendicitis (Norris), chronic appendicitis with ulceration (Walsham), and chronic inflammation (A. O. J. Kelly) are mentioned in 1 case each.

Adhesions were stated to be present in 15 cases.

In 2 cases, Beger and Elting (Case 30, *vide* List, p. 148), there was a fistula of three and a half years and six months duration respectively.

The growth may, as already pointed out, produce a stricture; further, by projecting into the lumen it may completely obliterate the lumen, even (as in Case 42) in microscopic sections.

A concretion was mentioned as being present in only three cases (Letulle and Weinberg [Case 10], Walsham, and Hurdon). This is a striking contrast to the frequent associations of calculi and primary carcinoma of the gall-bladder.

The average length of the normal appendix is about 8 or 9 cm. (Lockwood (46)). In the case of primary malignant disease the average length of the recorded cases was found to be 7·4 cm.

Secondary Growths.

In only 5 of the 42 cases, or 12 per cent., were secondary growths described as being present; in 3 cases (Fiske-Jones and Simmonds, Beger, and A. O. J. Kelly [Case 16]), the abdominal lymphatic glands were involved, in 2 cases (A. O. J. Kelly [Case 16] and Elting [Case 30]) there were

multiple growths on the peritoneum, and in Whipham's case there were growths in the liver and right ovary. In 2 out of the 5 cases the growth was a columnar-celled carcinoma (A. O. J. Kelly (Case 15) and Beger).

Whipham's case was the only one in which the metastatic growths were found at the autopsy; in the others the condition was seen during the course of operation.

The *situation of the growth* is given in 33 cases: The growth involved the whole length of the appendix in 4, it was situated at the tip in 7, near the tip in 9, in the middle in 4, at the middle and tip in 1, and near the base in 8.

Cases in which the growths involved the junction with the cæcum have not been included in our 42 cases, because, as already stated, it seemed necessary to avoid any possible inclusion of cases really primary in the cæcum. It is possible that some cases primary in the cæcal end of the appendix have thus been excluded. In the 33 cases here analysed at least 16, or 48 per cent., were growths localised in the distal third.

As already mentioned, the growths may occur at the site of stricture, and in Battle's case it occurred between two strictures.

The size of the growth varied from that of a pigeon's egg in Glazebrook's endothelial sarcoma to those of microscopical dimensions, as in Letulle and Weinberg's series. As a rule it was the size of a pea to that of a marble, nearly always white in appearance and firm in texture.

Microscopic Appearances.

Of the 42 cases of primary malignant disease of the vermiform appendix 37, or 88 per cent., were described as one form or another of carcinoma, 3 as endothelioma, and 2 as sarcoma.

From the tabular statement it is seen that of the 37 cases of primary carcinoma 17, or 45 per cent., appear from the descriptions given (*vide* Appendix, p. 144) to be polyhedral- or spheroidal-celled (1 being colloid), 6 cases as transitional

from the columnar-celled to the spheroidal-celled type, 6 columnar-celled carcinoma (1 being colloid), and that 8 cases are described merely as "carcinoma."

There are thus two distinct types of primary carcinoma of the vermiform appendix: (1) the columnar-celled, like that met with in the large intestine, and (2) the spheroidal-celled.

As already pointed out, the average age of the 5 cases of columnar-celled carcinoma of the vermiform appendix was 52 years, thus corresponding with the average age of primary carcinoma of other parts of the small and large intestines. The special character of spheroidal-celled carcinoma of the vermiform appendix is shown (*a*) by their benign nature (*vide* pp. 142, 143), (*b*) by the early age incidence, for the average age of the 14 available cases was only 24·2 years, the extremes being 37 and 12 years. Since the average age of the 6 of the 8 cases described merely as "carcinoma," in which the age is available, was 25·5 years, it is highly probable that many of them were examples of spheroidal-celled carcinoma. In this connection it is interesting to note that the average age of the 6 cases, showing a transition from columnar- to spheroidal-celled carcinoma was 32·7 years.

Some reference must be made to the histology of the spheroidal-celled type, as it differs so markedly from the columnar-celled carcinoma met with in the colon.

In Whipham's case, in which there were metastases causing death, the growth was an ordinary spheroidal-celled carcinoma of rapid growth arising in Lieberkühn's crypts. Our recent examination of the sections shows that the type of spheroidal-celled carcinoma is distinct from that about to be described; the cells of the growth are larger, and the alveoli do not show the vacuolation to be mentioned below. This is of significance in connection with the manifest malignancy of Whipham's case and the remarkable benignancy of the other type of spheroidal-celled carcinoma.

The following brief description applies to two specimens

(Cases 11 and 42) that we have examined at St. George's Hospital, and probably to many of the recorded spheroidal- or polyhedral-celled carcinomas.

The arrangement of the growth is alveolar, the cells occupying the alveoli are round and polyhedral, small, and somewhat resembling those of rodent ulcer. There is a scanty margin of clear protoplasm around the nuclei, which

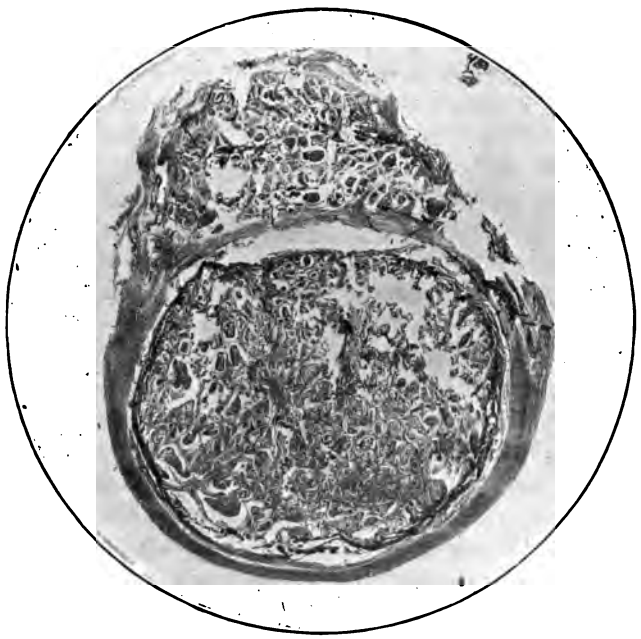

FIG. 1.—Section of primary spheroidal-celled carcinoma of the vermiform appendix (Case 42), showing growth filling up the lumen of the appendix and at one point infiltrating its wall. × 12. [Photomicrograph by Dr. H. R. Spitta.]

stain sharply and show nucleoli. The cells are in close contact and fill the alveoli, but in some alveoli there are one or more clear spaces, apparently due to degeneration of the surrounding cells. The spaces thus produced are more often empty, but may contain spindle-shaped cells like those forming the walls of the alveoli. This vacuolated appearence is a striking feature of the growth

(Fig. 1). The alveolar walls are delicate, and formed of spindle-shaped connective-tissue cells. It may be difficult to determine the starting-point of the tumour, but from an examination of sections from two cases at St. George's Hospital and one of Dr. Hurdon's (to whom we are much indebted for a slide sent by the courtesy of Dr. Bunting) we incline to the view that it is in the mucosa, which becomes replaced by spheroidal-celled growth, and from the cells of Lieberkühn's crypts.

These appearances resemble in a remarkable manner those in a group of cases, recently collected by Bunting (47), of multiple primary carcinomata of the jejunum or ileum (*vide* Fig. 2 of Plate). In addition to his own case Bunting gave the main points of five other examples (O. Lubarsch (48), 2, Notthaft, Walter, Oberndorfer), which all agreed in their structure and their benign character. Ransom (49) described and figured a case which had a similar structure, but differed from the others in the presence of numerous secondary growths in the liver.

In these multiple primary carcinomas of the small intestine a similar vacuolation of the alveoli, due to hyaline degeneration of the cells in the centre, was mentioned as giving the growth the appearance of a cylindroma, but as a connection could be traced between the epithelial cells of the mucosa and the growth (*vide* Lubarsch's Figs.) (48) in six out of seven cases they were regarded as carcinomatous; the remaining case (one of Oberndorfer's two cases) in which there was no manifest connection with the intestinal epithelium, was termed a "lymphatic endothelial carcinoma."

The histological nature of these multiple primary growths of the ileum and jejunum is evidently the same as in those spoken of as primary spheroidal-celled carcinoma of the vermiform appendix; further, the growths in both cases are nearly always benign, and in this respect, it is true, resemble some forms of endothelioma more than spheroidal-celled carcinoma.

Two closely allied forms of carcinoma of the skin, how-

ever, rodent ulcer and the basal-celled growths of Krompecher (50), of which fifteen cases of multiple growths of the scalp collected by Dubréuilh and Auchè (51) are examples, resemble the spheroidal-celled carcinomas of the small intestine and vermiform appendix both in structure and benignancy.

There is, however, an etiological difference between the multiple primary carcinoma of the ileum and the primary spheroidal-celled carcinoma of the appendix in the age-incidence, averaging 46·8 years in five of Bunting's cases, as compared with 24·2 years in the cases of primary spheroidal-celled carcinoma of the appendix.

The vacuolated appearance of the contents of the alveoli resembles that seen in some of the tumours regarded as endotheliomas, especially those of the parotid region and of the upper jaw. By the courtesy of Mr. Dudgeon we have had the opportunity of examining a section of the primary endothelioma removed by Mr. Sargent in which the appearances are so much like those just described as spheroidal-celled carcinoma that the difficult question of nomenclature arises, for it is obvious that what one observer terms endothelioma may be regarded by another as a carcinoma. Thus, from difficulty in determining the starting-point of what we have here spoken of as primary spheroidal-celled carcinoma, similar histological growths may in the future, as they have in at least one case in the past, be described as endothelioma. It would therefore be unsafe to insist on too sharp a distinction between the cases recorded as spheroidal-celled carcinoma of the vermiform appendix on the one hand and as endothelioma or sarcoma on the other hand.

Clinical Considerations.

From the cases available for analysis it would be useless to attempt to build up a clinical picture by which a diagnosis could be made; indeed, as has been already pointed out, the diagnosis has never been made before operation. This is hardly surprising, since the symptoms in nearly

every instance were those of appendicitis in one form or another.

The extension of the growth to the cæcum may mask its true origin if symptoms do not arise to call attention to it at an early stage. Kolaczek's case may have been of this nature; in one of Elting's cases (Case 30) the growth had spread, from its origin, far along the other viscera; the tumour was close to the cæcal apex in Fiske-Jones's and Simmonds's case, and in Bernay's case the fact of the cæcal apex being involved prevents its acceptance.

The past history of the patients.—In those cases in which the condition was found after death the growth was the cause of death in two only, namely in Wright's case from "peritonitis of obscure origin," and in Whipham's, which is remarkable in being the only one on record in which the growth proved directly fatal by its extension.

The reasons which led to the operation in the thirty-three patients from whom the appendix was removed during life were as follows:

Four of the operations, those of Hurdon, Jessup, Elting (Case 29, *vide* list), and Norris, were undertaken for the relief of symptoms referable to the female pelvic viscera, for retroversion of the uterus in Hurdon's case, and for salpingitis in the other three; in all these four the disease was wholly unsuspected before operation.

Beger's patient and one of Elting's (Case 30, *vide* list) underwent operation for the relief of a fistula dating from an iliac abscess that had refused to heal; in Elting's case this was thought to be due to tuberculous disease of the cæcum.

In the remaining twenty-seven the symptoms pointed to appendicitis in one form or another, and may be separated into four groups:

(*a*) Symptoms of the first acute attack, 10 cases.

(*b*) Chronic symptoms with an acute attack, 3 cases.

(*c*) Recurrent attacks, 9 cases.

(*d*) Chronic appendicitis, 5 cases.

In some, then, the condition appeared to be acute and of

short standing, while in others the symptoms had extended over many years, in one case twelve years.

Can these extremes be reconciled with the view that the growth is directly or indirectly the cause of the symptoms? Or must it be assumed that the growth is a mere accidental occurrence or the result of the real cause of the symptoms?

In the more acute cases it is easier to admit the possibility that the growth is the actual cause of the inflammatory trouble, for it may ulcerate and allow of infection of the walls of the appendix, it may block the lumen, or it may interfere with the nutrition of the tissues by compressing the blood-vessels.

In those cases, again, with long-standing symptoms, the obvious objection that the growth, if the primary cause, would long since have formed metastases, or have spread locally and caused the death of the patient, can be met in part by the fact that these tumours do not tend to form metastases.

On the other hand, Letulle and Weinberg and other authors have laid especial stress on the probability that chronic inflammatory change is the precursor of malignancy, just as carcinoma of the breast and stomach may be preceded by mastitis and gastric ulcer.

The growth, it appears, may be either the cause or the effect of the changes producing the symptoms, and may give rise to the symptoms of appendicitis; it is probably the cause in those cases with an apparently acute onset, or in which, the symptoms having been chronic, the growth is the main feature of the appendix.

It is probably the outcome of chronic irritation in those cases of obliterating appendicitis in which the growth is only recognised by the microscope.

The actual changes found to exist with the growth when a further examination is made have been dealt with under the Associated Conditions (*vide* p. 133).

The extent of the operation called for by the diseased appendix but rarely exceeded the simple removal of the appendix.

In three of the operations a portion of the cæcum surrounding the base of the appendix was excised with the latter organ (Fiske-Jones and Simmonds, Paterson, Kelly and Hurdon, Case 39). In one case (Fiske-Jones and Simmonds) it was necessary to remove some glands in the mesentery.

Beger operated for the relief of a persistent iliac fistula. Elting, operating for a similar condition, was forced to remove the cæcum and part of the colon and ileum owing to the wide spread of the disease (Case 30), and the sarcoma in Warren's case was so extensive as to require a similar operation.

The results, immediate and remote, of the operation, have been surprisingly good.

There were four deaths within two weeks of the operation. Beger's patient, who had had a fistula in the iliac region for three and a half years, did not survive the attempt to remove the condition.

One case of Elting (Case 30), also with a fistula, in whom the operation consisted in the removal of a large amount of intestine, died two weeks later; one case (A. O. J. Kelly [Case 16, *vide* p. 145]), a man of 63, in whom the growth had formed secondary metastases, also died; and the fourth patient was Paterson's, in whom it was necessary to remove part of the cæcum.

In the majority of the other cases recovery is definitely stated to have occurred.

The presence of the growth, unless it is so advanced as to require removal of some additional portion of the intestinal tract, seems not to increase the risk of the operation of appendicectomy. Of the twenty-nine patients who made recoveries, one died four months later (Harte and Wilson, Case 24) after an operation to relieve obstruction caused by a band in the right iliac fossa, but post mortem there was no recurrence.

None of the other patients—and some have been heard of years after the operation—can be found to present any suggestion of recurrence.

A case recorded by one of us (24) was at the time of the original report suffering from symptoms compatible with the view that a recurrence had occurred, and is mentioned by Howard Kelly and Hurdon in their monograph on 'Diseases of the Vermiform Appendix' as the only case in which recurrence was thought to have occurred. We are indebted to Mr. H. M. Ramsay for the information that she was in perfect health in July, 1905.

This is striking evidence of the slight malignancy of these growths compared with those in nearly all the other parts of the alimentary canal.

Conclusions.

(1) The disease is one which renders an accurate diagnosis impossible; every case in which the symptoms drew attention to this region exactly imitated appendicitis in some form.

(2) Most of the older reputed examples fail to withstand investigation; but as 80·9 per cent. of the 42 genuine examples have been reported since 1900, the disease cannot be quite so rare as has been thought. The microscopic size of the growth in some cases makes it probable that many such instances have been overlooked.

(3) Pathologically, several varieties of carcinoma have been reported, and also sarcoma and endothelioma. The growth is usually, however, a spheroidal-celled carcinoma which is peculiar in the early age-incidence, the slight malignancy, and the resemblance to endothelioma. Colloid change is not common, as has been hitherto supposed.

(4) The presence of concretions is only mentioned in 3 cases out of 42.

(5) The disease is not prone to affect one sex more than the other.

(6) Inflammatory changes, either chronic or acute, very frequently accompany the growth.

(7) The immediate prognosis and the prospect of freedom from subsequent recurrence after operation are very good, particularly in the spheroidal-celled carcinomas.

APPENDIX.

Forty-two Cases of Primary Malignant Disease of the Vermiform Appendix.

1882: (1) BEGER ('Berlin. klin. Wochens.,' 1882, xix, 616).—Male, aged 47, three and a half years before developed an abscess in right iliac fossa; incision; pus evacuated; wound refused to heal. Operation: fistula found to lead direct into appendix which was infiltrated throughout by carcinoma. Death soon after. Post mortem: Glands found affected; no other growth.

1895: (2) GLAZEBROOK ('Virgin. med. Monthly,' vol. xxii, p. 221. Quoted by Elting).—Male, aged 55, died of cerebral hæmorrhage; growth, the size of a pigeon's egg, found at post-mortem in appendix; many adhesions; appendix normal for proximal three inches; tumour hard and fibrous; walls of viscus infiltrated with nests of irregularly cuboidal and cylindrical cells, reported as endothelial sarcoma.

1896: (3) STIMSON ('Annals of Surgery,' vol. xxiii, p. 186).—Female, aged 44. Acute appendicitis ten years before, another attack one month before, a severe attack in which operation was performed; appendix 4 inches long and 1 inch thick, much thickened mucosa (projecting as a ring). Carcinoma.

1897: (4) MOSSE ET DAUNIC ('Bull. Soc. Anat.,' Paris, 1897, p. 814).—Female, aged 50. Found at post-mortem; death from heart disease. Diffuse growth; appendix 4 cm. long, 1·5 cm. thick; in parts growth was of cylindrical cells, while in parts it presented more of an alveolar arrangement. Lumen almost obliterated.

(5, 6) LETULLE ET WEINBERG ('Bull. Soc. Anat.,' Paris, 1897, p. 747).—Mentioned in a report on 12 cases of obliterating appendicitis, among which 2 cases had developed carcinoma at the site of stricture.

1898: (7) WARREN ('Boston Med. and Surg. Journ.,' vol. cxxxviii, p. 177, 1898).—Young male. Symptoms of chronic appendicitis for one month, recently with a definite swell-

ing. Operation: Appendix the site of round-celled sarcoma, spreading to mesentery; removal of cæcum; anastomosis by Murphy's button.

(8) WRIGHT, J. H. ('Boston Med. and Surg. Journ.,' vol. cxxxviii, p. 150, 1898).—Found at post-mortem of a case of general purulent appendicitis of obscure origin, slight adhesions around, but no actual perforation. There was a small primary adeno-carcinoma at the tip.

1900: (9) LETULLE ET WEINBERG ('Bull. Soc. Anat.,' Paris, 1900, p. 374).—Found post-mortem. Appendix hard and obliterated in its lower quarter, end of appendix practically a mass of carcinoma, with very small cells.

(10) IBID.—Child, aged 12. Acute appendicitis, August, 1897, leaving some tenderness in right iliac fossa; another attack in January, 1898, with a definite cæcal mass; recovery in ten days, leaving appendix thick and palpable; another slight attack on March 1st. Operation March 28th. Appendix 4 cm. long, adherent, containing pus and a concretion; definite stenosis, found to be carcinomatous with very small cells, infiltrating meso-appendix; tip, beyond, dilated, showing ulceration and chronic changes.

1900: (11) ROLLESTON ('Lancet,' 1900, vol. ii, p. 11).—Woman, aged 26. Fourth attack of appendicitis, formal amputation on day after admission, adhesions, no glands. Caseous-looking swelling, about the size of a marble, found to be spheroidal-celled carcinoma. Alive and well July, 1905.

(12) GISCARD ('Toulouse Imp. St. Cyprien,' 1900, 360, p. 51. Quoted by Elting).—Male, aged 37. First attack mild, two and a half years before, second attack severe, abscess opened in right iliac fossa, appendix found obstructed about centre by what appeared to be a cicatrix, found to be new growth between mucosa and muscle; superficially adeno-carcinoma; deeper, an alveolar arrangement.

(13) KELLY, A. O. J. ('Proc. Path. Soc. Philadelphia,' 1900, p. 109).—Full details not known. A case of acute gangrenous appendicitis. At distal end polyhedral-celled carcinoma.

(14) IBID.—Woman, aged 24. Attack of diffuse abdominal pain, with vomiting, one year ago; since then three other attacks; last attack three weeks before, when pain became localized to right iliac fossa. Appendix easily felt and found free from adhesions; 9 cm. long, 5 cm. thick; ordinary changes of appendicitis, and also endothelioma near base.

(15) IBID.—Male, aged 19. Eight days before operation all signs of ordinary acute appendicitis, with definite swelling. Small localized abscess found. Appendix 5 cm. long and 1 cm. thick. Chronic changes and small carcinoma near base.

(16) IBID.—Male, aged 63. Recently many attacks of acute pain and vomiting; signs of appendicitis. Appendix very adherent; numerous small "tubercles" on peritoneum and intestine. Glands enlarged. Death. Appendix 2 cm. long, 1·2 cm. thick. Firm and nodular, infiltrated throughout by growth of cylindrical and polyhedral cells; lumen obliterated in distal third.

(17) HURDON ('Johns Hopkins Hosp. Bull.,' vol. xi, p. 175).—Woman, aged 24. Symptoms of uterine trouble from birth of child eight years before. Pain and vomiting for eight months, ascribed to movable kidney. Operation on uterine condition; retroflexion found; also appendix adherent and kinked, distended at tip by concretion; also an oval tumour 10 by 5 mm., proving to be adeno-carcinoma, involving all the coats.

1901: (18) WHIPHAM, T. R. ('Lancet,' 1901, vol. i, p. 320).—Woman, aged 45. History of loss of flesh for six weeks and a swelling for fourteen days; thought to be malignant and inoperable. Post mortem, spheroidal-celled carcinoma at base of appendix, with secondary growths in liver, glands, and ovary.

(19) MCBURNEY ('Med. Record,' N.Y., vol. lx, p. 478).—Female, aged 23. Clear attack of appendicitis two years before, leaving some pain in right iliac fossa. Symptoms more severe for two months. Appendix 4 in. long, not adherent. Two strictures, and near the tip a small, white,

firm tumour, the size of a pea. Microscopically, carcinoma.

(20) LARTIGAN.—Male, aged 30. Mentioned without details by McBurney.

(21) GOFFE ('Med. Record,' N. Y., vol. lx, p. 14).—Female, aged 15. For more than a year steadily increasing pain in right iliac fossa. Diagnosis of chronic appendicitis. Appendix unusually long, thick, and tortuous; smooth, round, white body, the size of a pea, in extreme tip; on section, like fibrous tissue; by microscope, typical carcinoma.

1902: (22) JESSUP ('Med. Record,' N. Y., vol. lxii, p. 289).—Woman, aged 36. History of pain in right iliac region since an abortion. Operation on uterine appendages. Appendix found firmly bound down by adhesions; bent at an angle, and beyond this a dilatation occupied by a firm, white tumour; adeno-carcinoma, polygonal, and cylindrical cells, with alveolar arrangement.

(23) HARTE and WILLSON ('Trans. Amer. Med. Assoc.', vol. xx, p. 228).—Female, aged 24. Five years ago, supposed acute appendicitis; one year ago a recurrence, one month ago another attack, with formation of a lump; appendicectomy; organ 15 cm. long, no adhesions, constriction, or obvious growth. Most of lumen obliterated, central part necrotic, and small area of spheroidal-celled carcinoma.

(24) IBID.—Male, aged 25. Eight months before pain in right iliac fossa, when seen an acute appendicitis diagnosed; appendix found perforated, showing cubical-celled carcinoma beginning near tip; four months later admitted with obstruction by fibrous band near cæcum. Operation; death; post mortem, no recurrence of growth.

1903: (25) MOSCHCOWITZ ('Annals of Surgery,' vol. xxxvii, p. 891, 1903).—Male, aged 37. Symptoms supposed to be due to gastritis for eight months. For one day symptoms of acute appendicitis, with a mass in right iliac fossa. Operation, an abscess, appendix adherent; spheroidal-celled carcinoma near base, and acute changes.

(26) IBID.—Female, aged 20. Onset of pain in right iliac fossa ten days before without vomiting or fever; tenderness in right iliac fossa, no swelling; appendix removed, found adherent, with signs of acute inflammation and spheroidal-celled carcinoma beginning near tip.

(27) IBID.—Female, aged 24. Five days before being seen pain in hypogastrium, rigor; temperature 105°. No definite symptoms, but after two days condition so bad that abdomen was opened and appendix found three inches long with a thickened, obliterated, distal portion, which proved to be the site of a carcinoma of transitional type.

(28) ELTING ('Annals of Surgery,' vol. xxxvii, p. 549, 1903).—Male, aged 81. Found post mortem; death from cardiac disease; appendix 5½ cm. long, proximal 2 cm. normal. Distal, 3½ cm., swollen and filled with gelatinous contents, which in one place had fungated through the coats. Colloid carcinoma.

(29) IBID.—Female, aged 36. Attack of pelvic peritonitis eight years before. Recently return of symptoms, double salpingo-oöphorectomy performed and appendix also removed. Appendix 4 cm. long, about 1 cm. from distal end, a slight bulging, obliterating the lumen; author finds it difficult to say whether growth was an alveolar spheroidal-celled carcinoma or an endothelioma.

(30) IBID.—Male, aged 19. An attack of acute appendicitis, abscess opened and drained; six months later sinus had not healed but discharge was not fæcal. Diagnosed as tubercle of the cæcum. At operation mass in right iliac fossa, found to be new growth, involving appendix, cæcum, ileum, and colon—considered primary in appendix; spheroidal cells.

(31) WALSHAM, W. J. ('St. Bart's. Hosp. Reports,' vol. xxxix, Surgical Registrar's Report).—Male, aged 45. Several attacks of appendicitis; appendix thickened and ulcerated; microscopically columnar-celled carcinoma with alveolar arrangement. Concretion present.

(32) WEIR ('Med. Record,' N. Y., 1903).—Male, aged 23. Thirteen apparent attacks of appendicitis in two years.

Nothing felt *per abdomen*. Operation; clubbed, thickened appendix which showed the usual inflammatory changes and an adeno-carcinoma at the tip.

(33) NORRIS ('Univ. Penn. Med. Bull.,' 1903, p. 334).—Female, aged 27. Operation on right Fallopian tube for symptoms of two years' standing. Appendix found, thickened and inflamed, 7·5 cm. long, adhesions present; for 1·5 c.m. from the tip the lumen was occluded by friable mass of growth; "although the nests are almost solid plugs, yet vacant areas occur around which the cells are arranged with some regularity."

(34) PATERSON, P. ('Practitioner,' 1903, vol. lxx, p. 515. Male, aged 39. Uneasiness in right iliac fossa for three months; four attacks of definite pain; when seen, symptoms of subacute appendicitis. Thickened, firm, adherent appendix removed with portion of cæcum. Death. Post mortem, no trace of sarcoma elsewhere. Appendix 16·5 cm. long, 10 cm. round; very thick walls; much ulceration; round-celled sarcoma, infiltrating all coats except peritoneal.

1904: (35) FISKE-JONES and SIMMONDS ('Boston Med. and Surg. Journ.,' vol. cli, p. 566, 1904).—Female, aged 26. Four attacks of "colic," first attack twelve years ago, the last three months before. No swelling felt. At operation thickened area at base, through which appendix was ligated; area found to be spheroidal-celled carcinoma; second operation to remove stump and portion of cæcum.

(36) BURNAM ('Johns Hopkins Hosp. Bull.,' vol. xv, p. 136, 1904).—Male, aged 25. Recurrent attacks of pain in right iliac fossa; one attack subsiding at time of operation. Appendix found adherent, 6 cm. long, 75 cm. thick at base; cæcal end normal, outer two-thirds inflamed; at the tip a yellow core of growth, filling up lumen and replacing mucosa and sub-mucosa, cells arranged in small alveoli. Adeno-carcinoma.

1905: (37) BATTLE ('Lancet,' 1905, vol. i, p. 291).—Female, aged 14. Symptoms of appendicitis on four occasions; some fulness in right iliac fossa; nothing else

abnormal. Appendix 2 inches long; fibrinous exudate; congested thick walls, two constrictions, between which a marble-like structure, proved to be spheroidal-celled carcinoma.

(38) SARGENT ('Lancet,' 1905, vol. ii, p. 889).—Female, aged 12. First attack; three weeks' history; small mass to be felt. Appendix 3 inches long, acutely inflamed, deeply ulcerated but not perforated; obstruction ½ inch from cæcum by small mass, size of a pea. Reported as endothelioma.

(39) H. KELLY and HURDON ('Diseases of the Vermiform Appendix,' 1905).—Female, aged 30. Recurrent appendicitis for seven years; pain becoming severe; operation in quiescent period. Appendix much thickened, distal portion cystic, base being indurated, removed with V-shaped portion of cæcum. Examination showed case to be affected with columnar-celled carcinoma with alveolar arrangement.

(40) IBID.—Woman, aged 24. Two days' history of pain without other symptoms; previous history of indigestion. Appendix found adherent, with a bulbous tip; small nodule near tip, 6 inches in diameter. "Carcinoma."

(41) IBID.—Male, aged 19. Recurrent attacks of cramp, but no definite attack of appendicitis until ten days before admission, when mass was felt in right iliac fossa. Appendix densely adherent, with small abscess, 8 cm. long, central 2 cm., thick and dense. Microscopically small alveoli packed with cells.

(42) ROLLESTON AND JONES.—Female, aged 31. Six days' history of abdominal pain, with vomiting and distension. No previous attack. Cæcum found much distended; clear fluid in pelvis; appendix slightly swollen at tip, not adherent; at the tip a small, white, firm mass, proved to be spheroidal-celled carcinoma (case not previously reported).

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To Dr. Harold Spitta our sincere thanks are due for the photomicrographs illustrating this paper.

DISCUSSION

Mr. W. McAdam Eccles reported the following Case of Primary Carcinoma of the Vermiform Appendix:

I was asked on May 17th, 1904, by Dr. S. Verdon-Roe, to see a young gentleman, aged eighteen, with the following history:

He had had one or two slight attacks of pain in the right iliac fossa during 1903, but was never confined to bed or even to the house by them.

On April 6th, 1904, a more pronounced attack of pain supervened, and there was much tenderness in the appendix region. He was seen by Dr. Verdon-Roe, who found the temperature raised to 100° F., and a definite swelling in the right iliac fossa. He was kept in bed for fourteen days, then allowed up, and shortly afterwards went to Hastings.

A second sharp attack of pain occurred on May 12th, 1904. Again the temperature was somewhat above the normal, and there was distinct induration in the right iliac fossa. He remained in bed, and no evidence of suppuration appeared, though the swelling persisted.

When seen on May 17th, his temperature and pulse were normal; all the pain had gone, but there was marked tenderness in the right iliac fossa, and an easily palpable, hard, resistant mass was present.

As no symptoms indicating the necessity for an immediate operation existed, it was agreed to defer laparotomy until May 25th, 1904. On that day a "split-muscle" opening was made over the mass, exposing the cæcum fixed by adhesions in the fossa, and behind it a hard mass which was clearly a diseased appendix.

With some difficulty this was separated from the adhesions around and found to be an appendix one and three quarter inches long, pointing upwards and outwards behind the cæcum. It was greatly thickened, having an external circumference of two and a quarter inches.

One or two lymphatic glands were removed from the base of the appendicular mesentery, but unfortunately these were not preserved for examination.

The wound was closed in the usual manner, and the patient made an uninterrupted recovery. When seen on February 19th, 1906, he was perfectly free from any recurrence and quite well in health.

When the appendix was cut through longitudinally there were two whitish patches in its walls, one at a spot about one

third its length from its cæcal attachment, and the other a little more distal. These two patches were absolutely distinct from one another. They were taken to be probably of the nature of tuberculous deposits. There were no concretions within the lumen of the appendix. On microscopical examination, however, both the deposits proved to be spheroidal-celled carcinoma.

This case is another example of an undoubted carcinoma of the appendix, primary in origin, and occuring in a male of only eighteen years of age. It is also of interest in that two separate foci of carcinoma existed. It was impossible to diagnose their existence before operation, the signs and symptoms being only those of a chronic appendicitis.

It is satisfactory to note that the patient is in perfect health now, twenty-one months after the removal of the diseased organ.

The PRESIDENT said that the cases were etiologically interesting, especially with regard to the question whether the cancer was primary or secondary to inflammatory changes. The duration was remarkable. The diagnosis was, apparently, of academic interest only, since the treatment by removal was uniform with that of simpler inflammatory varieties of the disease with which it was usually confused, and, so far as experience as yet went, with equally good results. Subsequent histories of these cases would, however, be of interest to the Society, and he hoped that the authors would supply them.

Mr. T. JEFFERSON FAULDER quoted the case of a patient who had three attacks of apparent appendicitis. In 1902 the appendix was removed, and was found to be infiltrated with columnar-celled carcinoma undergoing spheroidal-celled transformation. The appendix contained some concretions. The patient made a good recovery, and was now, four years after the operation, in good health. Columnar-celled carcinoma undergoing spheroidal-celled transformation was, when it occurred elsewhere in the intestinal tract, regarded as actively malignant, whereas when in the appendix the growth did not seem to possess any great malignancy. He suggested that all such growths should be regarded as endothelioma.

Dr. NEWTON PITT said that another class of malignant growths, namely lymphadenomata, might start in the appendix. It was a point of interest whether there was any evidence of local infection when there were multiple nodules in the appendix, and whether the growths were opposite or close to one another. He remarked on the small size of the cells in these appendix tumours which thus markedly differ from those in the stomach. Were the central spaces empty alveoli with fibrous-tissue walls, or were they the result of central degeneration in the masses of cells?

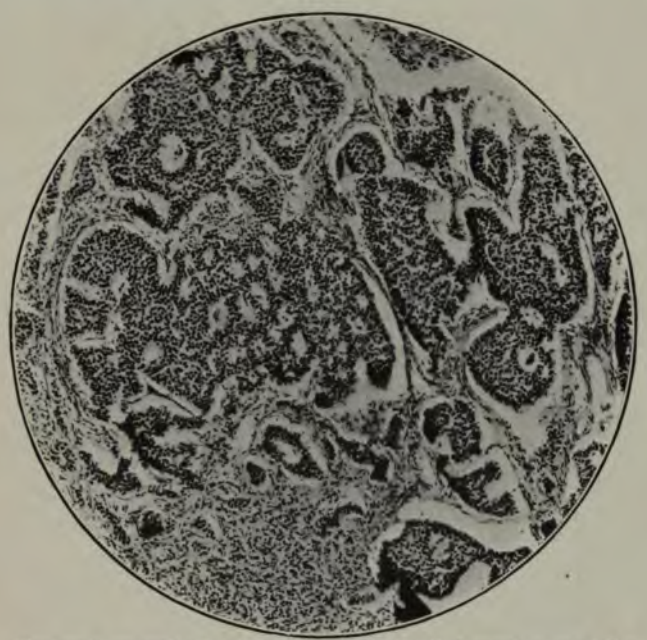
Dr. HERBERT FRENCH remarked on the small size of the growths. It would have been anticipated that so cellular a

tumour would have grown to a large size if carcinomatous. How could inflamed lymphatic tissue be differentiated from the growths? What were the microscopic characters of the tumours from which there were metastases as compared with those from which there were none?

Dr. ROLLESTON, in reply, said that he had been much interested in Mr. Eccles' case, and that it was interesting to note that the white appearance of the growth had suggested caseous tubercle, both in Mr. Eccles' case and in that reported by himself in the 'Lancet' in 1901. Mr. Eccles' case was also remarkable in the presence of two distinct growths, and these resembled Bunting's primary multiple carcinomata of the ileum. The question of the nomenclature of these tumours had been discussed in the paper, and the reasons why the tumours were regarded as belonging to the group of the carcinoma rather than to that of endothelioma had been stated. The tendency to apply the term "endothelioma" to any tumour merely because the appearances presented were anomalous was undesirable. In reply to Dr. French's question whether there was any known example of such a richly cellular tumour with slow growth and low malignancy, it was only necessary to point to rodent ulcer. The suggestion made that the appearances were due to inflammation of lymphoid tissue was not compatible with the histological appearances, which were also quite unlike those of lymphadenoma. The spindle-cells inside some of the vacuoles he regarded as portions of the alveolar walls cut transversely. The multiplicity of the growths in Bunting's case of multiple primary carcinomata of the ileum and jejunum could not be explained by supposing that local infection had taken place from a single primary growth.

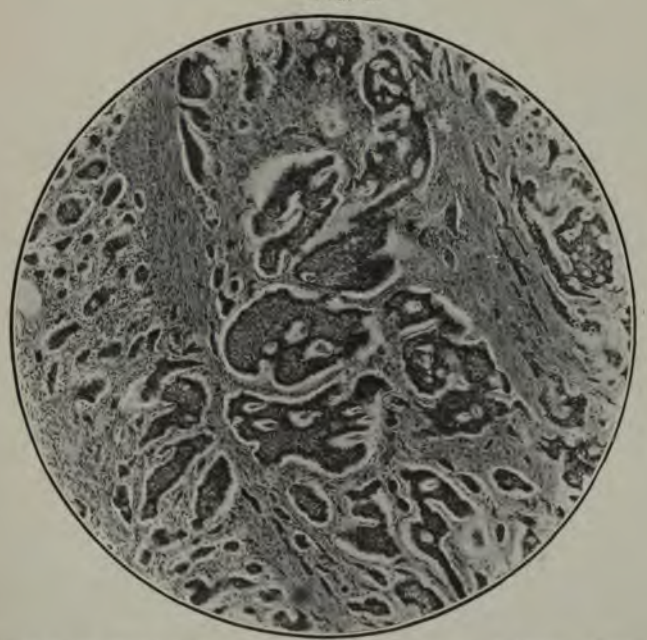
Mr. ECCLES added that there was nothing in his case to suggest infection from one focus to the other by contact. The nodules were separate and quite distinct; they were on the same side of the appendix, and one was considerably below the other.

FIG. 1.



Photomicrograph of primary spheroidal-celled carcinoma of the vermiform appendix, showing vacuolation (Case xi). × 175. (Photomicrograph by Dr. H. Spitta.)

FIG. 2.



Photomicrograph of multiple primary carcinoma of ileum, showing vacuolation (C. H. Bunting, 'Johns Hopkins Hospital Bull.,' vol. xv, p. 389, *1904*), from section kindly provided by Dr. *Bunting.* × *170.* (Photomicrograph by Dr. H. Spitta.)

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REPORT ON THE SECTIONS SUBMITTED

FROM THE TWO CASES (NOS. 11 AND 42) RECORDED BY DR. ROLLESTON AND MR. LAWRENCE JONES, AND FROM THE CASE RECORDED BY MR. ECCLES, TOGETHER WITH THOSE RECEIVED BY DR. ROLLESTON FROM DR. HURDON AND DR. BUNTING, AND COMPLETE SECTIONS THROUGH THE ENTIRE APPENDIX, FROM CÆCUM TO APEX, FROM A SIMILAR CASE OF NEW GROWTH OF THAT ORGAN REMOVED AT ST. BARTHOLOMEW'S HOSPITAL SINCE DR. ROLLESTON AND MR. LAWRENCE JONES' PAPER WAS READ

BY

F. W. ANDREWES, M.D.

AND

ALEXANDER G. R. FOULERTON, F.R.C.S.

In all these cases the new growth appears to us to be of almost precisely similar character, and we confirm the histological description of their sections given by Dr. Rolleston and Mr. Jones in their paper. We have no doubt but that in each case there has been a new growth arising in the appendix, and we agree that the essential cells constituting this new growth are generally spheroidal or polygonal in form, and that they are contained within the alveoli of a fibrous reticulum. In places, however, where the cells are arranged at the margin of the cell-masses, they are of cubical or columnar form.

In transverse sections of the new growth in several of the cases there is an appearance of vacuolation, possibly tubular, occurring in the cell-masses. In some of the cases the cells of the new growth appear to have extended along clefts, probably lymphatic, in the wall of the appen-

dix. But where this has occurred it does not appear to us that the cells have actually destroyed the muscular tissue of the wall which apparently bounds these clefts.

Although, at first sight, the general histological appearances are in accord with those which are generally considered to be characteristic of carcinoma, and in spite of the apparent penetration of the cells into the lymphatic clefts, we are unable to concur with Dr. Rolleston and Mr. Jones and Mr. Eccles in describing these cases as cases of malignant disease or carcinoma of the appendix.

The term carcinoma connotes something more than histological structure, and the complete data as to age-incidence, benignant course, and favourable prognosis which are furnished by Dr. Rolleston and Mr. Jones in their paper, together with the absence of satisfactory evidence that the new growth in those cases in which it undoubtedly originated in the appendix manifested the essential qualities of malignant disease—that is to say, progressive invasion of contiguous parts, or dissemination in remote parts—appear to us to prevent the application of the term carcinoma.

From the 42 cases of alleged primary malignant disease of the appendix which Dr. Rolleston and Mr. Jones have collected we would at once exclude 3 (Nos. 18, 30, and 35) as irrelevant, since there would seem to be no evidence that in these cases the new growth originated in the appendix rather than in the cæcum.

Out of the remaining 39 cases there are 2 (Nos. 14 and 38) which are described as endotheliomata, 2 (Nos. 7 and 34) described as sarcomata, and 1 (No. 2) described as an endothelial sarcoma, but in none of these was there any evidence of malignancy beyond that derived from histological examination.

There remain 34 cases of alleged carcinoma to be considered, in all of which the new growth apparently originated in the appendix; and amongst these 34 there are only 3 (Nos. 1, 16, and 28) in which what we take to be the criteria of malignancy are not absent. In one of Elting's cases (No. 28) the appendix was "swollen and

filled with gelatinous contents, which, in one place, had fungated through the coats: colloid carcinoma." In Beger's case (No. 1), in which there had been suppuration about the right iliac fossa for three and a half years, the appendix was found to be "infiltrated throughout by carcinoma," and some glands were found to be "affected," and in one of Kelly's cases (No. 16) the appendix was found to be "firm and nodular, infiltrated throughout by growth of cylindrical, columnar, and polyhedral cells," and there were numerous small "tubercles" on the peritoneum and intestine.

And not only has the ordinary anatomical evidence of malignancy been absent in most of the cases, but, as a rule, there has been a limitation of the extent of the growth in the appendix itself which we should not expect, under the given circumstances, in a series of cases of carcinoma. In practically all the cases the new growth was discovered accidentally, either in the course of an operation for the relief of what was supposed to be appendicitis, or during an examination after death from some cause other than the new growth found. It may reasonably be assumed, therefore, that in some of the cases the new growth had existed for a considerable length of time. But Dr. Rolleston and Mr. Jones write with regard to the entire series of 42 cases, "the size of the growth varied from that of a pigeon's egg in Glazebrook's endothelial sarcoma to those of microscopical dimensions, as in Letulle and Weinberg's series. As a rule it was the size of a pea to that of a marble."

Our doubts as to the generally malignant character of the alleged cases of carcinoma are increased when we consider the age-incidence of the disease. The age is given in 29 out of the 34 cases described as carcinoma, and in 16, or 55 per cent., the disease occurred at ages under thirty years. If we exclude the 3 cases (Nos. 1, 16, and 28) in which there were indications of malignancy other than those founded on histological examination, we have a series of 26 cases, in which the disease occurred at ages under thirty years in 16, or in 61 per cent.

Searching for growths of similar histological character in other regions of the body we have been struck by the close resemblance of the growths under consideration to certain tumours of the parotid gland—a resemblance so close as to amount, in some cases, to complete identity. The parotid tumours to which we refer are those commonly described as simple adenomata of the gland, in which the cartilaginous and myxomatous elements of the ordinary "mixed" parotid tumour are absent, in which the new growth consists entirely of cellular elements arranged in alveolar fashion and commonly presents areas of vacuolation quite similar to those seen in the new growths of the appendix which are under discussion.

We do not feel called upon to discuss here the vexed question as to the exact origin of these parotid tumours, whether they arise from the epithelium of the gland or whether they are of endothelial origin; we need only remark that their habitual encapsulation and their generally benign course stamp them, by common consent, as of a non-cancerous nature. But, exceptionally, a new growth of the parotid of the histological character described will show characteristics of malignancy, and the same is true of somewhat similar growths originating in the palate.

And we consider that the same rule applies to these histologically similar new growths of the appendix. Generally the new growth is of an innocent nature; occasionally, no doubt, a malignant new growth originating in the cells from which the innocent growth occurs may be met with. But since definite evidence of malignant character is wanting in all but three of the cases of alleged primary carcinoma of the appendix, which are quoted by Dr. Rolleston and Mr. Jones in their paper, we are unable to accept the conclusions of the writers as to the comparative frequency of carcinoma of the appendix, whilst we are in agreement with them entirely as to the essential histological structure of the growths which have been submitted to us.

July 16th, 1906.

"INTERRUPTED CIRCULATION" AS A THERAPEUTIC AGENT

WITH ILLUSTRATIVE CASES OF RHEUMATOID ARTHRITIS

BY

WILLIAM EWART, M.D., F.R.C.P.

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WHEN, as in the surgical use of the tourniquet, the arterial inflow and the venous outflow are suddenly checked in a limb by the application of a sufficient constriction near its attachment, the intimate circulation within the limb is profoundly modified. A still greater modification is brought about if, as a preliminary, the veins and lymphatics should have been drained by elevation and pressure, so as to leave beyond the tourniquet an abnormally small supply of the circulatory fluids. Whatever else may result, the direct effect upon the circulation itself is that of "an alterative." The object of this communication is to give further proof that this alterative action can also be in suitable conditions a beneficial action; and that as a therapeutic agent it possesses considerable scope and efficiency, as was shown in the cases mentioned in a short article in the 'Lancet' more than a year ago.[1]

Novelty is not the fault that need delay the discussion of this procedure, for it has been in daily use since Ambroise Paré. And, as to its risks, we have long since learned the worst from the severe tests to which it has been put

[1] 'Lancet,' August 13th, 1904, vol. ii, p. 442.

in modern operative surgery. Surgeons are ready to admit that the prolonged anæmia sometimes kept up during operations must be detrimental, though it has not usually been fatal, to the vitality of tissues; and it is obvious that beneficial effects could only be expected from applications of the tourniquet sufficiently brief to be free from any suspicion of harm.

Nevertheless neither this ancient standing nor this acknowledged safety had hitherto led to the suggestion of its systematic use as a remedy. And the extent of its remedial capabilities has remained unsuspected, in spite of Harvey Cushing's[1] original and apparently isolated employment of the tourniquet in a case of Raynaud's disease published in 1902. Such, at least, is the inference from the absence of any fresh contributions to the subject, beyond those which were referred to in the writer's article on "Interrupted Circulation as a Therapeutic Agent,"[2] in 1904, by N. S. Isambert,[3] who used successfully the elastic ligature in a case of threatening gangrene, and by L. Isnardi,[4] whose practice is to apply an Esmarch's bandage as a preliminary to any painful or difficult surgical dressing. In that article due reference was also made to George Oliver's pioneer work in the study of tissue-lymph in its relation to the circulation.

The evidence reported in 1904[5] had been obtained in cases of rheumatoid arthritis, and the opinion was expressed that the success recorded by Cushing in his case was, as in them, due to a local action upon the circulation rather than to any central influence reflected from the medulla.

The general conclusion was also drawn that the influence of "interrupted circulation" is clearly not limited to the blood-vessels, but must also intimately affect for

[1] 'Journal of Nervous and Mental Diseases,' Nov., 1902.

[2] The Oliver-Sharpey Lectures on "Recent Studies on the Tissue-lymph Circulation," 'The Lancet,' April 30th and May 7th, 1904.

[3] Cf. 'Semaine Médicale,' May 18th, 1904.

[4] Ibid., June 22nd, 1904.

[5] 'Lancet,' April 30th and May 7th, 1904.

better or for worse all the tissues of the ligatured limb.

Although substantial evidence has already accrued in support of the opinion that the beneficial effects noted in rheumatoid arthritis might probably be equalled in other peripheral disorders, as these observations are still in progress they cannot be included in the present paper, which must remain limited to a consideration of the arthritic group.

The technique.—A brief account of the procedure (which is essentially the same as in operations) had better precede the notes of the cases in which it was applied. In the absence of an Esmarch's tourniquet the simplest substitute is india-rubber tubing of suitable thickness, which is tightened round the limb in single or double loop outside a slight protecting pad. The tube can either be simply drawn tight, both ends of the loop being held, or else coiled over itself to any degree of tightness.

As a preliminary the limb is to be rendered anæmic, the patient being in the reclining posture. In many instances the profound anæmia obtained by Esmarch's bandage need not be resorted to, though it is an essential for the best results; but the raised limb must be squeezed empty and kept elevated until after the application of the tourniquet. The relative duration of the constriction will also influence the result, and will need to be varied according to the nature of the case. In my hands the shortest has been thirty seconds; the longest three to five minutes. I have not exceeded six applications at one sitting, with a duration of two minutes each, and with intervals of one to two minutes. Three applications at each sitting may suffice in most cases, and two sittings daily may be desirable.

It is important to liberate the artery suddenly; and a distinct advantage is gained by lowering the limb into the vertical position, if this can conveniently be done, just before removing the ligature.

With sufficient care the risk of any damage from ex-

cessive pressure at the seat of ligature is easily avoided. None of the cases hitherto treated have presented the slightest complication referable to the skin, to the vessels, or to the nerves. It need hardly be mentioned that inflamed or tender nerve-trunks are an absolute contra-indication, just as much as senile and calcified arteries.

THE CASES.

The following cases, some of which may be exhibited, have been under treatment during the last two months. Until then leisure had failed for any further observations. They will be given very briefly, as the essential question in each of them is limited to the local condition.

They belong to the following groups:

(1) Subacute, subpyrexial synovitis, persistent or relapsing, in young subjects of rheumatic tendency.

(2) Deforming soft puffy nodular arthritis in women, with chronic quiet intra-articular and peri-articular effusions and thickenings.

(3) Late massive arthritic thickenings, with fixation or with much stiffness.

The treatment was suspended in one case only, that of a stout florid coachman of gouty temperament with chronic effusion and synovial thickening of the right knee of eight months' duration. As no visible reduction of the swelling was obtained after three sittings, the further application of the method was postponed till other forms of treatment had been given a trial.

CASE 1. *Acute rheumatoid arthritis.*—A. W—, dressmaker, aged 26 (St. George's Hospital Medical Register No. 1081), was admitted on July 6th, 1905, for a first attack of rheumatism in the wrists, ankles, and knees. The pains and swelling did not yield satisfactorily to the full treatment by sodium salicylate, potassium citrate and iodide, although more amenable to aspirin; and in other points also, including the presence of decayed teeth, the

case wore a rheumatoid rather than an ordinary rheumatic complexion. On July 14th and 15th the tourniquet was applied to the left arm: an almost complete disappearance of the swelling and of the pain ensued on the first day, and complete relief on the second. The left ankle, however, remained swollen and painful. The tourniquet treatment was applied thoroughly to the thigh on July 17th. The effect of this single sitting was to completely relieve the swelling and pain. There was no return of the effusion into these joints, although the patient had a slight relapse of rheumatic symptoms whilst still under drug treatment.

CASE 2. *Relapsing subacute attacks of rheumatoid arthritis.*—K. C—, aged 23 (St. George's Hospital Medical Register, No. 985), a waitress, has been liable to sudden attacks of swelling, redness, and pain of the hands and feet since her first rheumatic seizure in 1900. Three of her attacks were described as "rheumatic fever." There is slight permanent disfigurement of the wrists with awkwardness and stiffness. She was treated with the tourniquet from June 26th, 1905, until July 7th, when she got up. The acute swelling had subsided; there was still some thickening, but a decrease in the slight puffiness which remained. The treatment was continued for seven days, although the chief result was obtained during the first three days.

CASE 3. *Subacute relapsing rheumatoid arthritis.*—Kate S—, aged 21, single, has been an inveterate rheumatic since her rheumatic fever five years ago. She had right pleurisy three years ago and lingering attacks of acute rheumatoid symptoms every year, but none so severe as the present one. This began with painful swellings of the ankles one month before her admission into St. George's Hospital on July 10th, 1905 (Med. Reg., No. 1080). Since then the knees have been affected, and the joints of the upper extremity, chiefly those of the

wrists and hands, have been swollen with excessive tenderness and painful stiffness of the muscles of the forearm. Her complexion was sallow and pasty, her aspect vacant and open-mouthed, her attitude characteristic, with helpless spade-like hands and wrists, and a wet palm. The phalangeal joints were also swollen and tender, without redness. No evidence of any visceral affection was noted except a systolic murmur audible at the cardiac apex and base.

She was ordered the usual antirheumatic treatment, viz. iodide of potassium, citrate of potassium, and sodium salicylate. The next day, as there was no marked improvement such as occurs in acute rheumatism, the right arm, which was the worse of the two, was selected for the special treatment. The tourniquet was applied with such good effect on July 11th, 12th, 13th, and 14th, that the soft puffy swellings, decreasing day by day, had almost entirely disappeared, leaving behind the thickenings of the hard structures. The left wrist, which had remained swollen as before, was now taken in hand with equally good results. The treatment was kept up henceforth for the sake of the peri-articular thickening, and on July 30th, when the patient was discharged, the Medical Registrar was able to conclude his report with the note "the joints are now practically normal." The temperature throughout the case had oscillated up to 100°, probably in connection with the irritation from decayed teeth.

CASE 4. *Chronic rheumatoid condition, with acute painful seizures of fixation of joints and muscles.*—Miss E. E—, aged 52, has always been healthy, in spite of a gouty tendency, but of late years has been increasingly liable to acute rheumatoid swellings of joints and stiffness of the muscles. Last autumn she had quickly recovered from her symptoms during a stay abroad; on returning to London she was seized the same night, and rendered quite powerless by stiffness and pains, from which she slowly recovered. Her present attack, the worst she has

ever had, began in April, 1905. When she came under treatment in June the very severe pain which she had suffered, apparently from acute neuritis, over the inner aspect of the head of the left tibia was less intense, but there were great aching and tenderness of the swollen left knee and of both hands, the shiny skin of which seemed to be too tight for the enlarged and stiffened phalanges. The temperature was normal or only slightly elevated at times. General treatment by saline laxatives, by colchicum and mercury, and local applications such as in particular of the compound liniment of iodide of potassium, did good. Neither these measures, however, nor massage made so marked and rapid an impression upon the stiffness, the swelling, and the pain as the treatment by interrupted circulation which was applied for upwards of three weeks, and the efficacy of which was demonstrated by limiting its employment to the left arm first, then to both arms, before it was applied to the left thigh. Great relief was obtained in the three limbs, with considerable though not complete loss of swelling. The patient was then sent to Aix to consolidate her recovery.

CASE 5. *Chronic deforming rheumatoid arthritis with effusion and rigidity, but without ankylosis.* Mrs. X. Y—, aged 37, thin, pale, and nervous, of the type known as irritable weakness, but viscerally sound and free from catamenial irregularities, came under treatment in June, 1905. She was then very feeble, stiff, and crippled in her knees and ankles (chiefly on the left side), and in her hands, which presented a wet palm and marked ulnar deflection. The finger-joints of the left hand were abnormally loose, those of the right showing more thickening, particularly the middle and ring fingers, the latter with a distinct float-shaped interphalangeal joint. The wrist-joints were thickened, and presented soft synovitic and puffy nodular swellings, with much stiffness, tenderness, and limitation of movement. The patient's expression and attitude were those of helpless-

ness and distress. This condition was the climax of progressive symptoms of four and a half years' duration.

The first symptoms after a wetting followed by a prolonged chill in church, had set in suddenly in January 1901, with painful swelling, numbness, and stiffness of both hands, and with severe pains over the whole body which kept her in bed for fourteen days. From that date onwards she was never free in some form or other from rheumatic pains or stiffness. She continued to attend to her avocations, often, however, with considerable difficulty; and the effort told severely upon her nervous system, which was naturally delicate, until she lapsed, in 1904, in a condition analogous to neurasthenia, for which she was treated in November 1904, with hot sulphur baths and ferruginous waters, without much or any benefit; and she seems to have then suffered from increased weakness and loss of flesh. The view was taken at that time and since that the arthritic condition was of neurotic derivation, and under neuropathic influence.

In September, 1901, the recurring painful red and shiny swellings of the right hand had been diagnosed as "rheumatic erythema." The same diagnosis was also given when she consulted in October, 1902. In the interval she had been confined, in May, 1902, of her second child, and had undergone much fatigue.

Her first pregnancy, twelve years ago, had been marked by the onset of dental decay, which eventuated in the extraction of seven teeth from the upper jaw, and of four molars from the lower jaw at a comparatively recent date. For the last fourteen years her residence has been on high ground, where the air is bleak and the water chalky.

Her feet began to suffer during a stay in Africa in 1904, and walking became very difficult, owing to the pain, stiffness, and swelling, which seemed to affect the whole foot as well as the joint of the great toe.

Her condition since then has oscillated without any permanent improvement. Although she was better at the end

of last winter spent in the Riviera, the cold wet weather which she encountered on her return determined a severe recrudescence. The knees, particularly the left one, became swollen and very painful, and the feet also swelled. The left knee has remained much swollen as a whole and fixed, but particularly tender and puffy over the inner aspect of the head of the tibia. The right knee is almost normal in size and movement.

The treatment was directed, as in Case 6, to the husbanding of the general strength, and to a general hygiene of the skin, muscles, and viscera, with fairly good results.

After a period of rest in bed and of massage, which was of service for the general health, the treatment by interrupted circulation was applied to the right arm first, as this was the worse affected. The effect upon the puffy swellings was decided and rapid. They disappeared, as in the cases of subacute rheumatism. After a few days the left arm was also submitted to daily treatment with similar results. The treatment was kept up steadily, and is still kept up, with a view to influencing, if possible, the thickening around the bones. Not only the patient herself, but all those best able to judge (including the husband, after an absence of three weeks), were agreed that the size of the wrists and of the float-shaped knuckles was perceptibly reduced, and the freedom of movement greatly increased.

The left knee, although getting all the advantage that general treatment, local applications, and rubbing could confer, had remained almost as greatly swollen as before, very tender, painful on attempted movement, and incapable of complete extension. The interrupted circulation treatment was at last resorted to three weeks before the date of this report, and is still being applied. The progress made during that interval has been great, the patient noticing first a relief and subsequently a disappearance of the pain and tenderness, whilst to onlookers the diminution in the general swelling and the return to a

more natural configuration and to greater mobility are quite obvious.

As a result of these gains (within seven weeks), for which the other instalments of treatment are also, doubtless, in great measure responsible, the patient has largely recovered from her depression and from her almost melancholic frame of mind, and is looking forward to continued progress towards recovery.

CASE 6. *Osteo-arthritis with fixation.*—Maria J—, aged 56, married, residing in Sheerness, was admitted into St. George's Hospital on June 14th, 1905 (Med. Reg., No. 925), in a crippled condition, not having been able to walk (or latterly to stand) without assistance for eighteen months past owing to fixation of the knees in a semiflexed condition, and to much limitation in the movement of the ankles, and being moreover disabled in the upper limbs by complete fixation of the right elbow and partial loss of movement in the left elbow, and by complete fixation of both wrists.

Her mother had suffered from rheumatism. She herself had never had rheumatic fever or any serious illness; and was fairly healthy-looking for her years. The menopause had occurred at the age of fifty-three.

For the last twelve to fourteen years the joints had gradually swelled and afterwards become stiff, without pain except on movement; the first joints to be affected were the metacarpo-phalangeal joint of the index finger and the metatarso-phalangeal joint of the great toe on both sides, all at one time. She had been under treatment during nearly the whole period without improvement.

On examination no evidence was found of any visceral disease. There were no teeth in the upper jaw, few in the lower. The temperature was normal; the pulse rate 96, and the respiratory rate 24. The first, second, third, and fifth metacarpo-phalangeal joints of both hands were swollen, with lipping of the cartilages and grating. The

proximal and middle phalanges of the fourth and fifth digits and their joints were swollen. There was ulnar deviation and much limitation of movement of the fingers. The right thumb was rigidly fixed at its proximal joint. There was much wasting of the interossei and of the muscles of both arms.

Both knees were enlarged, chiefly the left, and grated on any attempt at forcible extension.

The first metatarso-phalangeal joints on both sides were swollen, the ankles and tarsal regions were swollen and somewhat rigid, and there was some fibular deviation.

The hips and shoulders were comparatively free within the smaller range of movement, and the spine, neck, head, and jaw quite free. The patient could thus be placed in the sitting as well as in the recumbent posture; but in both positions was otherwise helpless.

The treatment included, besides cutaneous hygiene and laxatives, full doses of the hypophosphites and of the glycerophosphates of calcium, iron, and sodium, two ounces of olive oil and half an ounce of whisky every night, a full and suitable diet, massage for the muscles and passive movements of the movable joints, extension of the knees by weight and of the elbows by elastic traction (to facilitate which my house physician, Mr. Hetherington, constructed a convenient apparatus), continued flexor elastic traction for the wrists, and the encouragement of active movement, which had previously been limited to a feeble waving of the fingers, and to movements of the head and shoulders.

The "interrupted circulation" treatment was first applied to the right arm only, as this was the worse ankylosed, namely, one sitting every other day with three "turns" of two and a half minutes' duration. But complete anæsthesia of the limb could never be obtained, and the forcible manipulation of the rigid joints during the anæmia—one of the chief features of the treatment—could only be applied very gently on a small scale. Nevertheless distinct improvement was secured after three

sittings; and on June 30th slight mobility had been restored to the rigid wrist and elbow.

The treatment was later on applied to both arms with daily sittings, and finally to the left thigh. Previously, however, Sir William Bennett, after forcible treatment under an anæsthetic (on July 18th), had expressed an opinion that the left knee would never be perfectly straight. Most of the joints were moved that day with much creaking and grating; and both wrists were again moved under gas on July 28th. But on both occasions the advantage gained seemed to be lost again during the several days' rest entailed by the surgical interference.

Meanwhile the general strength and condition continued to improve, and on August 9th patient was able to stand, and a few days later to walk as far as the lavatory.

Daily systematic treatment of the arms and of the left leg was applied more regularly and efficiently after August 15th with progressive improvement. But before that day the patient herself was conscious of the diminution in the size of the heavy wrists, as well as of an increased mobility of the joints. The left knee also was now perceptibly less massive.

Further progress will be reported later.

The Immediate Effects of the Application.

In each of the three stages of the procedure we have to keep separate account of the objective as well as of the subjective effects.

(1) *The application of the ligature* (with emptied veins) gives rise to the familiar appearances well known to surgeons. The proof that the ligature has been effectively applied is the continued pallor of the limb, and the failing of the superficial veins to fill again.

As regards *subjective* effects: there is no pain, but only a sensation of pressure at the seat of the ligature, provided no accidental pinching of the skin between turns of the tubing has occurred; and this, of course, should be

carefully avoided. No immediate change in sensation is usually experienced below the ligature.

(2) *The period of anæmia.*—In most cases no change is perceptible in the appearances beyond a steady increase in the pallor of the skin during the first few seconds. In rheumatoid cases the softer puffy synovial and periarticular swellings may sometimes be actually seen to have subsided after a minute or two, though some of the swelling may afterwards return when the ligature is removed.

The subjective effects vary. In some individuals there is distinct numbness rapidly passing into anæsthesia. In others the numbness and loss of sensation are delayed, or the fingers or toes may retain almost unimpaired sensation throughout the short period of artificial anæmia.

In one particular all patients agree. The painful or tender joints are made easier. Pain and tenderness may even entirely disappear. At the same time there is a feeling of recovery of some degree of power for active movement; and when the stiffness is not due to any firm ankylosis, patients will sometimes spontaneously test the joints by active movements.

On the other hand no painful or discomforting sensations have ever been complained of even during the longest sittings employed (upwards of four minutes).

(3) *The removal of the ligature* is followed by a visible bright blush of the skin and nails. Never absolutely immediate, this occurrence is preceded by an interval which varies in different subjects, and is also apt to vary at different sittings in the same subject. This variability has its clinical importance as probably pointing to differences and variations in the function of the vaso-motor mechanisms. It is also worth mentioning as an instance among the many speculations and studies which are opened up by this method.

Together with the blush there also occurs the objective symptom of increased local heat. And there may be a slight visible return in some of the soft parts of the fulness which had disappeared, as, for instance, at the back

of the hands, in the inter-osseous spaces, and about the wrist.

Subjectively, the return of the circulation is always grateful to the patients. They usually dwell upon the pleasant warmth felt to pervade the limb. I have never heard a complaint of any painful sensation, much less of that severe pain which is often associated with the thawing of frostbitten extremities.

It is important to note that the marked relief from pain and tenderness obtained during the period of anæmia is not entirely evanescent, but that the limb remains permanently "easier."

The Clinical Results.

The therapeutical results obtained as regards the arthritic condition have been invariably satisfactory in the cases hitherto treated. Sometimes perceptible even to casual observers, they have always been obvious to the patients themselves (see cases). No complications or untoward effects of any kind have been observed. The results may be briefly summarised as follows:

(1) The recent puffy swellings in group (1) were rapidly amenable to a few applications, and in one case to a single application.

(2) The inveterate puffy swelling associated with fibrous, cartilaginous, and bony thickenings was sometimes visibly influenced during the application. Its almost complete disappearance after a short series of sittings revealed the articular deformities in their sharper nodular outlines.

(3) The peri-articular thickenings were influenced more slowly, but gradually diminished.

(4) The thickening of cartilages and of the joint ends of bones may conceivably be found to yield to prolonged treatment. At any rate some reduction has been observed in the diameter of the float-shaped knuckles, and of the swollen wrists and knees in Case 5. But how much of

this fining down may have been limited to the periosteum cannot be decided without more searching observation by means of systematic radiography.

(5) The great improvement to be secured with the help of this method in the condition of the articular surfaces in some cases of fixation or rigidity from adhesions, both as regards restoration of movement, diminution of creaking or grating, and actual reduction in the size of the joint as a whole, is evidenced in Case 6.

(6) In connection with the latter case attention may also be called to the fact that in limbs so long disused all the tissues must benefit indirectly from the restoration of movement, in addition to any direct advantage conferred upon them by the tourniquet.

General Remarks.

The phenomena which have been described in this paper can be easily verified by any observer, and they seem to furnish a sufficiently firm basis for clinical action. But their adequate explanation would be very difficult, nay, impossible, at this stage; and, moreover, it would be almost wholly a study in pure physiology. Only few words need therefore be devoted to theory and inference.

We seem to be dealing, as previously suggested, essentially with the vascular mechanisms, although *the nerves* must not be lost sight of. Their terminal fibrils receive a large share of the peripheral vascular effects. They are also immediately concerned in any associated vasomotor changes, and in any loss or depression of sensation.

Within the domain of the vascular system an instructive contrast is afforded by Bier's method of "passive congestion," which aims at overcharging the limb with venous blood and with venous plasma by closing the superficial venous outlets by a light ligature exerting but little pressure upon the arteries.

The aim in "interrupted circulation" is, on the contrary, to drain the limb of as much venous blood and

venous plasma as possible, and to furnish it with as fresh an arterial supply as can be obtained.

The central facts in Bier's method are the dusky swelling and the vascular turgor. Here the most striking appearances are the anæmia and the subsequent arterial flush; and these represent distinct and, to a certain extent, opposite events, which can be broadly defined as "absorption events" and "stimulation events."

The "absorption events" are rendered manifest in the group of cases under consideration, when the shrinkage which takes place in the synovial effusions or in the softer local swellings chances to be seen, or, as is sometimes possible, is verified by measurement, during the time of the application of the tourniquet. The inference is that, under the conditions of the experiment, the balance of circulation between the capillaries and the tissues is altered, and that, like an imperfectly saturated sponge, the capillary network tends to soak up any surrounding fluid. This view seems to be justified when we watch the capillary circulation in an ulcer of the leg. We then witness a gradual emptying of the capillaries which begins soon after the tourniquet is applied, and continues to increase for many seconds, until the red granulating surface is almost quite pale. What has become of the blood? Is its withdrawal due to a redistribution of the capillary contents of the more superficial and of the deeper districts? Or is it merely local and due to the blood being sucked up by elastic aspiration into the partly emptied arterial and venous channels? The slow and gradual establishment of the capillary ischæmia fits in with the view that it may be due to the relaxation of an initial extreme vaso-constrictive spasm, with partial reflux into the re-expanding arterioles. And we should not forget that at the same time the empty venules must also claim their accustomed influx. A third explanation, which would assume the occurrence, as in Bier's method, of an escape of some of the plasma into the lymph-spaces, seems to be inconsistent with some of the

appearances as well as with the probabilities. The opposite assumption has been made in this series of observations, namely, that the stronger suction is that exercised by the unfilled vascular system. Some evidence for this view is afforded by the observation that as the surface becomes blanched under the action of the tourniquet, it becomes at the same time less moist.

The "stimulation events."—These may be summed up in two words—"arterial irrigation" and "arterial movement"—which are a welcome sequel to the venous drainage of the limb. Anæmia, it is needless to point out, cannot ever be constructive: any beneficial effect from a sudden withdrawal of the nutrient blood could only be explained indirectly through its alterative effect upon the nerves, as a nerve shock. It may, nevertheless, as previously suggested, serve a quasi negative nutritional purpose. Not unlike forced expiration, which expels some oxygen from the alveoli, together with less useful gases, the soaking up of the plasmatic juices makes room for a freshness of supply not otherwise obtainable. Beyond this the local anæmia cannot avail to assist nutrition, for its continuance would mean "necrosis" if absolute, and "atrophy" if only partial.

The vitalising effect which must belong to a full supply of pure arterial blood under full pressure requires no comment, except, perhaps, a reference to the interesting fact that owing to the blood-forming properties of bone-marrow this local advantage may be a gain to the general nutrition.

It would occupy too much time to discuss the effects upon the general circulation and upon the general blood pressure which may result from the removal of the tourniquet; they are probably opposite to the consequences of its application. But there is another local influence probably not devoid of importance. In some instances the suddenness of the arterial flush is well marked, and suggests that each of the emptied arterioles and capillaries receives as it were a "ramming" charge.

Any sudden mechanical effect of this sort is unattainable in the spontaneous variations of the circulation. The impact conveyed to the capillary walls cannot fail to be communicated to the contiguous cells as well as to the fluids in which they are bathed, and this "cellular vibration" will be carried wheresoever capillaries extend, even into the inaccessible recesses of bone, in literal realisation of the poet's conception :

" . . . . . per ima cucurrit
Ossa tremor."

In conclusion, to meet the possible objection that this method is artificial or unnatural it may be said, not altogether in metaphor, that it is a modification of the familiar treatment by massage. It has just been suggested that interrupted circulation includes an intimate micro-massage of the tissues, but it might almost be added that ordinary massage owes some of its efficacy to the fact that its performance entails a definite though very brief interruption of the circulation at each spot influenced by the pressure of the hand.

I propose to deal in a future communication with the results obtained by systematic treatment in chronic ulcers. The main purpose of this paper, as stated on its first page, is to call attention to *the principle of "interrupted circulation"* as a definite therapeutic agent, and to the evidence as to its efficacy, and does not include any attempt to urge its adoption. Much remains to be made out as to the physiological mechanism, as to the advantages and drawbacks, and as to the scope in practical therapeutics which belong to that principle ; but above all, as to the most practical form under which it may eventually be applied. Upon all these matters I must reserve an opinion until further observation and the help of the experience of other workers shall have matured our conclusions.

ADDENDUM (JANUARY, 1906).

FURTHER REPORT ON CASES.

There is nothing to add concerning Cases 1, 2, and 3, no further reports having been received.

CASE 4.—This patient has not been seen recently, but she reports that although she has not entirely lost the articular thickening and stiffness, she has maintained the advantage which had been secured during her treatment in London, and her after-treatment at Aix-les-Bains, and she is able to follow her avocations.

CASE 5.—In this case, which ceased to be under my observation soon after this paper was written, the tourniquet treatment was resumed after the patient's return home, and continued at intervals; but she is unable to report any substantial improvement in the condition of the knee from this treatment, or from any of the other remedies which have been resorted to. The local treatment was discontinued because she complained of increased aching supervening in the knee some hours after its application. She writes that she is still unable to walk owing to the painful swelling and stiffness of that joint.[1]

CASE 6 (exhibited).—This patient has remained continuously under observation. There has been marked liability in damp weather to temporary aching and soreness of the joints, with increased stiffness, which have needed special relief by medication. Nevertheless she has lost none of the ground which she had gained, and has continued to improve in general health and in

[1] A later report, dated January 24th, describes considerable improvement. "Crutches have been discarded for the past few weeks, and the patient has taken short walks of half a mile or thereabouts, with no other support than a stick. The knee is less swollen, stiff, and contracted; but much walking or standing is still followed by a return of the pain and swelling. She is steadily putting on weight."

capacity for movement. She is no longer a cripple, walks rather stiffly, but without crutch or stick, and "she can do everything for herself." But the knees are not yet straight, and the right elbow has only a limited range of movement, apparently owing to the obstruction of a bony outgrowth. Comparatively little movement has been regained in the wrists. These joints are smaller, and are slowly improving; but their tendency to become fixed if strong passive movement should fail to be applied day by day has not yet been overcome. The mobility of the fingers continues to improve, greatly owing to the patient's own persevering exertions the favourable effect of which has doubtless had a considerable share in the benefit which she has secured during her prolonged stay in the hospital.

Additional Cases Exhibited.

Acute cases.—None of the *acute rheumatic cases* in which immediate relief was given by the elastic bandage and tourniquet are at present in the hospital, or available for demonstration. The method has not been systematically applied to all cases of acute articular rheumatism. But in none of the few cases (Nos. 1678, 1739, 1773, 1837, in the St. George's Hospital Medical Register) in which it was applied has it failed to effect a diminution in the acute swelling, an immediate relief of the pain, and an immediate restoration of some degree of painless mobility. Instead of the tourniquet simple digital compression of the artery was used in some of these cases.

Acute gonorrhœal arthritis.—In the two patients exhibited there was acute arthritis of the knee-joint. In the case of P. B—, aged 36, motor driver ('St. George's Hospital Medical Register,' No. 2010), acute swelling of the right knee-joint supervened some days after he had been in bed under treatment for symptoms of lumbago (the previous inquiry as to the existence of urethritis

having been answered by the patient in the negative). Four applications of the local treatment by interrupted circulation by my House Physician, Mr. Herbert J. Bankes, were sufficient, the first application having brought about considerable diminution in the swelling and pain, before the copaiba prescribed the same day could have influenced the condition. The same remark applies to the internal treatment in the following case:

J. B—, aged 34, shop assistant ('St. George's Hospital Medical Register,' No. 1919), was admitted with intensely painful and tender swelling of both knees and ankles. The diagnosis was made, and the treatment applied without delay to the right lower limb, which was even worse than the left. The pain in the knee was immediately relieved; and the patient was enabled to move slightly and without pain both the joint and the limb. This advantage was well maintained, together with perceptible reduction in the swelling, the next day; whereas the left limb was still utterly helpless. As there could be no further object in delaying complete relief, the local treatment was now applied to the left knee with the same immediate result. The effusion diminished day by day, and was almost imperceptible in the right knee on the *third day* after the first application of the tourniquet. The left knee also improved, and the local treatment was not pushed beyond three applications on each side owing to the lack of any further urgent indication; but it was resumed again on January 11th owing to the recurrence of slight painless effusion in both knees, chiefly the left. Meanwhile the patient has greatly improved in health, and remains under treatment.

Acute sprain.[1]—Patient, A. H—, aged 29, child's nurse ('St. George's Hospital Medical Reports,' No. 1883), suffering from chronic rheumatoid arthritis of nearly five years'

[1] This patient was unable to attend; the hands and the arms, which have greatly improved, being still unequal to an efficient use of the crutches.

duration, and from inability to walk or stand owing to almost absolute rigidity of both knees, and to considerable stiffness of both wrists and elbows, is a good instance of the relief afforded to the pain and swelling of acute sprain. On two occasions adhesions were forcibly broken down in the left knee, and the acutely painful swelling that resulted was treated some hours later by an application of Esmarch's bandage and tourniquet, with excellent results. The swelling not having completely subsided, and showing no signs of spontaneous disappearance, the limb was again treated by the method on January 10th and January 11th, with immediate improvement.

Chronic cases.—In contrast with the case of A. H—, patient E. B—, aged 56 ('St. George's Hospital Register,' No. 1808), illustrates the chronic non-adhesive synovitic form of the disease, with muscular stiffness and shortening of tendons, but no fixation of the swollen joints. She likewise illustrates the relief obtainable by even a few applications of the "interrupted circulation method," but also its unsuitability for subjects so extremely thin as she is. Sufficient protection was not afforded to the nerves by the wasted soft parts of the right arm, and two or three rather long sittings (upwards of five minutes' pressure) occasioned persistent numbness of the right hand, from which she completely recovered after three weeks. The interrupted circulation treatment was, nevertheless, applied to the right thigh regularly, and, after seven weeks' treatment, the right knee, which had been larger and less movable than the left, is now the smaller of the two; some effusion remains in the right knee-joint, but there is much more of it in the left. The right ankle has also improved. The internal treatment in this case included a draught of olive oil and milk at bedtime, and the strychnine and hypophosphite and glycerophosphate mixture.

Patient E. C—, aged 23, barman ('St. George's Hospital Medical Register,' No. 2012), affords another instance

of the nodular puffy, non-ankylosing variety, in this case beginning in boyhood with a prolonged rheumatic attack (two months in bed), which was followed at varying intervals by three similar attacks. Both hands, on admission, were much swollen at the wrist, as well as the knuckles and the interphalangeal joints; and the latter presented the float-shaped variety of deformity. The right hand being worse than the left, the tourniquet was used to the right arm on several occasions, the result each time being a diminution in the stiffness and in the puffiness. Meanwhile the rheumatism was treated by internal remedies, for which eventually a tonic treatment by hypophosphites, glycerophosphates, and strychnine was substituted.

Concluding Remarks.

Further observation in the cases narrated and in others confirms the estimate taken in this paper of the efficacy of the method in reducing the swelling and the pain associated with the intra-articular effusion of synovial fluid or the peri-articular effusion of lymph. The immediate relief afforded in the cases of acute arthritis, whether rheumatic or gonorrhœal, and of sprain in which it has been tried, is equally striking. But in joints chronically thickened or fixed the improvement reported has not hitherto resulted in any complete cure.

APPENDIX.

Mr. J. Y. W. MacAlister, our Secretary, has suggested to me that the condition shown in the accompanying reproduction of a photograph which was given to him some time ago by Mr. Thomas W. Nunn, namely, complete freedom of the ringfinger of the left hand from any swelling when all the other fingers are evenly swollen from rheumatoid arthritis might, perhaps, be due to a limitation

of the circulation in that finger by the tightness of the ring worn upon it.

The contrast between this and the other fingers is striking; on the other hand there can be little doubt that the relative constriction of the base of the finger must have modified its circulation both of blood and of

lymph. It would be impossible to base any conclusions upon this isolated instance. Moreover, the interference with the circulation was of the continuous rather than of the intermittent kind. Nevertheless, the mysterious aspect of the case as well as the ingenious suggestiveness of the explanation offered may be held sufficient excuse for appending this brief note to the paper.

NOTE BY MR. NUNN.

The hands shown in photograph are those of a woman aged 70, who had spent her life in non-laborious domestic service. The hands were characteristically deformed by rheumatoid arthritis, but, as is shown in the photograph, the ringfinger is perfectly normal. The case was so singular that I had the hands photographed to record indisputably a remarkable, and, to me, unaccountable fact. The photograph was made about thirty years ago. Recently a question has arisen in my mind as to whether some influence analogous to radio-activity had any share in modifying the nutritional changes in the tissues of the finger.

DISCUSSION.

Sir DYCE DUCKWORTH had had some experience of the method in rheumatoid arthritis and gonorrhœal arthritis, and had witnessed some relief of the symptoms in some of the cases. The method in acute stages of rheumatoid arthritis must be very painful, and he, therefore, thought that it was to the chronic cases that it was specially applicable. The blood vessels and lymphatic system were both greatly affected and stimulated by the application of the ligature. He, however, considered that other methods of treatment should be employed simultaneously with the interrupted circulation method.

Dr. EWART, in reply, said that in his own experience the most striking results had been those observed in acute arthritis. The relief immediately afforded to the pain, tenderness, and fixation of acutely swollen joints was remarkable, even in cases of acute rheumatism. It was worth noting that simple digital compression of the main artery of the limb was capable of producing satisfactory effects, as, in those acutely painful conditions, the usual procedure was more difficult to carry out.

THE USE

OF

RECTAL INJECTIONS OF AN ANTISTREPTOCOCCUS SERUM IN GONORRHŒAL INFECTIONS

AND IN

CERTAIN CASES OF PURPURA HÆMORRHAGICA

BY

W. SOLTAU FENWICK, M.D.,

AND

J. PORTER PARKINSON, M.D.

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MR. PRESIDENT AND GENTLEMEN,—During the course of a series of experiments upon the influence of various forms of serum, and of mixtures of different sera, on diseases commonly met with in hospital practice, we have obtained certain results which appear to us of considerable interest. This statement applies particularly to that large class of complaints in which the symptoms arise from a gonorrhœal infection, either recent or remote, and it is to such that we would at the present time invite your attention. Inasmuch, however, as we have also encountered two examples of hæmorrhagic purpura which rapidly benefited by the same method of treatment, it may be

excusable for us to include them in this communication. Originally it had been our intention to have collected a large number of cases before venturing to publish any report upon the subject, but we have found that in a hospital of only one hundred beds examples of gonorrhœal infection are inconveniently scarce, while the greatest difficulty is encountered in inducing men suffering from acute gonorrhœa to enter a hospital and to remain there long enough to permit of the examination and control experimentation which it is necessary to undertake. The following cases have been selected from a series of fourteen consecutive instances in which the presence of gonorrhœa was definitely ascertained and confirmed by bacteriological examination, and in which the symptoms and signs rapidly subsided under the use of the serum after having resisted the various methods of treatment usually recommended for the disease.

Gonorrhœal Pyæmia.

CASE 1.—A married woman, aged 39 years, was admitted into the London Temperance Hospital on March 31st, 1903, for what was supposed to be acute rheumatism. It was stated by a friend that about nine days previously the patient had been attacked by severe pains in the right wrist and left knee, had become feverish and restless, and for the last two days had been delirious. Beyond these facts no history could be obtained.

On examination the woman was found to be delirious; the body was fairly well nourished, and there was marked pallor of the face and lips. The skin was hot and dry, the tongue thickly coated with a greyish-brown fur, the temperature in the axilla 101·2° F., the pulse 102, and the respirations 28 per minute. The pupils were moderately dilated, the soft palate and fauces somewhat injected and covered with stringy mucus, and a few patches of erythema were visible upon the forehead and sides of the neck. The right wrist was swollen, and the

skin of the dorsum of the hand was reddened and pitted upon pressure. Both knee-joints were swollen, and contained a moderate quantity of fluid, while the right ankle appeared somewhat puffy, and the dorsum of the foot was œdematous. There was no purpuric eruption. The percussion note was hyper-resonant over both sides of the chest, and the expiratory murmur was prolonged. The apex of the heart was situated in the normal position, the impulse was feeble, and a soft systolic murmur was audible over the mitral area, and could be traced as far outwards as the left anterior axillary fold. At the base of the heart the sounds were clear. The liver was depressed by the emphysematous lung, and its edge could be felt one inch below the costal margin. Pressure upon the organ did not elicit any signs of pain, and there was no jaundice. The spleen was somewhat enlarged to percussion, but its edge could not be felt, while careful palpation of the abdomen failed to detect any tumour. There was a purulent discharge from the vagina, and the uterus was fixed on the left side, but no disease of the pelvic viscera could be detected. The urine withdrawn by a catheter showed a specific gravity of 1014, and contained a trace of albumin, but it did not give the salicylic reaction. The retinæ and optic discs were quite healthy.

Although the age and general condition of the patient seemed to indicate pyæmia rather than simple rheumatism, full doses of salicylate of sodium were ordered, and a small quantity of the vaginal discharge was collected for examination.

Two days later the temperature had fallen to 100° F., the pulse-rate was 98, and the respirations 28 per minute. The general condition, on the other hand, was worse, and both the urine and fæces were passed into the bed. As the vaginal discharge was reported to contain numerous gonococci, the salicylate mixture was omitted in favour of one containing quinine and iodide of potassium, and local treatment for the gonorrhœa was adopted.

During the next six days the patient remained in much

the same condition, the temperature ranging between 100° and 101° F., with a pulse-rate of about 112.

On April 8th it was noted that the patient had become decidedly worse. The temperature was now 103° F., the pulse 120, and the respirations 40 per minute. The tongue was dry, brown, and cracked, the features looked shrivelled, and the complexion had assumed a dirty, sallow hue. The mitral murmur, which was audible on admission, had increased in intensity, and a systolic bruit was now present over the aortic area. Numerous rhonchi and moist râles could be heard over the right lung, and there was a friction sound over the anterior part of the base of the left lung.

Six days later, on April 14th, the patient was practically moribund, and was apparently only kept alive by repeated injections of strychnine. There was complete unconsciousness; the mouth was foul, sordes covered the lips, the pulse was feeble, and varied in rate from 132 to 140 beats a minute; there were signs of œdema at the base of the right lung, and the friction sound at the left base had been replaced by the indications of a moderate effusion into the pleural cavity. A little turbid fluid which had been withdrawn from the chest showed a few gonococci enclosed in pus cells.

In this desperate condition 10 c.c. of the antistreptococcus serum, prepared by Burroughs Wellcome and Co., were injected into the rectum.

The following day, to our surprise, the patient was still alive, and was able to swallow a little nourishment. The temperature had fallen one degree and a half, but the pulse rate had not diminished. Another injection of the serum was therefore given.

At midday on the third day after the first injection, or approximately after the lapse of sixty-six hours, it was noted that the temperature, which had been rapidly falling since the second injection, was now subnormal. The pulse was 108 and the respirations 34 per minute. For the first time the patient was quite conscious, and

able both to speak and to swallow liquid nourishment with ease. The motions were no longer passed into the bed, and a wonderful improvement had taken place in the facial expression.

Although the temperature rose again the next day to 100° F., and continued about this point for nearly a fortnight, this febrile condition appeared to depend solely upon the pleuritic effusion, since it gradually declined as the latter became absorbed, and in no way retarded the rapid progress of convalescence. In all three doses of the serum were administered by the rectum within five days. Upon her return to consciousness the patient complained of some pain and stiffness in the affected joints, but within a few days these sensations disappeared along with the signs of swelling and effusion.

The only trouble during convalescence was insomnia, which proved very intractable, and had not entirely disappeared when the patient was discharged from the hospital on July 1st. In the last note upon the case it was observed that the apex of the heart was beating forcibly in the nipple line, and that the mitral murmur was still audible, though not so loud as it had been during the crisis of the illness. The aortic bruit, on the other hand, had disappeared. Deficient expansion of the lower half of the left chest, with enfeeblement of the vesicular murmur, pointed to adhesion of the two surfaces of the pleura in this region, and the urine still contained a trace of albumin, and had a specific gravity of 1012. The vaginal discharge had quite ceased.

Case 2.—A girl, aged 18 years, was admitted into the London Temperance Hospital on October 9th, 1903, for what was supposed to be acute rheumatism. None of her relatives had suffered from the complaint, and she had been quite healthy previously, with the exception of an attack of anæmia.

The present illness commenced a week before admission, with pains in the body and limbs accompanied by fever.

On examination the pains were found to be chiefly referred to the right knee, ankles, and wrists, the knee-joint containing a small quantity of fluid, while the other joints were enlarged and extremely painful. There was also complaint of pain in the lower part of the back and abdomen. The skin was dry, the tongue furred, and the temp. 100·5° F. The heart, lungs, and other organs of the body were apparently healthy.

The ordinary treatment of acute rheumatism was adopted, but in spite of the large doses of salicylate of sodium and other remedies, the condition of the joints grew steadily worse, and the temperature rose until at the end of eleven days it registered 103·2° F. In the meantime it had been discovered that the girl was suffering from gonorrhœa of several weeks' duration, and numerous gonococci had been found in the vaginal secretion. This condition was treated by local injections.

On October 21st, eleven days after admission, pleurisy developed at the base of the left chest, and a soft systolic bruit became audible over the mitral area of the heart. The administration of large doses of iodide of potassium combined with quinine produced no effect upon the course of the disease, pleurisy developing at the right base on October 23rd, while a pericardial friction appeared on October 24th. Small quantities of turbid serum withdrawn from the left pleura and from the right knee-joint were found to contain gonococci, and the urine presented one-tenth of albumin.

From this time onward the general condition of the patient grew rapidly worse; the temperature continued to range between 103° and 104°, the pulse-rate exceeded 130 beats per minute, and it was found impossible to move the girl in bed without inducing excessive pain in the affected joints. On November 3rd, when all other remedies had failed and the patient appeared to be sinking, 10 c.c. of the antistreptococcus serum prepared at the Wellcome Laboratories were injected into the rectum, and the dose repeated each day for a fortnight. After the second

injection the patient expressed herself as feeling much better, the pain and swelling of the joints rapidly subsided, the appetite and sleep returned, and, in spite of the effusions into the pleuræ and the pericardium, the pulse-rate and the temperature steadily diminished, until, on the thirteenth day after the first injection, they had both regained their normal state.

The patient made an uninterrupted recovery, but when discharged from the hospital there was evidence of some enlargement of the left ventricle, and a soft mitral systolic bruit was still audible at the apex of the heart.

The next two cases were examples of gonorrhœal arthritis.

Case 3.—A man, aged 32 years, was admitted into the London Temperance Hospital on May 29th, 1905, suffering from rheumatism.

It appeared from his history he had contracted gonorrhœa in India in 1898, and that a few weeks later he had been seized with severe "rheumatism" in the knees, ankles, and wrists, which had caused him to be invalided for nearly six months. Since that time he had frequently suffered from transient pains in the joints previously affected. The present attack commenced five weeks before his admission to the hospital, during the whole of which time he had been confined to bed. The right wrist and the ankle upon the same side were the first joints to become swollen and painful, but after the lapse of a few days the left knee and shoulder and the left temporo-maxillary joint also became involved. Careful inquiry elicited the fact, not previously divulged, that about three weeks before the onset of the rheumatism he had again contracted gonorrhœa and was still suffering from a urethral discharge.

On admission the temperature was 99° F., and the pulse-rate 84 per minute. The right wrist was enlarged, the dorsum of the hand was much swollen and œdematous, and this condition also extended for three inches up the

back of the forearm. Great pain was experienced if the joint was touched, and the patient was unable to move either the wrist or the metacarpo-phalangeal articulations. The right ankle was swollen, rigid, and tender, and the dorsum of the foot was œdematous. The left knee was enlarged and contained an appreciable quantity of fluid, and the left temporo-maxillary joint was swollen and so painful that mastication was almost impossible. The movements of the left shoulder were restricted, and manipulation was very painful. The heart and other organs of the body were healthy. The purulent discharge from the urethra contained gonococci.

For three weeks the patient was treated by large doses of iodide of potassium and quinine, it having been ascertained that, previous to admission, salicylate of sodium had been given without success, and each joint was subjected to radiant heat for half an hour daily. Local injections were employed for the urethral complaint.

On June 23rd, eight weeks after the onset of the rheumatism, it was noted that the patient felt no better, and that the condition of the joints was practically the same. The right knee had also become swollen and painful. The temperature of the body varied at night from 99·5° to 100·2°, being subnormal in the morning. The lips and conjunctivæ were markedly anæmic, the appetite was bad, and the man suffered much from loss of sleep and mental depression. The injections had improved, but not cured, the urethral discharge. It was, therefore, determined to stop all the treatment hitherto employed, and to inject 10 c.c. of the antistreptococcus serum from the Wellcome Laboratories into the rectum each day. Three days later, after four doses had been administered in this manner, the following note was made:—"The patient states that for the last twenty-four hours the pain in the joints has practically disappeared, and for two nights he has enjoyed excellent sleep. The appetite has improved, and he is now able to masticate with only little discomfort. The swelling and œdema of the right wrist joint has

almost subsided, and the extensor tendons upon the back of the hand are plainly visible. Although the various joints are said to feel stiff, he is able to flex and extend the hand to a perceptible degree, and to bend the fingers until the first phalanges form almost a right angle with the metacarpal bones. No fluid can be detected in the left knee-joint, and passive movements of the legs upon the thighs are not attended by pain. The tenderness and swelling of the right ankle and left temporo-maxillary joints have greatly diminished, and the urethral discharge has practically ceased. The temperature is still slightly elevated at night." No more injections of the serum were given, but the patient was put upon a full diet, while massage was ordered to the stiff joints. A week later he was able to walk about the ward without discomfort, and was discharged cured on July 18th.

CASE 4.—A married woman, aged 28 years, was admitted into the hospital on May 31st, 1905, suffering from pain and swelling of the wrists, ankles, and knees. Her history showed that two years previously she had had an attack of gonorrhœa, followed by severe "rheumatism," which had confined her to bed for six weeks. She had also been laid up with two attacks of "peritonitis." The present illness commenced, in the same manner as on the former occasion, with a purulent discharge from the vagina, and swelling of the wrists and left ankle, the pain of which had prevented her from walking for a fortnight.

On admission she still had a profuse discharge, in which numerous gonococci were found. The temperature was 100·1°, and the pulse-rate 88; the appetite was bad, and the pain in the joints interfered with her rest at night. Both wrist-joints were swollen and tender, and a puffy swelling extended several inches up the extensor surfaces of the forearms. The movements of the fingers were much impaired, and any attempt to flex or extend the wrist-joints gave rise to great pain. The left

ankle was also swollen and tender, and a little fluid was present in the left knee. A trace of albumin existed in the urine.

The treatment adopted consisted of antiseptic vaginal douches, followed by swabbings with a 2 per cent. solution of protargol, while internally large doses of salicylate of sodium, combined with quinine, were employed. The affected joints were also exposed for half an hour each day to radiant heat. The temperature fell to normal on the eleventh day of her residence in the hospital, and the vaginal discharge diminished, but the condition of the joints remained unaffected, while the right knee and right ankle also became swollen and tender. Subsequently the radiant heat was replaced by soda fomentations, and calomel and iodide of potassium substituted for the quinine and salicylate of sodium. At the end of another fortnight, practically no improvement having taken place in the condition of the joints, it was resolved to try the anti-streptococcus serum, and accordingly 10 c.c. were injected into the rectum every alternate day for six days. On the sixth day it was noted that the pain had almost disappeared from the ankles and knees, that the swelling of the wrists and forearms had subsided, and that, although the joints felt stiff and were inclined to ache towards evening, both active and passive movements could be undertaken without much discomfort. The treatment was continued for another week, at the end of which time the patient was able to walk about and use her hands without difficulty. She was discharged cured a fortnight later.

We have selected these two cases because they were not only exceptionally severe, but also represented a second attack of the complaint. In both instances the disease progressed during the patient's residence in the hospital, and the pain and swelling of the joints first affected were in no way relieved by three weeks' assiduous attention to the original complaint and the adoption of the ordinary methods of treatment of gonorrhœal rheu-

matism. In both instances, also, the effects of the injection of the serum were immediate, and more striking than the mere notes of the case would indicate, the pain being relieved after the second dose, and the tenderness and swelling rapidly subsiding after the third. The rectal injections being administered by a nurse, the patients were quite unaware that anything unusual in the way of treatment was in progress.

The fact that in the various cases we had treated in this manner the urethral discharge disappeared along with the other phenomena of the complaint naturally suggested that acute gonorrhœa might also respond to the serum. Unfortunately, however, considerable difficulty was experienced in inducing suitable cases to become in-patients at the hospital or to attend each day at the casualty department so as to permit the effects of the treatment to be carefully watched, but the results obtained in the few cases we have treated, of which the following is an example, permit us to hope that the serum will prove as valuable in the urethral complaint as in its sequelæ.

Case 5.—A man, aged 28 years, was admitted into the hospital in September, 1905, with acute gonorrhœa. He stated that nine days previously he had exposed himself to infection, and that five days later (or four days before admission) he had experienced a sense of heat and discomfort in the penis and perinæum, which was followed by severe scalding upon micturition and a discharge. He had had a similar attack four years previously.

On admission the penis was found to be much swollen, the lips of the meatus inflamed, and the prepuce œdematous. The inguinal glands on either side were enlarged and tender, and numerous gonococci were present in the purulent discharge from the urethra. The patient was ordered to remain in bed, and 20 c.c. of the antistreptococcus serum were injected into the rectum, and another dose of 10 c.c. was administered on the following morning.

No other treatment was adopted. After the lapse of three days, during which four injections had been given, the œdema of the prepuce was found to have disappeared, and only a drop of thick pus could be squeezed from the urethra. Two other injections were given in the course of the next week, during which time, with the exception of a little discomfort after micturition and an occasional erection at night, the man professed himself quite well. No discharge could be detected upon the lint with which the penis was kept covered, and only occasionally could a bead of pus be squeezed out.

The following cases were examples of purpura hæmorrhagica. In the first the condition was associated with chronic phthisis, and was one of the most severe and rapid that we have ever encountered. In the second all the organs of the body were apparently healthy, but since the child came under treatment as early as the second day of the complaint, it is impossible to say what course the disease would have taken. The fact, however, that after the lapse of twenty-four hours severe hæmaturia and bleeding from the mouth had set in, seems to indicate that the case would have proved a serious one.

Case 6.—A warehouse porter, aged 22, was admitted into the hospital on June 17th, 1905. He stated that he had suffered from cough and expectoration for about six months, and had lost much flesh during that time. There had been no hæmoptysis. On June 15th, two days before admission, he had felt ill, and blood had begun to issue from his mouth, while numerous red spots had appeared upon the legs and body. On the following day the urine contained blood, and he experienced great weakness. On the day of admission he had passed blood by the bowel.

When examined in bed the patient was found to be anæmic and very weak. The temperature was 97·2°, the pulse 106, the respirations 34. There were signs of consolidation of the upper lobe of the left lung, while rhonchi

and moist râles could be heard over both bases. The expectoration was moderate in amount, muco-purulent, and contained numerous tubercle bacilli. A loud systolic bruit was audible over the pulmonary area of the heart. Scattered over the whole of the body, but most profuse on the extremities, were purpuric spots, varying from the size of a pin's head to that of a sixpence, while here and there large ecchymoses could be observed.

The mucous surfaces of the tongue, lips, gums, and palate were pale, and covered with petechiæ of various sizes, some of which, near the roots of the teeth, were obscured by black crusts, from which blood constantly dripped into the mouth. There was also a discharge of blood from the nose. The urine, which was passed with some difficulty, was dark brown in colour, became almost solid when boiled, and deposited a vast number of red blood-corpuscles. Several loose stools, consisting almost entirely of altered blood, were voided, but there was no vomiting. A blood-count on admission indicated 60 per cent. red corpuscles, with about the normal number of leucocytes. There was no œdema. The patient was ordered a milk diet, the bleeding spots in the mouth were painted with adrenalin chloride, and a pill containing gallic acid and opium was administered every three hours. The following day the man appeared to be much worse, and suffered greatly from dyspnœa, but no change could be detected in the pulmonary signs. Numerous fresh hæmorrhages had appeared in the skin, and the bleeding from the nose, mouth, bowel, and kidneys was more profuse. The following day it was obvious that a fatal termination was rapidly approaching. The face was blanched, the pulse feeble and intermittent, and partial consciousness alternated with periods of muttering delirium. The hæmorrhages continued unchecked, and œdema of the feet and dependent parts of the body had supervened. The breath was also horribly offensive, and the gums were covered with black scabs, which bled profusely. Although no hope was entertained of doing good, it was determined to

pursue our usual practice of testing the effects of the antistreptococcus serum, and accordingly ten cubic centimetres were injected into the rectum. At 6 p.m., as the patient was still alive, the dose was repeated. The following morning, to our great surprise, the man was not only alive, but wonderfully better. The urine passed after a fair night's rest contained much less blood, the bleeding from the gums had almost ceased, very little altered blood had been voided by the bowel, and the pulse had improved in tension while the rate per minute had fallen to ninety-six. Encouraged by these symptoms of improvement, two more doses of the serum, of similar quantity, were injected into the bowel during the day.

The next day the temperature had risen to 99°, and the pulse rate had declined to 90. The bleeding from the mouth, nose, and bowel had entirely ceased, and many of the crusts upon the gums had separated, leaving the subjacent mucous membrane pale, but devoid of ulceration. The bowels had not acted, and the urine presented only a slightly smoky appearance. Two more injections were given, and a semi-solid diet allowed. On June 23rd, five and a half days after his admission, the patient appeared to be convalescent from his dangerous malady. The purpuric eruption was rapidly disappearing, the mouth was clean, and the hæmorrhages had entirely ceased. No more serum was therefore given, but an iron mixture was ordered and a full diet permitted. The blood-serum tubes which had been inoculated with blood abstracted from the arm on the patient's admission exhibited no bacterial growth. From this time onwards the tubercular mischief in the left lung developed somewhat rapidly, and a month later the case was discharged with the signs of a cavity in the upper lobe, but without any recurrence of the purpura.

The fact that the injection of the antistreptococcus serum in this case had synchronised with a rapid cessation of the hæmorrhage at a time when death seemed to be only a question of a few hours made us resolve to try the serum

again upon the next case of the kind that was admitted into the hospital. This opportunity occurred on September 19th, 1905.

CASE 7.—The patient in question was a girl, aged 10 years, who had enjoyed excellent health until two days previously, when she complained of pains in the back and limbs, lost her appetite, and looked ill. The next day the mother discovered many bright red spots upon the abdomen and legs, and found that the urine contained blood. There was also some spitting of blood. There had been no rheumatism in the family, and no cause could be assigned to the child's sudden illness.

On admission the girl was found to be very pale; the temperature was 99·5°, the pulse 96, and the respirations 24. The heart, lungs, and other organs of the body were apparently healthy. Several small petechiæ were present on the surfaces of the tongue and palate, while upon the inner surface of the upper lip on the left side, as well as upon the gum in contact with it, there were large black scabs, which bled spontaneously and freely.

There was a profuse purpuric eruption upon the legs, arms, back, and lower part of the abdomen, intermixed with ecchymoses about the size of a shilling. The urine was deeply coloured with blood, and deposited red corpuscles on standing. The bowels had not acted for twenty-four hours, and there was neither epistaxis nor hæmoptysis.

The next morning the purpuric spots were much more numerous, the hæmaturia was severe, and the child was evidently losing much blood from the mouth. It was therefore decided to try the antistreptococcus serum at once, and accordingly ten cubic centimetres were injected into the bowel, and a second dose administered in the evening. The following morning the hæmorrhage from the gums had ceased, and the urine was just coloured with blood. No more purpuric spots had appeared, and those previously existent were undergoing resolution.

One more dose of the serum was administered, and on the next day it was found that the black crusts upon the lips and gums had disappeared, while the urine only contained a minute quantity of blood. Convalescence was uneventful, and the child was discharged cured on October 10th.

As soon as we had assured ourselves that the antistreptococcus serum exerted an important influence upon gonorrhœal infections, we instituted a series of control experiments by means of simple enemata and rectal injections of the antidiphtheritic and other sera, while, at the suggestion of Dr. Dowson, who kindly provided us with the material for the purpose, normal horse serum in doses of 20 c.c. was likewise employed.

In no instance did the patients experience any relief of their symptoms as the result of these experiments, nor did the physical signs of the disease, in any way, improve until the antistreptococcus serum was substituted for the other forms of injection. The antigonococcus serum, specially prepared at the Wellcome Research Laboratories for the treatment of gonorrhœa, also proved of no value in our hands. In addition to the ordinary joint lesions of gonorrhœal origin we have met with several cases in which the inflammatory trouble was chiefly situated in the muscles of the lumbar region and spine. In two well-marked instances of this description, where the patients had been confined to bed for three and five weeks respectively, and were unable either to raise themselves or to turn over owing to the severity of the pain which such movements induced, three doses of the antistreptococcus serum completely removed the complaint, so that on the fourth day they were able to get up and walk about without experiencing anything worse than slight stiffness of the muscles of the back. We might add that during the last two years we have never encountered a genuine example of gonorrhœal rheumatism, either in hospital or private practice, that was not immediately benefited by an injection of the serum, nor any case which has suffered from a relapse.

In addition to its positive value in the treatment of gonorrhœal infections, we have had several opportunities of proving the negative use of the serum in diagnosis. Thus, in the case of a young woman who was admitted into the hospital suffering from gonorrhœa, associated with severe pains in the left ankle, right knee, and right hip, it was found that, while two injections of the anti-streptococcus serum into the rectum were followed immediately by a subsidence of the trouble in the ankle, and an alleviation of the vaginal discharge, the pain of the hip and knee continued unabated. Subsequent events proved that, in addition to the gonorrhœal affection, the patient was the subject of an acute tuberculous disease of the right hip-joint which necessitated surgical treatment.

We have laid stress upon the rectal administration of the serum because we think that the practical utility of this method has been greatly overlooked. For the last six years it has been our invariable custom both at the Temperance Hospital and in private practice to inject all varieties of serum into the bowel by means of a simple glass syringe, and we can safely assert that in not a single instance has the method proved inferior either in efficacy or rapidity of action to the usual mode of subcutaneous injection. But although its use in hospital cases may only be a matter of convenience, the value of the method in private practice can hardly be over-estimated, for not only does its adoption obviate the necessity of a special syringe with its constant sterilisation and other antiseptic precautions, but both the pain of the injection and the mental perturbation so often experienced by the patients and friends at what they term "the operation" are done away with. Moreover, in a suspicious case of inflammation of the throat, as well as in any other condition where an experimental employment of a serum may seem advisable, a dose can be given by the bowel without creating the alarm or inconvenient inquiry which the hypodermic injection usually calls forth.

It is worthy of notice that we have never obtained any

results from injections of the serum into the urethra, either in acute gonorrhœa or its sequelæ, from which fact it is probable that should the serum prove of value in gonorrhœal ophthalmia it will be by absorption into the general circulation and not by its local application.

It may also have been remarked that the term "an" antistreptococcus serum has been employed instead of a more general appellation. The reason for this is that there are at least seven varieties of antistreptococcus serum on the market, but it has only been with one of these, namely, that prepared at the Wellcome Research Laboratories, that we obtained the results we have mentioned. By this we do not mean to infer that the other forms are useless, but that this particular preparation has been the one with which we have obtained the best results, and upon which we now entirely rely. We are informed by Dr. Dowson, the Director of the Wellcome Laboratories at Herne Hill, that this special preparation is termed by them the "polyvalent" antistreptococcus serum, in order to distinguish it from several other varieties prepared at the same laboratories, and that in its manufacture forty-three different strains of streptococcus are employed, taken from such diverse clinical conditions as septicæmia, ulcerative endocarditis, puerperal fever, malignant sore throat, and acute rheumatism.

With this shot-gun remedy it is naturally impossible to determine whether the effects of the serum are due to one or all of the strains of the micro-organism, and we have consequently been obliged to remain content that every effort will be made to perpetuate the different cultures until the value of the treatment has been definitely ascertained.

With regard to the dosage of the serum we have found that double the ordinary amount (namely, 20 c.c.) followed by three or four injections of 10 c.c. each on consecutive days is usually sufficient in the majority of cases, it being only in gonorrhœal pyæmia and in severe examples of

hæmorrhagica purpura that two injections a day are necessary.

We have never seen any abnormal symptoms ensue from the use of the serum, with the possible exception of a slight elevation of temperature, and no eruption upon the skin has been observed to follow an injection. When the serum exerts a beneficial influence it always does so within three days.

It is interesting to note that since this paper was written we have been informed by Dr. Dowson, who had kindly undertaken some experiments for us with reference to the cultivation of the gonococcus, that he had found, to his great surprise, that while the micro-organism readily grew in a medium to which the antigonococcus serum had been added, it failed to grow in the presence of one of the other sera prepared at the laboratories, and that this serum was the antistreptococcus serum. A second series of experiments undertaken upon the same lines has produced even more striking results.

We adduce no theories to explain the results we have brought to your notice; we are conscious that the number of cases at our disposal is too small to permit of anything more than a hopeful conclusion being drawn from them; but we feel sure that a careful and extended examination of the subject at the hands of the Fellows of this Society will prove that many, if not all, gonorrhœal infections derive immediate benefit from rectal injections of this polyvalent antistreptococcus serum, and that at least one variety of hæmorrhagic purpura is capable of cure by a similar method of treatment.

DISCUSSION.

Mr. STEPHEN PAGET described a personal experience of an injection of antistreptococcus serum, one of the first in this country, for an infection acquired at an operation for septic peritonitis. It seemed to be of no importance in the cases recorded in the paper whether the serum was used in an acute or chronic gonorrhœal infection. Was its value in purpura hæmorrhagica ascribed to the same mechanism as in septic infections? Had it ever been tried in any case of hæmophilia?

Mr. CAMPBELL WILLIAMS alluded to the fallaciousness of the term gonorrhœal rheumatism, since arthritis of a genital or urethral origin was not necessarily due to the gonococcus. It might result from ordinary sepsis. There were three varieties or symptoms of the complaint. First, the cellulitic, which appeared like a streptococcic infection, having the aspect of threatening suppuration; but an incision yielded only a little serum with, perchance, a few flakes of lymph in it. In this form the serum would probably be more than useful. Secondly, one got the arthritic form, either hydrops alone, or with marked implication of the soft tissues. And, thirdly, the arthralgic variety. In this there was no swelling, but only pain—subjective, not objective symptoms. Neuritis and periostitis fell into this category. The arthralgic form was possibly due to a circulating toxin acting on fibrous tissue, in contradistinction to the actual presence of transported micro-organisms in the tissues. The paper bore out the idea that the so-called gonorrhœal rheumatism was a condition which might be sequent to the action of various, or even mixed, germs, thus explaining the good effect of the polyvalent serum. It seemed that absorption through the rectum into the blood induced a change in the serum, which conferred upon it its lethal influence over the micro-organisms, since the direct contact of the serum in the urethra failed to affect them. He alluded to two cases of gonorrhœal rheumatism which followed puncture of œdematous prepuces. Vaginal arthritis after operation was a comparable condition. The method seemed to be a valuable one and worthy of extended trial, even in such conditions as gonorrhœal salpingitis.

Mr. P. LOCKHART MUMMERY supported the method of giving the serum by rectal injection, and alluded to the value of serum injections in preventing sepsis after operations, in which septic

infections were likely to arise, as in excision of the rectum, or operations on the mouth. The great difficulty in treating gonorrhœa was in its later stages, in the condition of gleet, and the authors of the paper had not mentioned the subsequent condition of the patients treated by serum injections. Before pronouncing any case of gonorrhœa as cured it was necessary to make certain that no gleet was left.

Dr. PORTER PARKINSON, in reply, said there was no special preparation of the rectum beyond its being washed out. The serum had not been tried by them in hæmophilia. Purpura they had considered to be due to toxins or micro-organisms. In two of the cases the gonococcus, and that alone, was found both in the urethral discharge and in the pleura. The serum might be of use in gonorrhœal ophthalmia.

CAPILLARY CIRCULATION AND BLOOD-PRESSURE AND THE CONDITIONS THAT CONTROL THEM

BY

ALEXANDER HAIG, M.D.

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A FEW hours, or even moments, of clinical observation suffice to show that there is a definite relation between capillary circulation and blood-pressure. In one bed in a ward we may see (let us say) quick capillary circulation and subnormal blood-pressure with a temperature of 102°, and in the next may be found very slow capillary circulation and high blood-pressure with subnormal temperature in a case of Bright's disease. But in every case and in all conditions there is similar, though less marked relation between capillary circulation and blood-pressure, and I propose in this paper to consider this relation, its causes and effects, and some of the conditions which it helps us to understand and control.

In the cases just mentioned it is clear that the low blood-pressure cannot be the cause of the quick capillary circulation, and equally clear that the high blood-pressure cannot be the cause of the slow capillary circulation, because the arteries in which this high blood-pressure is found are not contracted, thus shutting off the blood, but are

more than usually dilated, as is easily shown by measuring them in one condition or the other. There remain, then, I think, only two possibilities: (1) that certain vessels between the capillaries and the artery are contracted, causing high blood-pressure behind them, thus shutting off the rush of the blood from the capillaries and causing slow capillary circulation; or (2) that there is an obstruction in the capillaries themselves which effects high blood-pressure in all the vessels between these capillaries and the heart which is driving blood towards them.

It may be remembered from some of my other writings that Raynaud's observation of the conditions of circulation in the disease which bears his name, first directed my attention to measuring the rate of the capillary circulation in the skin; and that Raynaud showed the obstruction was neither in the arteries nor veins, but in the capillaries. It is easy to see the obstruction is not in the veins, for venous obstruction (*e. g.* thrombosis) causes a quickening and not a slowing of the capillary circulation. That it is not in the arterioles is perhaps more difficult to demonstrate, but I shall now give some reasons for suggesting that obstruction in the arterioles will not explain all the phenomena with which we have to deal. Raynaud believed the local troubles of which he wrote were probably due to spasm of the small vessels or capillaries affecting the surfaces and extremities, but there can be, I think, no doubt for those who have investigated this disease with care that circulation all over the body is similarly defective and the defect is not confined to any one part, though that part, owing to local cooling (the effects of which I shall treat later), might pass into gangrene. But there is evidence (and Raynaud himself mentions such evidence) that the defective circulation acts, not only on surfaces and extremities, but also on the internal organs, *e. g.* the kidneys.

In the smaller arteries, just as in the larger, we get a thickening of the muscle coats which might be attributed to their constant work in keeping up by contraction the

high blood-pressure; but in the small arteries, *e. g.* in the brain, there is often obvious dilatation and hypertrophy, not only of the muscle coats, but also of the fibrous coats outside these, though this, however, can only be a reaction against pressure from within. It is obvious, then, that the smallest arteries, equally with the large ones, are engaged in resisting pressure, not in producing it, and that in small and large alike there is some dilatation as the result of their inability to overcome this pressure. If the small arterioles were causing high blood-pressure, it is obvious that there would be no need of hypertrophy of their outer fibrous coat, as the high blood-pressure would be all inside the muscles. But if, on the other hand, the small arteries are, equally with the large vessels and the heart, engaged in overcoming pressure, then there is need for hypertrophy of their outer fibrous coat to aid the muscles in their struggle, and to some extent relieve their work. It is thus clear that the obstruction is not in the arteries or arterioles and not in the veins, but, as Raynaud said, in the capillaries.

What, then, is the nature of this capillary obstruction? It cannot be muscular, for the capillaries have no muscles, and we are confronted with the only remaining possibility, namely, that it is mechanical and due to some condition in the blood itself which hinders its passage through the smallest vessels. Again, Raynaud's disease is spasmodic; that is, it may completely disappear and leave no effect behind. It cannot, therefore, be due to structural defects in any vessel. Further, it is difficult to believe (supposing it due to muscular spasm) that any muscle could remain contracted till the tissue of which it forms part passes into gangrene; for surely a muscle must relax before this stage is reached as the result of failing nutrition? Later on we shall see that all these difficulties disappear if the possibility of a mechanical obstruction of capillaries by a condition of the blood itself is admitted. We shall also recognise the reason why Raynaud's disease is limited to surfaces and extremities, a fact almost certainly fatal to the hypothesis of this trouble as originating in the nerve centres; for the

same nerves are often distributed both to the surface and the deep tissues, and yet the disease is limited to the former. We shall also understand why it is paroxysmal, as this character establishes its identity of causation with migraine and other paroxysmal troubles due to similar circulation changes similarly produced. Some years ago, on arriving at this point, I observed in my investigations of migraine that high blood-pressure in that trouble was always associated with excess of uric acid in the blood and urine, and low blood-pressure, with its more or less complete absence from both. Further investigation extended this observation to all conditions, so that what I had found in migraine was but one instance of an invariable law. I next investigated the matter by means of an artificial circulation and found that uric acid in colloid form blocked the capillaries more than any other substance which I could suspend in the circulated fluid. Indeed, it was the great difficulty met with in separating this colloid substance from the urine by filtration which led me to suppose that uric acid might block the lumen of the capillaries in the same way as I constantly saw it blocking the interstices of the filter.

When we remember that in the more severe conditions of collæmia uric acid can be precipitated in the blood drawn from the vessels in bulk equal to one fourth or even one third of that of the red cells, we have no difficulty in believing that a viscid colloidal substance (though more or less invisible till a precipitant is used) must, nevertheless, when present in such quantities, greatly affect the viscosity of the blood and hinder the passage of both cells and plasma through the more minute capillaries. It can hardly be mere chance that in all conditions where we find slow capillary circulation there is excess of uric acid in the blood, and that in all conditions where rapid capillary circulation exists there is more or less complete absence of this substance. This relation is also susceptible of very simple demonstration, for it is an easy matter to alter the quantity of uric acid in the blood in either direction either by administering uric acid itself or by drugs

which alter the solvent power of the blood and so increase or diminish the amount of uric acid held in solution. In all these conditions (as can be demonstrated in a few hours in a number of cases) everything that increases the quantity of uric acid in the blood slows the capillary circulation, and everything that diminishes the quantity quickens it.

In this paper, therefore, I propose to treat two points: (1) the constant relation between the quantity of uric acid in the blood, the rate of the capillary circulation, and the height of the blood-pressure, which latter is partly dependent upon the rate of the capillary circulation; and (2) the clinical and pathological phenomena which this correlation enables us to understand and, to a large extent, to control.

Having noticed this correlation of capillary circulation and the quantity of uric acid in the blood and urine, and having further found that by controlling the uric acid in these I was able to alter the former, I looked round for a method of measuring that circulation accurately. I first of all began to watch the capillary circulation in the eye, as it affected the function of that organ in recovering from fatigue, and this resulted in my finding that the rate of disappearance of the "fatigue image" varied from morning to evening with the amount of uric acid in the blood, the "fatigue image" always disappearing more slowly in the morning hours when capillary circulation is slowest and the blood contains most uric acid, and disappearing more quickly in the evening hours when capillary circulation is quickest and the blood contains least uric acid. But this, as will be seen from my book, was a difficult process to carry out, and depended largely on the individual factor, as it could only be seen by the person operating, and not by others. While considering this I noticed Raynaud's observation that the capillary circulation in his disease was extremely slow, so that a pale spot on the surface produced by pressure might take as long as thirty seconds to recover its colour. I saw this was exactly the test I wanted, and concluded that if Raynaud's disease were

(as I had every reason to believe) due to excess of uric acid in the blood, I could probably find out, by careful measurement of the rate of capillary circulation, the power of the resisting force in other conditions, and thus ascertain whether it corresponded with the amount of uric acid in the blood. It then became clear that the only thing necessary was to apply a known pressure to a known surface for a calculated time, and to watch the return of the colour, accurately measuring the duration of the return process. It was also necessary that this should be done with the skin at the normal temperature of the body and on a level with the heart, since either above or below that level (as at the end of a dependent extremity) the time of the return of the colour altered. The instruments I adopted for this purpose were simply an inverted spring balance, by which I could obtain a known surface and pressure, and a metronome set to beat half-seconds, and all my work on the capillary circulation in recent years has been carried out with these instruments. I had previously been measuring blood-pressure for a number of years with various instruments, but was not long in discovering that this bore constant relation to the capillary circulation, and that, given a normal heart, the slower the capillary circulation the higher would be the blood-pressure and *vice versâ*. The methods which I now use for estimating the blood-pressure are—(1) three fingers, educated by more or less constant practice; and (2) a sphygometer as invented by Dr. Hill and Mr. Barnard; and besides these there are the alterations of the heart-sounds, which are practically constant in their relation to high blood-pressure, and give of themselves quite sufficient evidence of the conditions present. With regard to the educated finger, I may say that in working with an instrument like that of Hill and Barnard it is possible, in course of time, to train the fingers to estimate pretty accurately the small changes in pressure. It is therefore my constant practice to estimate blood-pressure with my finger, writing down the result before I apply the instrument; and it is not often, when due care

is exercised, that there is much difference between their records. I had previously obtained very similar results with Dr. Oliver's instrument for measuring the size of the artery, and this also demonstrated that with slow capillary circulation there was always an enlargement of the artery corresponding to the increase of blood-pressure, so that there are really a great number of ways of measuring these changes in capillary circulation and their results.

With regard to the sounds of the heart which accompany slow capillary circulation and its resulting high blood-pressure, I may briefly say that the first sound is more or less prolonged, the prolongation at times becoming a distinct re-duplication, and that this alteration is best heard at a point midway between the apex beat and the lower end of the sternum. The other important alteration is a marked increase both in the loudness and sharpness of the second sound, especially at the right base, and in certain conditions there is more or less re-duplication of the second sound also, owing, I believe, to difference of pressure in the pulmonary and systemic circulation, which causes the valves on the two sides to close at somewhat different rates. It is, then, recognisable that there is a correlation between capillary circulation and blood-pressure, slow capillary circulation practically always accompanying high blood-pressure and quick capillary circulation low blood-pressure. In physiological conditions we meet with relatively slow capillary circulation in the morning hours, from five or six a.m. up to ten or eleven a.m., and with relatively quick capillary circulation in the evening hours, from seven or eight up to eleven or twelve, or later, and in the same way blood-pressure is higher in the morning and lower in the evening. Under normal morning conditions in those who live on uric-acid-free foods capillary circulation takes about six half-seconds to restore the colour in a white patch, out of which the blood has been pressed, by the application of fifteen ounces of pressure applied for six half-seconds, and with this, supposing the heart to be normal, there should generally be found a blood-pressure

of 120 mm. of mercury. In the evening the capillary reflux would be found to be somewhere about five half-seconds, or slightly less, and the corresponding blood-pressure about 100 mm. of mercury. In pathology it may be stated generally that all conditions in which there is a large amount of uric acid in the blood (*e. g.* chronic gout, Bright's disease, diabetes, etc.) the capillary reflux may be as slow as ten, twelve, or fourteen half-seconds, and, while the heart remains strong, a blood-pressure corresponding to this will be somewhere about from 150 to 180 or even 200 mm. of mercury. In the opposite pathological conditions of fever, where there is almost no uric acid in the blood, the capillary reflux may be very quick indeed, only two or three half-seconds, and the higher the temperature the quicker (other things equal) will the reflux be, but even a temperature of 99° or 100° will quicken the reflux to four or five half-seconds. The blood-pressure in the early stage of fever corresponding with the very quick capillary reflux will generally be found about 70 or 80 mm. of mercury.

There are certain pathological conditions, however, which form exceptions to the rule just mentioned, and some of these are extremely instructive. If the heart is weak it is obvious that with the same amount of obstruction in the capillaries the capillary reflux will be slower than when the heart is strong. I mention this because, apart from weakness of the heart, it is generally possible to tell pretty accurately what the blood-pressure will be from the capillary reflux; that is to say, with a capillary reflux of seven or eight one would expect to find a blood-pressure of 150, but if the heart is weak we may get a capillary reflux of seven or eight, with a blood-pressure of only 130. I give these figures as merely approximate, and to illustrate my main points, but it is necessary to bear in mind the condition of the heart, otherwise we may draw a totally wrong inference from the rate of the capillary reflux alone. On the other hand, it is possible, by measuring both the capillary reflux and the corresponding blood-

pressure, to tell whether the heart is or is not weak. If we have a capillary reflux which would lead us to expect a blood-pressure of 150, but, on measuring the blood-pressure, we find it to be only 120 or 130, we must infer that the heart is weak, and look for other signs of this condition, such as increased rate of action and changes in the heart-sounds.

Again, any blocking of the veins beyond the capillaries will, other things being equal, increase the rate of the capillary reflux. Thus a tight sleeve, or (still more) thrombosis, will greatly quicken the capillary reflux in the limb on the affected side. To give figures, a capillary reflux of six or seven on the arm of the unobstructed side will be contrasted with one of four or five on the side where the vein is obstructed, and those who wear tight sleeves often have the capillary reflux very decidedly quickened in their hands, so that the record from the hands is of little or no value in these cases. The only trustworthy record is that to be obtained on the front of the chest on a level with the heart, and at the natural temperature. Local inflammation of all kinds also greatly increases the rapidity of the capillary reflux at the seat of inflammation. and this is very interesting, as it may be remembered that Sir Alfred Garrod many years ago pointed out that in blood drawn from the site of a local inflammation he could find no trace of uric acid. This is the explanation, no doubt, of the quick capillary reflux, because, as we shall see in this paper, in all conditions where the blood is clear of uric acid the capillary reflux is quick.

Then there are circumstances in which blood-pressure and capillary reflux do not completely correspond, and one of these is the presence of severe pain. Thus it is possible for a patient to have a capillary reflux of, say, 6 and a blood-pressure of 120, and then, owing to severe pain (let us say) in a tooth of which the nerve is exposed, to have the blood-pressure still further raised by ten or even twenty mm. of mercury. This rise of blood-pressure is out of proportion to the capillary reflux, and is not

accompanied by any slowing of it, and the rise is really due, I believe, to a temporary contraction of the muscles of the arterioles as the result of the local pain, being probably an effort on the part of Nature to shut off blood from the seat of suffering. But this is never much more than a temporary condition, and I mention it merely as one of the exceptions in which one may find that blood-pressure does not keep its normal corresponding relation to capillary circulation.

Other conditions which may just be mentioned as altering the ordinary circulation and blood-pressure are those which remove fluid from the body, such as vomiting and purging, or when fluid has for several days been withheld, so that the total quantity of the blood is approximately nine or ten pints as against the possible eleven or twelve pints when of normal amount. It is obvious that under these conditions of reduced fluid with the same obstruction in the capillary circulation and the same power of the heart, the general rise of blood-pressure cannot be so high when fluid is wanting as when it is present, and this is the explanation of the great value which has for long years been justly attached to a free action of the bowels under such conditions of dangerous high blood-pressure as are often seen in relation with cerebral hæmorrhage.

With regard to drug action, I may say shortly that a drug which clears the blood of uric acid quickens the capillary reflux and lowers the blood-pressure, and a drug which brings an increased quantity of uric acid into the circulation slows the capillary reflux and raises the blood-pressure. As nearly all the drugs in the Pharmacopœia have one or other of these actions to a more or less marked extent, I shall not take up space by enumeration, but will mention one or two of the more important that act in either direction.

I have already said that in fever the blood is cleared of uric acid and the capillary reflux is therefore quick, and if we take a case of acute rheumatism in which, as Sir Alfred Garrod has shown, there is little or no uric acid in

the blood, we shall find that the capillary reflux (antecedent to the administration of drugs) is three to four half seconds, with a temperature of, say, 102° or 103°. If we now administer salicylate of soda or any other preparation of salicylic acid, we shall find that in a few hours the capillary reflux has altered and slowed to eight, nine, ten or more half-seconds, and if we examine the blood we shall find that uric acid which was previously almost absent from it, is now present in large quantity. The old treatment of rheumatic fever was by alkalies, and these have a very similar effect both on the amount of uric acid in the blood and on the capillary reflux. On the other hand, the drugs which have most marked effect in clearing the blood of uric acid, and thus quickening the capillary reflux, are the metals, such as mercury, or an acid in any form which can best be absorbed from the stomach and which diminishes the solvent powers of the blood for uric acid. If we take a patient who suffers from migraine or from a stage of chronic Bright's disease, and administer to him, when his capillary reflux is nine or ten, several small doses of mercury or similar doses of some acid mixture, we shall find that in the course of an hour or two, or less, his capillary reflux has quickened by at least one or two half-seconds, and that the blood-pressure has fallen to a corresponding extent.

It may be worth while to mention here briefly the effect of diet on such a condition as that of migraine, which is commonly associated, in those who suffer, with a capillary reflux of seven, eight, or nine half-seconds, and a blood-pressure of 140 and above. If such a case is put on a uric-acid-free diet, it will be found, roughly speaking, that the capillary reflux will quicken by about one half-second in every three to six months, and that blood-pressure will fall by a corresponding amount, and both these will probably touch somewhere near normal, in uncomplicated cases (*i. e.* in those who have not for any particular reason an unusually large amount of uric acid in their body), in from eighteen months' to two years' time.

Where we have albuminuria or actual Bright's disease, the change may not only take very much longer, but an absolute resumption of normal conditions may be more or less impossible. In Bright's disease and all similar conditions of defective combustion, if the blood can be cleared of uric acid and the capillary circulation sufficiently quickened, we shall find we have put an end to defective combustion, the temperature rises to normal, the albumen falls to a trace, and the trouble is at an end. Migraine is but an epitome of Bright's disease and all similar conditions of defective combustion, and when, as the result of a correct diet, the circulation has been cleared of obstructing uric acid not only does capillary reflux quicken, blood-pressure fall, and headache cease, but such related symptoms as mental depression, dyspepsia, congestion of the liver, all similarly due to obstructed and defective circulation, disappear also. Thus we have in this functional trouble an epitome of the whole field of circulatory troubles produced by uric acid; for headache, epilepsy, mental depression and other mental changes represent its effect on the cerebral circulation and nutrition, asthma on the lungs, diabetes on the muscles and liver, and Bright's disease and anæmia on the metabolism and combustion of the whole body, more especially of the skin and great glandular organs. Every one of these is represented in the ordinary symptoms of migraine, and migraine if untreated and unrelieved is certain to pass into either Bright's disease or, more rarely, diabetes associated more or less with mental changes or severe brain lesions similarly brought about, with constant and incurable anæmia.

Again, in those who are free from exogenous uric acid, it is possible, by the administration of pure uric acid in doses of three or four grains, to slow the capillary circulation in the course of two or three hours and raise the blood-pressure to a corresponding extent; and thus in three hours' time a capillary reflux of five or six half-seconds might be slowed to one of seven or eight. It will remain slow for some five, six, or seven hours longer

and then gradually quicken to normal as the amount of uric acid in the blood again becomes normal for the individual experimented on.

We see, then, that in many conditions it may be truly said that the capillary reflux is an absolutely certain measure of the amount of uric acid in the blood, both in physiology and pathology, and also in drug action and the administration of uric acid itself, always subject to the exceptions already mentioned. I may add here that there are one or two physical conditions which also contribute to alter both the capillary circulation and its relation to blood-pressure—as, for instance, increased intra-abdominal pressure from tumours or ascites. This, other things being equal, interferes to some extent with the action both of the diaphragm and of the heart; it will, therefore, appreciably slow the capillary reflux out of proportion to the uric acid present in the blood, and its interference with the action of the heart will possibly prevent blood-pressure from being so high as the slowing of the capillary reflux would lead us to expect. The practical point, therefore, is that it may be impossible to clear the blood of uric acid and to make the capillary circulation good while the circulation in the abdomen and chest is hampered by such conditions. There are certain conditions in the chest which also influence the capillary circulation. One we have already spoken of, namely, weakness of the heart and morbus cordis, and practically all forms of morbus cordis give a capillary reflux which is somewhat slower than it ought to be in relation to the amount of uric acid in the blood, and a blood-pressure which is often not quite so high as one would expect in relation to the rate of the capillary reflux.

Again, all forms of obstruction in the pulmonary circulation, and such conditions as emphysema, bronchitis, and pneumonia, have as their effect a diminished oxidation in the body, and (as I have long pointed out) the result is increased alkalinity of the blood because the formation of acid products by oxidation in the body is hindered. The

consequence of this increased alkalinity of the blood is that, other things being equal, it will contain more uric acid and the capillary reflux will therefore be slowed. I will give one or two figures to illustrate this. In a case of pneumonia with a temperature of 102° there may be possibly a capillary reflux of eight or nine half-seconds, and the blood-pressure will, if the heart is strong, fully correspond with this; let us say 150 mm. of mercury and the pulse rate at about 100. Later on, let us suppose that the heart fails badly and dilates. You may then get a capillary reflux of eleven or twelve half seconds with a blood-pressure of only 100 or 110 mm. of mercury, and with this the heart rate has risen to, say, 140. But if we had had to deal with a temperature of 102°, without dyspnœa, the capillary reflux would have been three or four half-seconds and the blood-pressure 70 or 80 mm. of mercury.

Certain cerebral and intra-cranial conditions may also alter the blood-pressure very considerably. I refer to such things as tumour, hæmorrhage, or any such growth or inflammation in bone or membrane as causes increased intra-cranial pressure. These may to some extent raise the blood-pressure out of proportion to the capillary reflux, and I have always considered that they do this by causing direct contraction of the muscles in the walls of the arterioles, just as I speak of this same factor causing similar results in the case of severe local pain. So it will be evident, I fully acknowledge, that blood-pressure may be raised in certain conditions by contraction of the muscles of the arterioles and of the larger arteries as well, but, nevertheless, the result of my whole investigation goes to prove that in the majority of conditions high blood-pressure has no relation to such muscular obstruction, but a definite and constant relation to the amount of uric acid in the blood and the corresponding slowing of the capillary circulation.

There is also an interesting relation between capillary circulation and time of year. I have already mentioned the correlation of capillary circulation and time of day, a simple explanation of which exists in the fact that there

is always more uric acid in the blood in the morning hours and less in the evening hours. In the same way there is always more uric acid in the blood in the warmer seasons of the year and less uric acid in the colder. This takes place because warmth favours elimination of acids from the body in visible and invisible perspiration, and this elimination of acids raises the alkalinity of the blood and increases its solvent powers for uric acid. I have pointed this out at great length in my book 'Uric Acid' and I shall not allot much space to it here, but the interesting point is that it follows from this that capillary circulation will be slower and blood-pressure higher in the early part of the warmer season (spring and early summer), because there is more uric acid in the blood at that time, and that there will be quicker capillary circulation and lower blood-pressure in the early part of the cold season (autumn and early winter) because the blood is a less satisfactory solvent of uric acid and contains less of it at that time of the year. So that if we compare days and years, the morning hours of the day correspond with spring and early summer, and the evening hours of the day correspond with autumn and early winter. It is an interesting fact that the diseases of these two periods also absolutely correspond, and that all the diseases associated with excess of uric acid in the blood are met with generally in the morning hours, in spring and early summer, and in the decline of life, when failing metabolism again increases the alkalinity of the blood and therefore tends to flood it with uric acid. On the other hand, diseases such as arthritis and bronchitis are associated generally with evening and night hours, with winter and with the period of growth, adolescence and adult life, because the active metabolism of growth increases the formation of acids in the body, diminishes the alkalinity of the blood, and therefore lessens the solvent powers for uric acid. In a word, the collæmic diseases are found in those periods of day, year, and life when the capillary reflux is at its slowest and all precipitation and

local diseases at those times of day, year, and life when it is quickest. The relation of the collæmic troubles—headache, epilepsy, mental depression, and suicide—to menstruation, about which I have written so much in 'Uric Acid,' is simply their relation to the large quantity of uric acid which this function brings through the blood on the way to the kidney (see 'Uric Acid,' Fig. 31). It also explains why women during menstrual life do not suffer from gout, because they do suffer from these collæmic diseases associated with a large excretion of uric acid in the urine.

With regard to brain function, we find that in those whose capillary reflux is slow, who are meat-eaters and uric acid takers, this function is to a large extent impaired in the morning hours, when capillary reflux is at its slowest and blood-pressure at its highest. Brain function, in fact, is at its best in the evening hours, when capillary reflux is at its quickest and blood-pressure at its lowest. In the same way it is at its worst in the spring and at its best in the autumn, and mental depression, suicide, and other effects fluctuate in the same way. I believe that all the functions of the special senses are influenced by time of day, time of year, and time of life, and I may give one very interesting instance of this, mentioned to me by Dr. Bruce of Grimsby; he pointed out (being himself a volunteer and a marksman) that men accustomed to shoot well at a range in a cool northern county had their brain and eye functions and all dependent conditions much unsettled by coming south and shooting under conditions of greater heat; the effect of the heat being, no doubt, to bring some stored uric acid into the blood, slow the capillary circulation, and hinder the brain function as well as the eye function, so that they could neither co-ordinate the action of their muscles, nor could they sight the target so well as they had been accustomed to do in a more bracing climate.

There is an almost precisely similar relation between the lung function and time of day, year, and life, for here, also, as I have long shown, the excretion of water from the lungs is dependent on the amount of uric acid in

the blood and the rate of the capillary reflux. Here, again, we get diseases such as asthma (which is an exaggeration of the effects of uric acid on the capillary circulation of the lungs) keeping time with that period of the day, of the year, and of the time of life at which there is most uric acid in the blood. In exactly the same way, also, we get functions of the heart affected, and I have pointed out in 'Uric Acid' that in olden days, when my capillary reflux was slower and my blood-pressure higher than now, my heart would very often flutter, and falter, and drop out a beat when working against the high blood-pressure produced by uric acid in the blood (see 'Uric Acid,' edition 6, page 213). Here, also, the heart troubles produced bear a quite definite relation to time of day, time of year, and period of life; *e. g.* angina in early morning hours (see 'Uric Acid,' p. 655), a relation which it holds in common with headache, epilepsy, mental depression, and asthma, all of which are collæmic diseases.

Precisely the same conditions affect the functions of the arteries and their nutrition, and therefore the condition of their walls, resulting in various forms of arterial degeneration; and these also bear a special relation to time of life, though their real relation is to blood-pressure, for we find arteries markedly degenerated even in patients in the early twenties if they have been exposed to abnormal circulatory conditions and abnormal pressure for some years, as, for instance, in cases of Bright's disease. In exactly the same way the circulation, and consequently the functions of the liver, stomach, and intestines, are influenced by the amount of uric acid in the blood and the rate of capillary circulation in relation to time of day, time of year, and period of life, and all these troubles tend to be worse exactly at those diurnal and annual seasons when, under physiological conditions, there is most uric acid in the blood and the slowest capillary circulation. With regard to muscles, there is also a point of considerable interest, for those who have the most active and

powerful muscles and suffer least from fatigue are those in whom the circulation through these tissues is most free. Now, the circulation through the muscles will, as we see, be freer in the later part of the day and the autumn and winter, and in the period of growth and prime of life. With regard to climate, those who swallow uric acid will have the best circulation in their muscles in the evening hours, in autumn and winter, and in cold climates, and it has been observed that in this country, where the food in many places is now very much alike, men will do more work in the South of Scotland than in London, and more in London than on the south coast of England. For, other things being equal, the capillary circulation will be better in Scotland than in London and better in London than in the south coast of England, since the warmer the climate the more uric acid will there be in the blood, the less satisfactory will be the circulation and the greater the tendency to lethargy both in mind and body. (See also previous remarks on the functions of brain and eye under changes of climate.)

With regard to the skin, we have the fact that its circulation is always slower in the morning and quicker in the evening, and that its nutrition is therefore better in the evening and worse in the morning. In the same way the nutrition of the skin and skin structures, such as hair, is worse in spring and early summer, and better in autumn and early winter; and this, I believe, accounts for the fact that constitutional alopecia is often met with in a very marked manner in spring and early summer. At the same time of the year we often find many conditions such as those of hardening, thickening, defective nutrition of the skin up to Raynaud's disease itself, and these also tend to be most marked in the spring and early summer months.

With regard to the blood, its nutrition corresponds with that of the skin and other tissues, and is worse in the morning, better in the evening, worse in the spring and early summer months, better in the autumn and early winter; better during the high nutrition period of adoles-

cence, worse in the slack period of nutrition which follows it (from seventeen to twenty-five, especially in girls), better during the high nutrition period of middle life, and worse again in the low nutrition period of declining years. The blood, in fact, is, like all the other tissues, dependent upon the satisfactory condition of the metabolism of the body, and more especially upon the correct functioning of the great glandular organs, and these, as we can now understand, are absolutely dependent upon capillary circulation, which in its turn is controlled by the amount of uric acid in the blood, and so bears the above mentioned relation to time of day, time of year, and period of life. Hence in all uric acid consumers the blood is better in autumn and winter, worse in spring and summer. Almost precisely the same remark applies to the temperature of the body, and this is one of the best possible indications of the goodness or badness, and of the rapidity or slowness, of the metabolism—in other words, of the combustion of the body. The temperature of the body and especially of its surface varies with the time of day, time of year, and period of life, in accordance with the amount of uric acid in the blood. The surface temperature, however, is always lower in the morning and higher in the evening, and tends to be lower in the spring and the early summer months, and higher in autumn and the early winter months. It also tends to be higher during the rapid development of childhood and in the high nutrition period of adult life, and to be lower in the decline of life. In fact, everything that quickens the combustion of the body will raise the temperature of the surface, and everything that slows the combustion of the body will lower its temperature. Thus fever, which is of the nature of a general inflammation (we have already seen the action of a local inflammation), diminishes the amount of uric acid in the blood, quickens the capillary circulation with the metabolism and combustion of the body, and causes a rise in the excretion of the products of combustion—that is, of urea. But the uric acid cleared by fever out of the blood has not been cleared out of the body,

and when the fever disappears this same uric acid re-enters the blood in increased quantity, and we get the exact reversal of the effects produced by fever. We have now excess of uric acid in the blood, and in consequence slow capillary circulation; we have (if the heart is strong) high or rising blood-pressure. We have defective combustion as the result of defective circulation, and subnormal temperature especially on the surface of the body, because the precipitation of colloid uric acid is, as I have already pointed out, most marked on the surface, since cold is a direct precipitant of this substance. During the fever we had quick capillary circulation, low blood-pressure, rapid metabolism, rising urea; in the post-febrile conditions we have exactly the reverse of all these, slow capillary circulation, rising blood-pressure, diminished metabolism and combustion, falling temperature; and you have but to prolong this condition and intensify it to get, not only a falling excretion of urea, but also some uncombusted albumen in addition, for the albumen which has not been katabolised in the tissues into force and urea remains in the blood and is excreted by the kidneys as a foreign product. Albuminuria is therefore a mere exaggeration of the defective katabolism produced when the capillary circulation is slowed by an excess of uric acid in the blood, and hence it so frequently follows scarlet and other fevers. In the same way, as the result of defective capillary circulation in such an organ as the liver, we get, either with or without albuminuria, the presence of an excess of uncombusted sugar in the circulation, and consequently its passage from the blood through the kidney into the urine. Glycosuria is thus, like albuminuria, but a slightly modified result of defective combustion, and defective katabolism is in this and all other conditions the mere result of defective capillary circulation, which again is the result of excessive uric acid in the circulation.

I may mention in passing that albumen is always present in larger quantity in the morning hours, when the amount of uric acid in the blood is largest and consequent inter-

ference with circulation and combustion greatest, and that sugar also is more abundant in morning than in evening hours; so much so, that in most cases two ounces of bread if given at breakfast will produce a marked rise in the excretion of sugar but will have little or no effect if given in the evening.

In albuminuria also it is often possible to arrive at a diagnosis simply by noticing whether the albumen follows the natural curves of combustion or breaks them, for all albuminurias due to defective combustion (*i.e.* of the nature of Bright's disease) are more in the morning and less in the evening; but albuminurias due to other causes, such as oxaluria or other forms of gravel or stone, not infrequently reverse this procedure, the albumen being present in largest quantity in the evening or night and least in the morning. But in all these conditions, in glycosuria, albuminuria, all defects of combustion, obesity, anæmia, skin troubles, Raynaud's disease, liver and stomach diseases, in lung and brain troubles, the defective function is much intensified if the power of the heart should fail; for it is obvious that uric acid in obstructing the capillaries and producing defective capillary circulation will have its power for evil intensified by any failure on the part of the driving power of the heart, since lessened heart power means lessened driving force of the blood through the capillaries. This induces slower circulation in the capillaries, and the longer the blood is exposed by slow circulation to cold in the capillary vessels, the greater will be the precipitation of uric acid and the more persistent, therefore, the blocking of circulation which results. Here we have clearly before us the causation of Raynaud's disease and the reason why it proceeds to absolute stasis of circulation and local gangrene in surfaces and extremities, *i.e.* in parts most exposed to cold. We have also here a complete explanation of another fact in relation to Raynaud's disease; its relation to weakness of the heart, and hence its great preponderance (80 per cent.) in the female sex, since women have

naturally a weaker muscular system and especially a weaker heart. In two patients, male and female, there may be an equivalent amount of uric acid in the blood and an equivalent amount of friction in the circulation from that uric acid, but in the female (with the weaker heart), the friction will have a greater local effect in upsetting metabolism and combustion, and there will also be a greater and more permanent precipitation of uric acid and a more serious interference with nutrition from what is precipitated, so that in the two individuals, originally equal as regards their available uric acid, the one with the weaker heart will be most likely to enter the final stages of Raynaud's disease and to suffer from local gangrene.

It is no doubt possible to argue that uric acid causes contraction of the muscles of the arterioles and thus shuts off the blood from the capillaries, and that the weaker the heart and the colder the surface the worse will be the result; but this is open to the objection already urged, that a muscle cannot remain contracted through all stages of failing nutrition up to gangrene. On the other hand, if we are dealing with a mere mechanical obstruction of capillaries by colloid uric acid, there is no reason why this should not increase and lead to complete stasis and death of the surrounding tissues; indeed, it is almost certain to do so, for the more the circulation slackens the greater will be the exposure of its fluids to cold, and the more complete and permanent will be the precipitation of uric acid in them. There is nothing vital about this process and nothing, therefore, which need come to an end with the onset of gangrene.

Obesity, again, affects just those times of life when combustion is at its worst, as from 17 to 25 in girls, and in both men and women in the decline of life; and, again, a slight deficiency in heart power is often the factor which determines that one member of a family shall be stout and the other thin. The stout man has the weaker heart in relation to the work required of it, has more marked de-

ficiency of combustion, and is therefore more likely both to get pneumonia and to die of it than the thin man; public opinion is that the stout man is the stronger, but the truth is just the reverse.

Probably the most interesting correlation of capillary circulation and blood-pressure is that with the excretion of water from the kidneys. Many years ago in my early investigations of the excretion of uric acid, I noticed that the water and the uric acid almost invariably moved in opposite directions—that when the water rose uric acid fell, and when uric acid rose the water fell. Now this fact obtains a quite simple explanation, if, as we now believe, uric acid in the blood blocks the capillary circulation; for the more uric acid there is in the blood the greater will be the block in the renal capillaries, and the less water will it be possible for them to pass into the urine. Since then I have also pointed out that precisely the same relation holds between the uric acid in the blood and the excretion of water in the air expired from the lungs, and this also has, no doubt, a similar explanation. In relation to time of day we find that the water from the kidneys is most per hour in the evening, when uric acid in the blood is lowest and capillary circulation quickest, and least in the morning, when uric acid in the blood is highest and capillary circulation slowest. In pathology we find that the excretion of water is greatest in early stages of fever when there is little uric acid in the blood and the capillary circulation at its quickest; it is less in conditions of severe collæmia (such as those of uric acid headache), when capillary circulation is slow and blood-pressure high. In drug action, again, we find that every drug which clears the blood of uric acid increases the excretion of water from the kidneys. Many drugs which clear the blood of uric acid while retaining it in the body produce a diuresis. Indeed, I believe there is no drug which produces a diuresis which does not at the same time clear the blood of uric acid; and this is a fact which is extremely suggestive with regard to the action of uric acid in controlling

capillary circulation; for drugs which are solvents of uric acid (*e. g.* alkalies and salicylates) as their first effect bring more uric acid into the blood and slow the capillary circulation, thus raising the blood-pressure, and in these conditions they do not increase, but diminish, the excretion of water from the kidney. Later on, however, when a large amount of the available uric acid has been passed out by the kidneys the blood becomes less charged with this substance, the capillary circulation gets somewhat quicker, the blood-pressure tends to fall, and with this there comes more or less marked diuresis. In the case of salicylates, as I have pointed out, this is likely to come on the second or third day of their action, and somewhat later still in the case of alkalies, but in all cases the time of the diuresis is dependent on the amount of available uric acid in the blood of the individual to whom these drugs are given. Before leaving the subject of the relation of the circulation to these various functions I may mention shortly the effects of gravity on the blood-pressure and the interesting way in which it enables us to estimate certain conditions of the circulation. If we measure the blood-pressure in the arm of a patient (1) raised above the head, (2) on a level with the heart, and (3) sunk downwards and forwards between the knees, we find that if it is normal on the heart level, it will be sub-normal when raised above the head, and above normal when lowered between the knees. Now this is due to the addition or subtraction of the weight of a column of blood, roughly equal to the length of the arm; the pressure is diminished by this quantity when the arm is raised above the head, and is increased by this quantity when the arm is lowered between the knees. There is an interesting fact with regard to this constant force which we have at our disposal, and it is this, that when the artery is unduly distended by a raised blood-pressure the addition of this force of gravity will scarcely distend it very much more, while in more normal conditions the added force of gravity causes a very marked increase in distension. We have

thus within our power a comparatively easy and simple means of judging whether an artery is or is not somewhere about its utmost limit of distension, and whether it has or has not been in the past still more distended than it is at present.

I will also add here one word as to arterio-sclerosis, and this is, that I believe it is never physiological, but is always, under all conditions, pathological; that it is never to be seen in old age except as the result of disease; and that if those who follow us in the future will live an absolutely healthy life on correct foods this will not be met with to any marked extent, even in quite old people I do not for a moment doubt that such factors as alcohol, syphilis, and strain greatly increase the tendency of the coats of the vessels to degeneration, but I believe also it is none the less true that the great cause of this degeneration (being also the one great cause of more or less constant strain) is high blood-pressure. Defective circulation in the vasa vasorum, as the result of those changes in the circulation which uric acid produces, will, by hindering the passage of blood through the capillary vessels, cause defective circulation in the walls of the arteries and arterioles themselves.

Thus these vessels, being subjected to more or less constant pressure and strain from within, producing dilatation and some displacement of structures, and also at the same time to defective nutrition of all their tissues from defective circulation, are certain to undergo degenerative changes which must steadily increase both in extent and severity as time goes on.

In conclusion, I would point out that by merely touching a patient with the point of the finger and watching the rate at which the colour returns in the surface thus made pale by pressure, we can learn—(1) the temperature, for abnormal rise of temperature will co-exist with an abnormally quick capillary circulation if there is no dyspnœa. If, on the other hand, there is dyspnœa, and therefore defective oxidation throughout the body and

its tissues, then the alkalinity of the blood may not be diminished by fever, and it will remain a good solvent of uric acid; there will continue to be a larger or smaller quantity of uric acid in the circulation and the capillary reflux will not be quickened. (2) We can tell the blood-pressure more or less acurately if there is no weakness of the heart or morbis cordis, this being a matter which I have already gone into. We can recognise the probable presence or absence of such conditions as headache, epilepsy, mental depression, glycosuria, albuminuria,—in a word, all the conditions of defective combustion, for, with the presence of these conditions of defective combustion, will co-exist subnormal temperature and slow capillary reflux.

Lastly, we can tell with very considerable accuracy the approximate quantity of uric acid in the blood and urine. In fact, the rate of the capillary circulation is practically in all conditions a measure of the amount of uric acid in the blood; for though in fever we may have, as above remarked, a slow capillary circulation if there is dyspnœa, this capillary circulation is slow because fever does not, in these circumstances, clear the blood of uric acid. Again, though in weakness of the heart or morbus cordis the capillary circulation will be somewhat slower than can be accounted for by the amount of uric acid, we can easily find the other factor of this causation in the diminished power of propulsion by the heart.

The final conclusion is, I think, that there is no escape from the fact that uric acid controls the capillary circulation of the whole body throughout life, and conditions everything that is secondary and dependent on this circulation. There may possibly be room for two explanations of the way in which it produces this effect, but it seems to me that there is a large and increasing number of facts which suggest that it does produce it, in all probability mechanically, by the more or less constant and continuous interference of small colloid particles with the passage of the circulating fluid through the tiny capillary vessels.

DISCUSSION.

The PRESIDENT said no quantitative estimation of the amount of uric acid in the blood or urine had been given, but perhaps these had been set forth in a previous paper.

Dr. F. PARKES WEBER said that Dr. Haig concluded that various symptoms (including migraine and Raynaud's phenomena) were due to mechanical obstruction in the capillary circulation caused by the presence in the blood of uric acid in colloid form. He ventured to speak in regard to this point because he had endeavoured in various patients to ascertain by actual examination of their blood what was the resistance in its flow through a capillary tube, as compared to the resistance in the flow of water; that was to say, he had endeavoured to estimate the viscosity-coefficient of the blood. Since, however, venesection was nowadays rarely considered necessary, he had not yet been able to examine many specimens of blood in this way, but his results, as far as they went, pointed to changes in the degree of blood-viscosity being usually chiefly dependent on the number of blood-corpuscles. In these viscosity experiments coagulation was prevented by directly collecting the blood, as it flowed from the venesection wound, into a glass vessel containing a little of a 50 per cent. aqueous solution of potassium citrate (as suggested to Dr. Weber by Sir J. McFadyean); 1 c.c. of this citrate solution should be present in every 100 c.c. of the citrated blood. The viscosity of the citrated blood was in each case estimated by the help of what might be termed a "viscosity tube," made for Dr. Weber by Messrs. Baird and Tatlock after a pattern kindly recommended to him by Prof. A. Schuster of the Victoria University, Manchester. This tube consisted of a capillary portion, 30 cm. long, with a bulbous portion above the capillary portion. The liquid the viscosity of which was to be estimated was sucked up by means of an indiarubber mouthpiece till the upper surface of the fluid column rose above the bulbous portion of the tube. The liquid was then allowed to fall, whilst the tube was kept in a vertical position, and the time taken by the upper surface of the liquid to sink from a mark above the bulb to a mark below the bulb was carefully ascertained. Professor Schuster pointed out that if the time taken in the case of two different liquids were t_1 and t_2 respectively, and p_1 and p_2 were the respective specific gravities of the two liquids, and n_1 and n_2 were their viscosity-co-efficients, then (when the temperature was constant) $\frac{n_1}{n_2} = \frac{t_1 p_1}{t_2 p_2}$, so that, if for one liquid n_2 was known, n_1 might be

easily calculated out. For practical purposes it was convenient to compare the viscosity co-efficient of blood to that of water at ordinary room-temperature, taking the latter as 1, and this was done in Dr. Weber's own observations referred to in the following notes, but C. Hirsch and C. Beck ('Deut. Arch. für klin. Med.,' 1901, vol. lxix, p. 503) had compared the viscosity of normal human blood to that of water, both at 38° C., and J. Bence ('Deut. med. Woch.,' April 13th, 1905, p. 590) had followed Hirsch and Beck's method. Taking the viscosity co-efficient of water at 38° C. as 1, Hirsch and Beck had estimated that of normal human blood at the same temperature as 5·1 and Bence as 5·4. This applied to the foreign observations quoted amongst the following remarks. In the blood from the case of splenomegalic polycythæmia which Dr. Weber described in the 'Med-Chir. Trans.' (1905, vol. lxxxviii), he found the viscosity co-efficient was about 11·5 when there were 9,230,000 red corpuscles and 4800 white corpuscles present in the cubic millimetre of the (citrated) blood. In two other cases of splenomegalic polycythæmia he was able to ascertain (by the kindness of Dr. R. Hutchison and Dr. T. D. Acland respectively) that the viscosity co-efficients were in the first case (August, 1905) 11·8; in the second case (December, 1905) about 6·7. The latter case had, however, been treated by copious bleedings. Dr. Weber here remarked that Lommel ('Münch. med. Woch.,' December 19th, 1905, p. 254) had recently by Hirsch and Beck's method found the viscosity co-efficient to be over 11·0 in a case of splenomegalic polycythæmia and that Bence (*loc. cit.*) in another case of splenomegalic polycythæmia obtained co-efficients varying from 15·9 to 20·9. In a recent case of cyanosis, probably of both chronic pulmonary and chronic cardiac origin, he (Dr. Weber) found the viscosity co-efficient to be 6·5, when the citrated blood contained 6,350,000 red cells to the cubic millimetre (rather too much citrate solution was, by mistake, added to the blood in this case). In a man, under Dr. Weber's care, with great cyanosis, probably of chronic pulmonary origin, he found (April, 1905) the viscosity co-efficient to be 11·8 when the citrated blood contained only 6,850,000 red cells to the cubic millimetre. That patient's condition gradually improved greatly in the hospital, and Dr. Weber had little doubt that the improvement was partly due to frequent inhalations of oxygen and to the prolonged use of iodide of potassium, since it was claimed that both oxygen inhalation and potassium iodide tended to lower the blood-viscosity. Bence (*loc. cit.*), in three cases of cyanosis in heart disease and in one case of bronchitis with emphysema found viscosity co-efficients varying from 6·93 to 8·2. In a specimen of venesection blood kindly furnished by Dr. R. Hutchison from a case of aneurysm Dr. Weber found the viscosity co-efficient of the citrated blood only 4·0, when

there were only 3,662,500 red corpuscles to the cubic millimetre. These observations were, Dr. Weber thought, sufficient to show that the variations of the viscosity co-efficient generally depended mainly, though not entirely, on the proportion of blood-corpuscles in the (circulating) blood. His first experiments in this respect were made with Dr. J. H. Watson on citrated horse blood, and they illustrated the same point. It was found, for instance, that horse's blood-plasma artificially mixed with two millions of red corpuscles to the cubic millimetre, took 84 seconds to pass through the bulb of the "viscosity tube," whilst a sample containing four million red corpuscles to the cubic millimetre took 110 seconds to pass through the bulb of the same tube ('Clin. Soc. Trans,' 1904, vol. xxxvii, p. 130). Dr. Weber concluded by asking Dr. Haig whether it might not be possible to employ a "viscosity tube" similar to those used in these experiments, in order to investigate the actual effect of the presence of uric acid in colloid form on the viscosity of fluids (and their passage through capillary tubes). R. Burton-Opitz, of New York, found, it might be noted, that the viscosity of a dog's blood could be much lowered by withholding food and much raised by feeding it on a meat diet, and he also found that the rise in viscosity from meat diet was chiefly due to the increase in the number of blood-corpuscles.

Mr. MALCOLM said that he had carefully studied the condition of the vessels with reference to surgical matters, and he wished to make some observations with a view to eliciting information, or possibly to persuading the author of the paper that the arteries were the more important agents in opposing the blood-flow. Dr. Haig inclined to the view that there was a difficulty in the passage of the blood through the capillaries, caused by a change in its physical characters when it contained much uric acid. He pointed out that in Raynaud's disease there was a hypertrophy, not only of the muscular, but also of the fibrous coat of the vessels throughout the body, the smallest as well as the largest being affected, and therefore, he said, it was obvious that all were "engaged in resisting pressure, not in producing it." The argument seemed to be that an increased muscular activity was developed in order to overcome the resistance to the flow of blood through the capillaries, when this was increased by the changes caused by an excess of uric acid in the blood. But the speaker submitted that contraction of the vessels would not act in this way. It would tend to increase the peripheral resistance to the blood-flow. The smaller vessels had comparatively much more powerful muscular walls than the larger and, of course, the effect of a contraction was greater in proportion to the smallness of the tube. The arterioles also, being more numerous, affected a much larger quantity of blood. The area of a cross section of all the

capillaries had been estimated as 700 times that of the aorta (Landois and Stirling), and the cross-section of the arterioles was nearly the same. Moreover, contraction of the arteries, when reflexly induced, began in the smallest vessels. Thus the power of the contraction of the vessels to restrain the blood-flow, which had been called the stop-cock action, was very great. In discussing blood-pressure writers had often omitted, and Dr. Haig had omitted, to state where the blood-pressure was estimated. The speaker maintained that when the pressure was raised in the large vessels by contraction of the small arteries, the pressure in the arterioles, and beyond them, was lowered. On the other hand, when the arterioles relaxed, the pressure in the main vessels was reduced, but the small vessels became larger and fuller, the blood-pressure in them was increased, and therefore the blood went bounding through the capillaries. Thus, a relaxation of the arterioles was the only physiological action that could *mechanically* counteract a slow current caused by increased resistance in the capillaries. As the speaker understood these changes he therefore could not agree with Dr. Haig's statement that it was "clear that the low blood-pressure cannot be the cause of the quick capillary circulation, and equally clear that the high blood-pressure cannot be the cause of the slow capillary circulation." On the contrary, he held that, if the amount of blood and strength of the heart were constant, low blood-pressure in the large and medium vessels was necessarily accompanied by a high blood-pressure in the arterioles, and therefore fully accounted for the quicker capillary circulation and the increased flow of urine; whilst high blood-pressure in the larger vessels was associated with opposite conditions, namely contracted arterioles, low blood-pressure in them, a slow capillary circulation, and diminished secretion of urine. That a long-continued contraction of the arterioles existed was proved by the condition of hypertrophy of their muscular walls, and therefore the evidence that there was an obstruction in the capillaries caused by a change in the constitution of the blood did not seem conclusive. It was pointed out that every stimulation of a sensory nerve caused a contraction of the small vessels and a rise of blood-pressure in the large. In certain diseases, such as gout, there was a chronic irritation of the tissues throughout the body, from the presence of uric acid or perhaps of some other poison or irritant, and this fully accounted for a tonic vascular contraction. That there was an irritant was shown by the effects, after a time, on the kidneys, and increased vascular tonicity was shown by the hypertrophy in the vessel-walls.

Dr. Francis W. Hare said that he would like to make a few remarks upon the relation of uric acid to migraine or periodic sick-headache. Dr. Haig had shown that under a steady per-

sistence in his well-known scheme of diet, which was practically purin-free, migraine in many cases tended to recur at increasing intervals and with diminishing intensity. This fact, which did not lack ample confirmation, was consistent with the view that the amount of uric acid circulating in the blood was an essential factor in the migraine paroxysm. But there were facts which directly contravened this view. Periodic sick-headache might in many cases be completely relieved and held in absolute abeyance by means of a dietary which so far from reducing largely increased the amount of uric acid circulating in the blood. This was exemplified in the following case: A stout woman, aged 35, had suffered from typical unilateral migraine for fifteen years. The attacks occurred every fortnight or three weeks. They lasted two, and sometimes three, days, and were accompanied by complete anorexia and bilious vomiting. Her diet was the ordinary mixed diet. This was altered. She was given fish or meat, or both, at every meal, and tea, coffee, meat extracts, and green, non-starchy vegetables were allowed *ad. lib.*, but sugar and fats, except a little butter, were interdicted, and starch foods were reduced to two or three ounces a day. To this diet she adhered strictly for six months. Throughout the whole of this period she had no trace of headache or any migrainous symptom. She then returned to her ordinary mixed diet. At the end of the first fortnight she had a typical attack of migraine identical in all details with her previous attacks, and these continued to recur thenceforward at their old intervals and with their old severity. Subsequent experiment in this case showed that the intake of starchy foods could be raised to about five ounces a day without inducing migraine, but that beyond that amount attacks were again induced. Similar examples were easy to find and it must, Dr. Hare thought, be conceded that in them at any rate the purin intake, and consequently the amount of uric acid which passed through the blood on its way towards renal excretion, was not an essential factor in migraine. It might be contended that in such cases the uric acid was retained and stored extra-vascularly in the tissues and did not therefore flood the circulation. If this were true, it would have to be admitted that the tissues have an indefinite capacity for storage. One of Dr. Hare's patients who had suffered from periodic sick-headache every three or four weeks for more than thirty years had adhered to the above scheme of diet for upwards of six years. His attacks finally ceased immediately his diet was changed, and he had been in perfect health ever since. It must be admitted that the migraine paroxysm was associated, as Dr. Haig had shown, with marked variations in the excretion of uric acid. But considerable evidence could be adduced to show that these variations were merely symptoms of the migrainous attack; they were probably, in fact, effects and not causes of it.

Dr. HAIG, in reply, alluded to the method of estimating the amount of uric acid in the blood by throwing down granules with a chloride of ammonium reagent, the comparative number of the granules in relation to the red cells being the index of the amount of uric acid. He thought that the body had unlimited power of storing uric acid, and that in respect of some persons the simile of a pillar of salt was no exaggeration. By swallowing pure uric acid it was possible to alter the number of granules in the blood at pleasure and to produce the circulation effects he had described. He said that he was much interested in the instrument shown by Dr. Parkes Weber for estimating the viscosity of fluids, and he would be happy to try by means of this instrument what effect uric acid would show on the viscosity of fluids. With regard to the viscosity of blood, and Dr. Weber's evidence that it varied with the number of red corpuscles, Dr. Haig said that he was merely suggesting that the addition to this fluid of colloidal uric acid would still further increase the viscosity. But it was not entirely a matter of red cells, as it could be shown from his own researches that those who are for years on a uric-acid-free diet have quick capillary reflux and normal blood-pressure, yet have, nevertheless, as a rule, more than the average number of red cells. Moreover, it would not, he thought, be maintained that fever diminished the number of red cells in the blood, yet did not fever in two or three hours change a capillary reflux of 7 or 8 into one of 4 or 5? and with this there was a corresponding fall of blood-pressure and a change in the granules in the blood and the uric acid in the urine. Indeed, fever, by causing diuresis, would diminish the water and increase the relative number of corpuscles in the blood, and yet this did not slow the capillary reflux or raise the blood-pressure. He was much interested in the experiment quoted by Dr. Weber in which viscosity of a dog's blood had been raised by feeding it on a meat diet. In his own experiments on dogs he had been able to increase the amount of uric acid in their urine by feeding them with meat as compared with farinaceous food and milk. With regard to what Mr. Malcolm said, Dr. Haig pointed out that a vessel which dilated with every rise of blood-pressure and contracted as it fell could not be responsible for such rise of pressure, and using the instrument he had mentioned in his paper, the blood-pressure was measured as directed by the inventors of the instrument in the radial artery. It was easy to show that the diameter of the radial artery increased with the rise of pressure and diminished with its fall, and it appeared obvious that a vessel the diameter of which diminished with falling blood-pressure could not be the cause of an increased rate of capillary circulation. If the artery in question had dilated with the fall of blood-pressure, it might have been the cause of the change in capillary circulation. Dr. Haig quite admitted that contraction

of muscles in the walls of the arterioles could cause a rise of blood-pressure and a dilatation of the vessels behind them. He also admitted that the stimulation of a sensory nerve might cause contractions of such arterioles, and he showed that these conditions could be distinguished from those of ordinary collæmia by the rate of the capillary circulation, which did not in this case bear its usual normal relation to blood-pressure. Dr. Haig maintained most strongly that there was a constant relation between capillary circulation and blood-pressure and between the amount of uric acid in the blood and the two other factors. He did not believe that irritation of a sensory nerve could account for such a condition as the high blood-pressure of Bright's disease, lasting steadily over many years; and then, again, it was possible for a sensory nerve to be irritated during fever and yet, in the absence of uric acid from the blood and with the free circulation in the capillaries, there was under these circumstances little or no appreciable rise of blood-pressure. Every drug that cleared the blood of uric acid quickened the capillary reflux and lowered the blood-pressure, and it would do this with little or no regard to the irritation or stimulation of a sensory nerve. But he acknowledged that such irritation of a sensory nerve would cause a further rise of blood-pressure in addition to that produced by capillary obstruction; but this was generally a small matter and only of temporary duration, whereas the obstruction produced by uric acid might be continuous for months and years and, as in Raynaud's disease, might eventuate in the death and destruction of the parts. But he had yet to learn that any muscle could remain contracted till it and the surrounding tissues had passed into a condition of gangrene.

AN IMPROVED METHOD OF PERFORMING THE "PANCREATIC" REACTION IN THE URINE

BY

P. J. CAMMIDGE, M.B.Lond., D.P.H.Camb.

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In March, 1904, I described a new method of examining the urine in suspected cases of pancreatic disease, the results of which, when considered in conjunction with the clinical symptoms, had been found by Mr. Mayo Robson and myself to be of considerable assistance in diagnosis(1). Since then numerous experiments have been made with a view to freeing the test of disturbing factors which, either from errors in manipulation or from inherent defects in the method, were liable to obscure the issue or render its interpretation, at times, a matter of difficulty, especially in inexperienced hands. I do not propose to describe these experiments in detail, as that would occupy too much time, but only to deal with so much as will make clear the reasons for employing the improved method I now bring forward. Before doing so, I should like to correct an erroneous impression which some appear to have received from my original paper. It was not my intention to suggest that the presence of

glycerine in the urine had been proved in pancreatic disease, nor did I wish it to be thought that the methods of examination I described were tests for that substance; the glycerine theory was merely mentioned to make clear the genesis of the reaction finally described.

In the original method two specimens of urine, one of which had been treated with mercuric chloride, were boiled with hydrochloric acid, and, after the excess of acid had been neutralised with lead carbonate, were examined by the phenylhydrazin test. The presence of active inflammatory disease of the pancreas was indicated by a difference in the amount of deposit shown by the two samples when they were allowed to cool undisturbed. This method had the great disadvantage of being a comparative test not capable of accurate measurement, and therefore dependent to a certain extent for its interpretation on the experience of the observer. In addition errors in technique, unless carefully guarded against, were liable to occur and to confuse the issue. The improved method has got rid of the first of these difficulties, and the test is now an absolute one, depending on the presence or absence of a precipitate in a single preparation, but the manipulation is slightly more complicated, and still requires a reasonable amount of care, particularly in the details of the experiment.

Examination of the phenylhydrazin precipitate derived from the urine in cases of pancreatic inflammation, after treatment with hydrochloric acid, showed that it consisted of two parts, one a phenylhydrazin compound of glycuronic acid and the other the osazone of a sugar. Although there is reason to believe that the excretion of glycuronic acid is increased in pancreatitis, an augmentation of the output occurs in so many other pathological conditions, that no helpful diagnostic method could be based upon this in the present state of our knowledge. Further investigation of the precipitate obtained from the urine after treatment with mercuric chloride showed that it consisted entirely, or almost entirely, of a glycuronic acid

compound of phenylhydrazin, so that the difference noticed between the *a* and *b* reactions in characteristic cases of pancreatic disease was probably dependent on some substance other than glycuronic acid. If, therefore, the glycuronic acid could be removed previous to employing the phenylhydrazin test, the result might be expected to be more definite and the necessity for two comparative tests be done away with. This was found to be possible by taking advantage of the fact that glycuronic acid is precipitated by basic lead acetate from acid solutions, while the sugars are only thrown out when the reaction of the fluid is alkaline. Many minor difficulties had to be overcome before a practical working method giving reliable results could be arrived at, and a large number of urines had to be examined by the old and new tests before their comparative value could be ascertained. The result was that the newer method was found to be a distinct improvement as regards the definiteness of the data on which an opinion could be formed. The details of this method I will now describe.

A specimen of the twenty-four hours' urine, or of the mixed morning and evening secretions, is filtered several times through the same filter-paper and examined for albumen, sugar, bile, urobilin, and indican. A quantitative estimation of the chlorides, phosphates, and urea is also made and the centrifugalised deposit from the urine examined microscopically for calcium oxalate crystals. If the urine is found to be free from sugar and albumen, and is acid in reaction, 1 c.c. of strong hydrochloric acid (sp. gr. 1·16) is mixed with 20 c.c. of the clear filtrate and the mixture gently boiled on the sand-bath in a small flask, having a long stemmed funnel in the neck to act as a condenser. After ten minutes' boiling the flask is well cooled in a stream of water and the contents made up to 20 c.c. with cold distilled water. The excess of acid present is neutralised by slowly adding 4 grammes of lead carbonate. After standing for a few minutes to allow of the completion of the reaction, the flask is again cooled in running water

and the contents filtered through a well-moistened close-grained filter-paper until a perfectly clear filtrate is secured. The filtrate is then well shaken with four grammes of powdered tribasic lead acetate and the resulting precipitate removed by filtration, an absolutely clear filtrate being obtained by repeating the filtration several times if necessary. Since the large amount of lead now in solution would interfere with the subsequent steps of the experiment it is removed either by treatment with a stream of sulphuretted hydrogen or, what I have found to be equally satisfactory and less disagreeable, by precipitating the lead as a sulphate. For this purpose the clear filtrate is well shaken with 2 grammes of finely powdered sodium sulphate, the mixture heated to the boiling point, then cooled to as low a temperature as possible in a stream of cold water, and the white precipitate removed by careful filtration; 10 c.c. of the perfectly clear transparent filtrate are made up to 18 c.c. with distilled water and added to 0·8 grammes of phenylhydrazin hydrochlorate, 2 grammes of powdered sodium acetate, and 1 c.c. of 50 per cent. acetic acid contained in a small flask fitted with a funnel condenser. The mixture is boiled on a sand-bath for ten minutes and then filtered hot through a filter-paper moistened with hot water into a test-tube provided with a 15 c.c. mark. Should the filtrate fail to reach the mark, it is made up to 15 c.c. with hot distilled water, but in my own work I find this is rarely necessary, as after a little practice it is possible to regulate the boiling process so that the final result always comes out at between 15 and 16 c.c. In well-marked cases of pancreatic inflammation a light yellow flocculent precipitate should form in a few hours, but it may be necessary to leave the preparation to stand over-night before a deposit occurs. Under the microscope the precipitate is seen to consist of long, light-yellow, flexible, hair-like crystals, arranged in sheaves which, when irrigated with 33 per cent. sulphuric acid melt away and disappear in ten to fifteen seconds after the acid first touches them.

The precipitate should always be examined microscopically, as it may be difficult to determine the characters of a small deposit with the naked eye, and so cases giving only a slight reaction may be overlooked. To exclude traces of sugar, undetected by the preliminary reduction tests, a control experiment is carried out by treating twenty c.c. of the urine in the same way as in the test described excepting for the addition of the hydrochloric acid.

TABLE I.

Group.	Diagnosis.	Number of cases.	"Pancreatic" reaction in the urine.	
			Positive.	Negative.
I	Chronic pancreatitis; stone in third or fourth part of the common duct	9	9	—
II	Chronic pancreatitis; no stone found at operation	19	19	—
III	Cancer of the pancreas	5	1	4
IV	No pancreatitis; stone in gall-bladder, or in first or second part of the common duct	9	—	9
V	No pancreatitis; miscellaneous	30	—	30
VI	Normal	22	—	22
VII	Cases from Group I re-examined after operation	2	—	2
VIII	Cases from Group II re-examined after operation	4	—	4

In the tabular statement of results obtained by this method I have arranged the cases in eight groups corresponding to the clinical diagnosis and the condition found at operation. For this information I am indebted to those who kindly supplied me with particulars of the cases I have examined for them in my laboratory, and particularly to Mr. Mayo Robson, who has operated on many of the cases included in Groups 1, 2, and 4. The urines here dealt with form a consecutive series of 100 specimens, derived from 94 persons. All have been examined under the same conditions by the method I have described.

From 29 specimens a more or less abundant deposit of crystals was obtained, but in 71 no crystalline deposit could be found even with the aid of the microscope. In nine cases (forming Group 1) a stone was found in the pancreatic portion of the common duct at operation, and the pancreas was said to show evidence of disease. In 19 (Group 2), although no stone was found at the time of operation, there was said to be enlargement and hardening of the head of the pancreas. I found a gall-stone in a specimen of fæces sent to me from one of these cases, and in another case included in this group I am informed that biliary calculi had been discovered in the stools shortly before the examination of the urine was made. No reaction was obtained in 4 cases diagnosed as cancer of the pancreas (Group 3). One case in which the clinical symptoms and after-history of the case pointed to malignant disease of the pancreas yielded an abundant deposit. A preparation made from the urine of this case by the original *a* method [1] showed a mixture of fine crystals dissolving in 33 per cent. sulphuric acid in fifteen to twenty seconds and many coarse, broad crystals that took five to six minutes to disappear. The urine was also found to contain a very large amount of bile and urobilin, and the excretion of chlorides was much diminished, while the urea and phosphates were approximately normal. In addition the fæces when examined by the method I have recently described (2) were found to be acid in reaction, to contain a

[1] Ten c.c. of the filtered urine are boiled in a small flask fitted with a funnel condenser, with 1 c.c. of strong hydrochloric acid for five to ten minutes. A mixture of 5 c.c. of the urine and 5 c.c. of distilled water is then added, and the flask well cooled in running water. The excess of acid is neutralised by adding 4 grammes of lead carbonate and the precipitate removed by careful filtration through a well-moistened close-grained filter-paper, after the mixture has been reduced to as low a temperature as possible in a stream of water. The clear filtrate is made up to 15 c.c. with distilled water and boiled with 2 grammes of sodium acetate, 0·75 grammes of phenylhydrazin hydrochlorate, and 1 c.c. of 50 per cent. acetic acid, for five minutes. The fluid is then filtered hot through a moist hot filter-paper and the filtrate made up to 15 c.c.

large amount of undigested muscle-fibre, and to yield not a trace of stercobilin. An estimation of the fats showed a total of 64·7 per cent., of which 56·3 per cent. was "neutral fat" and only 8·4 "fatty acid." So that the laboratory results, taken as a whole, confirmed the clinical diagnosis and pointed to cancer of the head of the pancreas, with complete obstruction of the common duct and a considerable degree of secondary inflammation. Of the remaining 67 specimens which gave no reaction 9 were from cases of jaundice in which a calculus was found at operation in the gall-bladder or in the common duct above the pancreatic portion (Group 4). In all these cases the pancreas was said to be normal in appearance and consistency. Fifty-two were examined as controls. Of these 30 were from patients suffering from diseases in which there was no reason to expect that the pancreas was involved (Group 5). They included cases of cancer of the stomach, colon, rectum, or liver, gastric ulcer, duodenal ulcer, gastritis, colitis, appendicitis, tuberculosis of the intestine, intestinal obstruction, cirrhosis of the liver, hepatic abscess, nephritis, floating kidney, tuberculosis of the kidney, cystitis, and Addison's disease. Twenty-two were from healthy individuals (Group 6). I have placed six cases in Groups 7 and 8 which were under the care of Mr. Mayo Robson, and in which I had the opportunity of examining the urine one to two weeks after a cholecystenterostomy had been done for the relief of pancreatitis. All had given a well-marked reaction when the urine was examined shortly before the operation, and are included in Groups 1 and 2, but when the second examination was made no reaction could be obtained.

I am not at present prepared to contend that at all times and under all conditions the results given by this improved method of examining the urine are indicative of the presence or absence of pancreatic inflammation, as my experience of it is not as yet sufficiently great, but I think that the evidence available suggests that it may be of considerable assistance in diagnosis, and that by means

of this, and other methods of investigation I have described, the 50 per cent. of cases of pancreatic disease now said to be only recognised post mortem might be reduced to a much more creditable figure.

My experience suggests that it is always advisable to control the urine examination by an investigation of the fæces, for if the results agree the chance of a mistaken opinion is considerably reduced and is probably very small. The examination of the fæces is particularly useful in cancer cases, as the instance quoted in a former part of the paper clearly shows. It is of the utmost importance that malignant and inflammatory conditions of the pancreas should be clearly differentiated, for, as Mr Mayo Robson has pointed out, while suitable operative interference in chronic pancreatitis and obstruction of the common duct by a calculus is a most satisfactory procedure, operation in cancer is to be avoided as it may tend to precipitate the fatal issue. Clinically it is often a matter of great difficulty; but if the results of the examination of the urine and fæces, carefully and conscientiously performed, are considered in conjunction with the history and symptoms, the chance of an erroneous diagnosis is materially reduced. I should, however, like to emphasise the fact that the laboratory investigations require a considerable amount of care and that it is necessary to weigh all the evidence obtainable in forming a conclusion. The "pancreatic" reaction is only one factor that has to be taken into account in making a diagnosis in suspected cases of pancreatic disease or of jaundice in which it is sought to determine whether there is a gross obstruction to the free flow of bile into the intestine, and whether this obstruction when present is of a simple or malignant nature.

References.

1. 'Lancet,' March 19th, 1904.
2. 'Brit. Med. Journ.,' October 28th, 1905.

DISCUSSION.

Mr. A. W. MAYO ROBSON said that Dr. Cammidge had tested many of his cases on which he had afterwards operated, and confirmed the accuracy of the test. The test required very special knowledge to carry it out. The validity of the test did not depend on the presence of glycerine; the crystals were a derivative of a form of sugar. He had received great help from the test in diagnosis, especially in common bile-duct cases, for if the pancreas were involved longer drainage was required. It also helped in the differentiating of inflammatory from malignant disease of the pancreas. A case on which he operated two years ago was that of a man with deep jaundice, suggesting the presence of malignant disease, but in which the reaction was against it; the appearances, moreover, seemed to be those of malignant disease at the operation, but it subsequently proved to be a case of common duct cholelithiasis, but with no malignant disease. His favourable experience was based on nearly two hundred cases. The test was not meant to be in itself conclusive, but only as a help in diagnosis, and to be taken along with an examination of the fæces.

Dr. H. H. TOOTH asked if it were likely that the test could ever be carried on at the bedside.

Dr. CAMMIDGE, in reply, thought it was not likely.

INFLAMMATION AND PERITONITIS REGARDED AS PHYSIOLOGICAL PROCESSES

BY

JOHN D. MALCOLM, F.R.C.S.EDIN.

SURGEON TO THE SAMARITAN FREE HOSPITAL

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IN offering for discussion a paper on Inflammation and Peritonitis, it would appear to be desirable to begin by stating as accurately as possible the meaning that is to be attached to the word "inflammation." Scientific writers are not dogmatic on this subject, and it is doubtful if any universally acceptable definition, or even short description, of inflammation has yèt been made. Moreover, it seems to me that certain phenomena occurring not infrequently in connection with abnormal peritoneal conditions have a significance, in regard to the nature of inflammation, which has not been sufficiently recognised. I therefore propose to consider the nature of inflammation, as described by physiologists, in connection with the phenomena of inflammation of the peritoneum as they appear to me from a clinical point of view, and to endeavour to bring our knowledge of inflammation and of peritonitis into a more perfect harmony than at present exists between the most authoritative and widely accepted descriptions of the two conditions.

The Nature of Inflammation.

There is a general agreement amongst physiologists that inflammation may be brought about by mechanical, thermal, or chemical injuries, and also by the action of minute living organisms which may be introduced into the tissues by violence, or may gain access to them without any obvious lesion.

Professor Adami, in the article on "Inflammation," in Allbutt's 'System of Medicine,'[1] wrote that "throughout this article inflammation has been considered as the reaction following injury and the response to it." He considered[2] that "the attempt to mark off sharply inflammations caused by mechanical and chemical noxæ from those produced by bacteria and their products must be given up," and he added[3] that "the various forms of inflammation merge insensibly one into the other."

In the 'International Text-Book on Surgery' it is stated by Mr. A. Pearce Gould and Dr. J. Collings Warren[4] that "inflammation may be divided into two principal varieties—simple and infective. To the former belong those produced by trauma or injury. . . . The infective inflammations are those by bacteria or the chemical substances evolved from them.

"In *simple inflammation* we have a disturbance in the nutrition of a part, brought about usually by trauma, which has been best expressed by the word 'damage.' It may be defined as a lesion in the mechanism of nutrition, owing to which its efficiency is impaired, but which, if not so severe as to cause death, is followed by changes favourable for the protection and repair of the part."

In their 'Manual of Surgical Treatment,' Mr. W. Watson

[1] Allbutt's 'System of Medicine,' vol. i, p. 114.

[2] *Loc. cit.*, p. 129.

[3] *Loc. cit.*, p. 128.

[4] 'International Text-Book on Surgery,' by A. Pearce Gould and J. Collings Warren, 1902, vol. i, p. 45.

Cheyne and Mr. F. F. Burghard[1] state that "inflammation may be defined as the first series of changes that occur in a tissue as the result of an injury, provided always that this has not been of sufficient violence to at once destroy the vitality of the part. Whenever an injury is done to a part, whether it be of a chemical or a mechanical nature, a certain series of changes at once commences there, and this series of changes, so long as it is of an exudative or destructive character, we call inflammation."

Although the view that inflammation may be due to various causes is taught by physiologists, it is not very unusual to find men talking and writing as if inflammation could not occur without the presence of micro-organisms, and Professor Adami attributed this view especially to surgeons. He said that "surgeons strive to restrict the idea of inflammation to acute pyogenic disturbance."[2]

There is no doubt that this assertion with regard to surgeons contains a certain amount of truth.

In most text-books on surgery there is a description of the nature of inflammation according to the teaching of physiologists, but in a still considerable number there is little or no further notice taken of aseptic inflammation. As far as I understand his writings, Lord Lister is in no way responsible for the view that all inflammations are caused by infective germs. His description of "The Early Stages of Inflammation"[3] was founded chiefly on observations of the effects of the application of various stimuli to the web of the frog's foot. Mechanical, thermal, and galvanic irritations and those caused by such agencies as mustard and carbonic acid were used.

Lister arrived at the conclusion[4] "that the various physical and chemical agents which, when operating powerfully,

[1] 'Manual of Surgical Treatment,' by W. Watson Cheyne and F. F. Burghard, Part I, p. 1.

[2] Allbutt's 'System of Medicine,' vol. i, p. 120.

[3] 'Phil. Trans.,' vol. cxlviii.

[4] *Ibid.*, p. 689.

extinguish the life of the constituents of the animal body, produce by a somewhat gentler action a condition bordering on loss of vitality, but quite distinct from it, in which the tissues are, for the time being, incapacitated for discharging their wonted offices, though retaining the faculty of returning afterwards, by virtue of their own inherent powers, to their former state of activity, provided the irritation have not been too severe or protracted. This suspension of function or temporary abolition of vital energy is the primary lesion in inflammatory congestion." Inflammation was not attributed to the influence of micro-organisms in any portion of this paper.

Moreover, the method of surgery introduced by Lister was not described by him as being directed to the prevention of inflammation. He wrote[1] that the "antiseptic system of treatment consists of such management of a surgical case as shall effectually prevent the occurrence of putrefaction in the part concerned."

But the discoveries of Lister and their clinical application have led to most brilliant results in facilitating recovery from operations without *dangerous* inflammatory reaction, and apparently it is on account of these results that some surgeons talk, and would seem to think, of the prevention of inflammation by various precautions, when the prevention of septic contamination was all that was claimed for the antiseptic method of treatment by its author.

It appears to be forgotten by many that, when septic changes in an injured part are successfully prevented, the simple inflammation described by Lister, Paget, Watson Cheyne, and others still exists as the result of every wound. "A certain amount of inflammation, as caused by direct irritation, is essential to primary union."[2]

Other surgeons maintain that all inflammations are caused by micro-organisms. As far as I understand those who adopt the latter view, it is held by them that the results of a wound, when not complicated by the presence

[1] Introductory Lecture, University of Edinburgh, 1869.

[2] Lister, 'Phil. Trans.,' vol. clxviii, p. 700.

of infective material, are only the physiological changes connected with its healing; that, clinically, inflammation does not exist under aseptic treatment; and that, when obvious symptoms of inflammation arise, there must have been some failure in the application of the means employed to prevent infection.

That the changes following the infliction of an aseptic wound may be regarded as physiological is beyond dispute. Healing and the processes which accompany it are natural, and therefore physiological, results of any injury the action of which is not too prolonged, and which does not kill.

On the other hand, that inflammation does not exist under perfect aseptic treatment, and that obvious signs of inflammation indicate a failure of the means employed to secure asepsis seem to me to be propositions which are distinctly opposed to the teaching of physiologists and which are not supported by clinical experience.

In the paper on "The Early Stages of Inflammation" from which I have already quoted it was proved that living tissue has an inherent power of recovery when damaged, if the injury be not too great. Numerous experiments were recorded in support of this conclusion. For example, it was shown that the movements of the cilia of a portion of a frog's tongue separated from the body were arrested by heat, and recommenced when the source of heat was withdrawn, and that this arrest and return of movement could be brought about no less than five times before all evidences of vitality ceased.[1]

In the same paper it was stated, and other observers have also shown, that one of the early changes caused by an irritation of the tissues was a slowing of the movements of the blood-discs and eventually a complete arrest of their progress through the vessels of an injured part, although the blood-vessels in and around the irritated area were widely dilated. As a result there was a redness of the tissue caused by the close aggregation of the coloured

[1] *Loc. cit.*, p. 694.

blood-corpuscles. Evidence was brought forward showing that the arrest of these corpuscles was due to a stickiness of the cells induced by their contact with the damaged walls of the capillaries, and this adhesiveness was compared to that arising when blood is removed from the body. The congregation of the red corpuscles was one of the most obvious effects produced, but it was also shown that "one of the earliest abnormal appearances is that of white corpuscles adhering in large numbers to the walls of arteries, capillaries and veins as first described and accurately figured by Dr. Williams."[1]

And again it was asserted that "when the irritation has been very slight the white corpuscles, which are susceptible of much greater adhesiveness than the red (as we learn from examining blood outside the body), acquire some tendency to stick to the vascular parietes. . . . As the irritation increases the vessels become crusted with them, often to a remarkable degree. . . . Sometimes, especially in young frogs, capillaries become obstructed throughout their entire length by white corpuscles alone."[2]

It has also been shown that these white corpuscles may pass through the walls of the capillaries into the tissues, and it is believed by some that this takes place even when there has been no irritation of the parts.[3]

To prove by actual demonstration that the leucocytes pass out of the vessels in health is obviously difficult, if not impossible, because the manipulation necessary to see the tissues may be the cause of sufficient irritation to promote a condition favouring the escape of the white cells. But as it is certain that they can escape from the vessels when the latter are irritated, and as we know that cells similar to the white blood corpuscles "are found in the lymph, in adenoid tissue, in bone marrow, and as wander-

[1] Lister, 'Phil. Trans.,' vol. clxviii, p. 670, quoting 'Principles of Medicine,' by C. J. B. Williams, M.D.

[2] 'Phil. Trans.,' vol. clxviii, p. 671.

[3] 'Landois' 'Human Physiology,' 5th English edition, p. 181.

ing cells in the connective tissues of various parts, as well as between glandular and epithelial cells," [1] it seems highly probable that the leucocytes are capable of considerable independent movement in the tissues outside the vessels in health.

More recently Professor Metchnikoff has emphasised the importance of the activity of the leucocytes in retrogressive processes, and has shown that the parts to be removed are taken up by them in the form of particles and therefore in a measure are eaten. He "designates the cells with these activities as devouring cells—phagocytes. Thus they act as *chondroclasts* and *osteoclasts* in the absorption of cartilage and bone respectively. Cells of similar activity are found in the tails of batrachia and which take up portions of the tissue, as, for instance, fragments of fibrils, in the disappearance of the tails during the process of metamorphosis. . . . Schizomycetes, or particles of other substances that have gained entrance into the blood, have been found taken up in part by leucocytes. Later, the leucocytes yield up these substances to the endothelial cells of the capillaries of the liver and the lungs, less commonly of the spleen." [2]

Thus one function of these colourless cells seems to be to remove effete and foreign matters by absorbing and digesting them and carrying them away.

Moreover, it is said that in the blood in the healthy vessels the white corpuscles are much more numerous than in blood outside the body,[3] and it seems certain that they may be found in any part of the living organism in which their services may be required, even in non-vascular tissues, such as the cornea. In an inflamed area the blood-plasma also escapes from the vessels. The swelling of inflammation is due "chiefly to the escape of plasma into the tissues." [4]

[1] *Ibid.*, p. 45.
[2] *Ibid.*, p. 46.
[3] *Ibid.*, p. 70.
[4] *Ibid.*, p. 189.

In healthy conditions nutrition and removal of effete matters are constantly going on in all parts of the system, more actively in some than in others.

Superfluous cells on the skin and mucous membranes are shed from time to time when they cease to be of use. The materials of the deeper tissues are made removable from one part to another either as waste products, or for nutritive purposes, by physiologico-chemical processes, the full details of which are not understood, and the mechanism of which is not of a nature that can ever be detected by the aid of the microscope alone.

It is, however, so probable that one may regard it as certain that, in an area which has been subjected to a severe bruise, or to the effects of heat or of chemical irritants, or through which a knife has been drawn, although some of the damaged cells recover because of their inherent powers, others must continue to undergo retrograde changes, and must hasten to become effete, or to develop effete matter more quickly as a consequence of the injury they have sustained than they would if they had been left to follow the natural processes of nutrition and decay.

Hence a necessity for the removal of an excessive quantity of waste products from an injured part must exist as a result of the irritation, until all damaged cells have recovered their full vitality or have been absorbed.

In the paper on "The Early Stages of Inflammation" above quoted it was argued that the arrest of the flow of blood through an injured area was due to the blood-cells being partially devitalised by coming into contact with the damaged walls of the vessels in the part affected.

But "in warm-blooded animals the leucocytes exhibit movements for a long time upon a warm stage, at the temperature of 40° C. for about two or three hours,"[1] and the circumstances in which an arrest of the blood-flow is produced by an irritation of tissue seem to me to indicate that the leucocytes may be gathered together for a definite purpose. The suggestion arises that the arrest of the

[1] Landois, *loc. cit.*, p. 47.

leucocytes is due to an active physiological process rather than to a simple diminution of their vitality caused by damage done to them by contact with the walls of vessels which have been injured.

Landois says that "the leucocytes exhibit still another interesting peculiarity, namely, that of chemotaxis (chemotropism), which consists in the attraction of freely motile cells—like some lower organisms—by certain substances and their repulsion by certain others; especially the metabolic products of pathogenic and non-pathogenic micro-organisms exert a strong attractive influence upon the leucocytes. If, therefore, colonies of staphylococcus (bacteria of suppuration) collect at a given part of the body, their metabolic products attract the leucocytes from the neighbouring vessels, and in this way inflammatory reaction and suppuration result."[1] But we have seen that when a "very slight" irritation is applied to the web of the frog's foot, "sometimes, especially in young frogs, capillaries become obstructed throughout their entire length by white corpuscles alone."[2]

Moreover, this effect of slight irritations, acting temporarily, is always followed by a return of the circulation to a healthy condition after a short time, and an arrest of the blood-flow has been observed under circumstances in which it is hardly possible that bacteria of any kind could have been present to attract the leucocytes.

For instance, on a drop of chloroform being applied to the web of a frog's foot,[3] "the corpuscles instantly become checked in their progress by sticking to each other and to the capillary walls, and move on slowly in masses with considerable intervals." It seems to me that as one of the functions, and certainly not an unimportant function, of the leucocytes is to digest effete material—in absorbing cartilage or bone, for instance—and to carry it away for disposal elsewhere, the chemotaxis which they exhibit as

[1] Landois, *loc. cit.*, p. 46.
[2] Lister, *loc. cit.*, p. 671.
[3] Lister, *loc. cit.*, p. 663.

regards colonies of staphylococcus may also be an inherent peculiarity which attracts them to any area of the body in which damaged tissue and consequent excess of metabolic products requiring removal may be found.

If the property of chemotaxis, the property of being attracted by some substances and repelled by others, draws the leucocytes in large numbers into an irritated area with the direct purpose of absorbing effete matter, there can be little doubt that, when the individual leucocytes have absorbed as much as they can hold, a repulsive action will come into play, and the white cells will, by virtue of their chemotaxic properties, seek to retire from the irritated area, and will effect this purpose either by returning to a capillary or by entering the lymphatic system. It is obvious that the exudation of plasma which takes place into the interstices of the affected tissues must greatly facilitate the movements of the leucocytes into and away from the parts which have been damaged, whilst this plasma will also afford pabulum for their nourishment, and may exercise a solvent action on effete matter and a destructive power as regards micro-organisms. There can be no doubt that a circulation and exchange of products between the blood and lymph on the one hand and the injured tissues on the other must continue even in severe inflammatory conditions. If the supplies of nutritive material were completely arrested, the tissues would die.

Inflammation is, therefore, an exudative process, but the exudation seems to be part of a process of absorption.

There are, however, two forms of exudation consequent on an injury, such as an incision, which involves division of tissue, and these must not be confounded. An immediate effect of cutting the tissues is a discharge of blood and lymph caused by the division and opening of the lymph and blood-vessels. Sometimes also oily matter may be seen oozing from the fat of very stout people. A discharge from large vessels may give rise to a lymphatic fistula or to serious haemorrhage, but smaller vessels close after a short time. This immediate exudation from the

surface of a wound is a purely mechanical effect, and is not due to inflammatory or other physiological causes. Its arrest is brought about by vital changes. In a wound healing by perfectly natural processes, in a dog, for instance, these discharges escape and are lost. But a surgical wound is usually closed by sutures, by which discharges may be retained. From an extensive wound, such as the incision necessary for the removal of a breast, even if all visible vessels are carefully tied, a large amount of red-stained serum, sufficient to soak through two or three inches of dressings, over an area of a square foot or more, may be discharged in the first twelve hours when drainage is free. Firm pressure checks this flow, and the most perfect and natural closing of a wound is by pressure just sufficient to prevent any accumulation, and so applied as to allow the discharges to escape between the lips of the incision whilst still keeping the surfaces in accurate apposition.

In nature such discharges are never retained unless by a valve-like action of different layers of tissue when an injury is extensive and deep. When this happens healing is apt to be interfered with.

This mechanical exudation, if it collects or is retained between the lips of a wound and is *not* absorbed, may prevent union mechanically, or by causing tension.

The tissues are, however, capable of absorbing a certain amount of such exudations, and a wound heals most quickly when all discharges are promptly taken into the circulation or escape on the surface of the body.

Thus, the exudation from a raw surface which is an immediate and mechanical effect of an incision is quite a distinct process from the exudation of leucocytes and plasma which takes place into the interstices of damaged tissue, and also on to the surface of an incised wound, as a result of the irritation.

The exudation immediately flowing from a cut surface may be harmful if in too great quantity, or if retained and not absorbed. On the other hand, the exudation into the

tissues brought about by their irritation seems to have a definite and always beneficial purpose. When the irritation is not septic, and when the conditions are otherwise favourable, union invariably takes place, and it seems to be at least highly probable that the object of the whole series of phenomena following an injury is an introduction of leucocytes into the damaged area in numbers sufficient to remove by physiological processes the products of the excessive decay of tissue induced by the injury.

In fact, although the damaged tissues continue to undergo the processes of nutrition and decay which are always in action, and some of the cells degenerate more rapidly as a consequence of the injury, it seems to me that in all other respects the processes set at work by an aseptic injury are of a constructive character and are not in any way destructive, and also that inflammation is not a process of impaired action, but a process of effective reaction to a call for increased physiological activity.

Phagocytosis and the passage of fluids and of leucocytes from the vessels into the tissues, and from the tissues back to the vessels, are normal physiological processes which are carried on to an unusual degree in an irritated area, and I see no reason to suppose that an aseptic inflammation is other than a physiological process in any of its details.

Here it may also be noted that when an injury is of the nature of an incision the changes connected with healing of the wound commence at once and progress rapidly under favourable circumstances. These changes are certainly constructive in character, and it would appear that the exudation of white blood cells and plasma into irritated tissues constitutes the initial stage both of inflammation and of repair.

It is an important point in connection with the results of an injury that the signs of inflammation are apt to be more obvious when a dense than when a lax tissue is concerned. According to the view I have suggested this is very easily explained; for, if leucocytes and plasma must be thrown into the tissues to accomplish resolution, it

is obvious that this can take place more easily when swelling of the part is not interfered with in any way. This is the more important if, as I conjecture, the leucocytes and the plasma move with considerable freedom into and out of the inflamed area.

In the same way the evil effects which always follow tension in a wound may be explained. Tension must make the necessary exudative processes more difficult.

The Merging of Inflammatory into Natural Processes.

If inflammation depends on a diminished vitality of injured tissues and if the inflammatory process consists of the physiological changes necessary to remove effete matter which is produced in excess because of a localised irritation and diminution of vitality, it is clear that an injury to one cell or to a hundred cells adjacent to each other, or to any number of cells, must produce changes of exactly the same kind, varying, if the circumstances be otherwise the same, chiefly or perhaps only in degree.

Hence it is a very difficult task to define the beginnings of inflammation, and indeed they must merge insensibly into natural processes.

In a paper on "The Fate of the Ovum and Graafian Follicle in Premenstrual Life,"[1] Dr. Thomas G. Stevens has published a series of drawings of microscopic sections, which were exhibited at a meeting of the Obstetrical Society, and these show the changes which take place in the ovaries of children under 10 years of age. At this age the ovum and the Graafian follicle develop and advance to a certain extent and then atrophy, and are absorbed without rupture of the follicle taking place.

As retrograde changes progress, the ovum is destroyed by a phagocytic action which, in Dr. Stevens' opinion, is carried out by the cells of the membrana granulosa, and the fibrous tissue surrounding the follicle "undergoes a well-marked series of changes which result in the

[1] 'Obstet. Soc. Trans.,' vol. xlv.

formation of a kind of granulation tissue. The first change noted is increase of capillary blood-vessels in the fibrous coat, sometimes to a remarkable degree. . . . Along with this increase in the vessels there is a proliferation of the connective-tissue cells in the fibrous tunic, the whole producing a richly cellular, very vascular tissue, extending eventually all round the follicle. This layer is easily distinguished from the membrana granulosa by the presence of so many vessels in the former, while there are none in the latter. This layer rapidly increases in thickness, and the blood-vessels form definite capillary loops such as are constantly associated with granulation tissue."[1] A layer which appears to consist of coagulated lymph is "thrown out from the blood-vessels, and in it new connective tissue begins to form in the follicle."[2] Dr. Stevens believes that some of the cells of the membrana granulosa take on a phagocytic action, whilst others simply disintegrate. "Before much contraction occurs in the follicle, nearly all the cells of the membrana granulosa have disappeared."[3] A delicate connective tissue fills up the follicle, "upon which the granulation tissue gradually encroaches, compressing it and possibly reabsorbing some of it."[4] Eventually nothing but a scar is left.

No evidence of the occurrence of diapædesis was observed and Dr. Stevens says that "every recent research points to the fact that it is not only the white blood cells which exert phagocytic powers."[5] Although "no leucocyte was seen emerging from a vessel," it seems probable that leucocytes must assist in eating up the disintegrated cells of the membrana granulosa, and there can be little doubt that effete matter is carried away by them, whilst pabulum and very likely also the actual cells or some of the cells for the building up of the cicatrix are supplied from the blood in

[1] 'Obstet. Soc. Trans.,' *loc. cit.*, pp. 475-6.
[2] *Ibid.*, p. 476.
[3] *Ibid.*, p. 475.
[4] *Ibid.*, p. 477.
[5] *Ibid.*, p. 474.

the " richly cellular vascular tissue " which temporarily surrounds the follicle when the retrograde process is going on.

In this description of the phenomena by which the ovum and the follicle are absorbed without rupture, the process is shown by which unnecessary tissues—organic foreign bodies —are removed and the surrounding parts are consolidated. The mechanism of the process consists of a phagocytic action and a formation of cicatricial tissue.

Again, from a study of the changes by which the tadpole loses its tail Metchnikoff first observed and described a process of phagocytosis, and in the sloughing of the umbilical cord on the abdomen of a newly-born mammal there is a natural procedure which cannot clinically be distinguished from that of healing under a scab, and which in all probability involves some degree of phagocytic action as the parts separate. It is certain that in connection with the separation of the umbilical cord, with the casting of the tadpole's tail, and with the absorption of the child's ovum and follicle, phagocytosis and the formation of a cicatrix are purely physiological phenomena.

The differences between the changes connected with these physiological processes and the changes following an injury seem to me to be very slight, if any exist at all.

If we consider the human body as a piece of machinery, the development of ova and follicles and their removal in the child, and also the separation of the umbilical cord and of the tadpole's tail, may be regarded as part of the work of the machine, arranged for by specially adapted mechanisms. The healing of a wound is carried out by a method involving identical processes; but as the infliction of an injury is not a natural occurrence, recovery from it may not be so readily accomplished, and consequently the accidental irritation throws the action of the affected area out of gear for a time.

There is a sudden unexpected call for extra work and for the introduction of an abundance of leucocytes and serum into the injured part to do this work.

These changes, however, seem to be only an exaggerated activity of a normal process by which phagocytic cells are conveyed to or developed in any area where there is effete matter to be disposed of.

When an accident occurs to a machine made by man, the whole of a complicated system of works may have to be stopped before an injured part can be put right; and a patient may be killed by an injury, or he may have to be kept absolutely quiet in bed until the damaged tissues are mended. On the other hand, only a very slight, temporary, and local inconvenience may be caused.

Repair, whether in a piece of machinery or in a living organism, is usually carried out deliberately, but proceedings for the removal of damaged structures and for the adaptation of parts which, although injured, may still be of use for a time, are often carried out hurriedly and with a certain amount of excitement. It would seem to be the series of phenomena necessary for the removal of effete matter from damaged tissues by natural processes that constitutes inflammation in the human machine.

From this point of view, also, the changes taking place in the process of inflammation are the same as those which lead to cicatrisation. When the cells thrown into an irritated area have absorbed and removed all effete products, if there be a solution of continuity, or, as in the case of the unruptured follicle, if there be a cavity to fill up, the same or similar cells are transformed into cicatricial tissue, and so resolution is completed.

Inflammation does not necessarily involve changes obvious to the naked eye or any constitutional reaction which may be recognised by a rise of temperature or pulse rate. When, in adult life, the Graafian follicle ruptures there is necessarily a solution of continuity in the tissues, and the changes taking place at the point of rupture must be very similar to, and probably exactly resemble, those described by physiologists as being brought about by an irritation of tissue. The rupture of a follicle is certainly a physiological process, but it is also of the nature of an

injury. Probably a few capillaries are blocked and a somewhat unusual number of leucocytes find material requiring their attention at the point of rupture, quite apart from the absorptive and constructive actions necessary for transforming the corpus rubrum into a scar.

Thus it would appear that at the point of rupture of a Graaffian follicle there is produced a very small area in which changes take place which differ in no way from those of inflammation, but which are certainly induced by a physiological act, and which, therefore, must be resolved by physiological means.

The thrusting of a fine needle into the tissues must also cause a certain amount of damage and a necessity for removal of an excess of effete matter, with a consequent congregation of leucocytes around the injured part.

The damaged tissues may hardly exceed in extent those implicated when a Graafian follicle ruptures, so that the effects produced might not be greater in the one case than in the other. But if the local changes brought about by the needle are exactly the same in nature as those which occur at the point of rupture of a Graafian follicle, the fact that their cause is abnormal does not alter the character of the changes which are produced. These changes are still physiological.

It might here be suggested that, as inflammation was long regarded as a disease of a damaging nature, if it is now to be considered as a physiological process, it would be well to retain the word "inflammation" for the destructive action which is generally effected by micro-organisms —a view which seems to be very generally adopted.

But although the changes caused by an injury merge into physiological action in their simplest forms, when only a small area is involved, there is no doubt in my mind (and I hope to be able to show) that these changes may give rise to a disturbance which is of a most acute kind, but which, in my opinion, continues to be a physiological reaction, and is not necessarily associated with putrefactive changes, but which it may be difficult, or even impos-

sible, in some stages, to separate clinically from effects which may be produced by micro-organisms in a wound. Hence, not only does inflammation in its simplest form merge into natural processes, but "the various forms of inflammation merge insensibly one into the other," and it is quite as difficult to say where the line is to be drawn between a simple and a septic inflammation as between normal and inflammatory changes.

A short incision, in a part which is little liable to movement, causes hardly a greater disturbance than the puncture of a needle. So, if there is a small clean aseptic wound in tissues adapted for considerable movement, such as those over a finger-joint, as long as the parts are kept quiet the healing process progresses with little, if any, evidence of local irritation. But if the joint be used after the first forty or fifty hours, when adhesion of the surfaces of the incision is fairly firm, and if the wound does not reopen, it will show marked evidences of inflammation, in the shape of redness, swelling, and pain; and during a period of some four or five days it may be possible to produce or to allay these signs of inflammation at will, simply by using the joint or by keeping it quiet. By movement the process of resolution is prolonged, the cause of this being the fresh injury involved in stretching and straining the healing parts. Under these circumstances there are obvious effects of the inflammation visible to the naked eye.

But, however painful and obviously inflamed a small clean wound over a joint may be, if it heals without breaking down, it seldom, if ever, causes any recognisable constitutional symptoms, and, when the wound does not re-open, there is no evidence that micro-organisms are concerned as the cause of the inflammation which is obviously produced by movement.

To say that micro-organisms must exist in the affected tissues because signs of inflammation develop is to beg the whole question.

When a large wound is made, such as that for the removal of a breast, if the parts are kept quiet and union

takes place by first intention, there may still be little or no evidence of inflammation in the form of quickened pulse, or elevated temperature, or in the appearance of the incision. But in such cases, if the temperature remains low, the skin acts profusely, and the urine is loaded with lithates after the operation.

These are evidences of increased tissue change throughout the body. They are also, under the circumstances, evidences of febrile reaction. Dr. Donald McAlister has stated that "high temperature is not necessarily fever, and fever is not necessarily accompanied by high temperature. . . . It is the excessive thermogenesis with the excessive catabolism of nitrogenous tissue which that involves that constitutes fever."[1]

It has been suggested to me that excessive sweating and concentration of urine follow violent exercise, and, therefore, that these changes do *not* indicate fever. But if the effect of a wound, when it heals by first intention, and when the patient and the injured part are kept as quiet as possible, is a production of as much sweating and concentration of urine as if he were taking violent exercise, the proof seems complete that the wound has given rise to very great and unusual tissue changes, and these changes, when thus induced, are described by physiologists as constituting fever. The increased metabolism brought about by an extensive incision differs from that induced by violent exercise in the nature of its cause. It is a physiological effect of an abnormal stimulus. Moreover, in a very large number of cases a slight rise of temperature, although it may be a very slight rise indeed, can be detected after any considerable[2] operation, if accurate records are made.

Peritonitis.

Before discussing the origin of the excessive metabolism which accompanies large injuries it will be convenient to

[1] "Gulstonian Lectures," 'Brit. Med. Journ.,' 1887, vol. i, p. 670.

[2] *Vide* p. 296, *infra*.

consider some of the phenomena of inflammation as they are exhibited in the peritoneum, and as they are modified by the presence of micro-organisms.

The peritoneum encloses, or constitutes, a large lymphatic space without any opening visible to the naked eye, except at the orifices of the Fallopian tubes in the female. It consists of a thin layer of fibroid tissue containing white and elastic fibres[1] and lined by a single layer of cells.

Owing to the arrangement of the serous membrane in relation to the various viscera, the space enclosed has a very complicated shape, and there are numerous recesses and partial separations of one part of the peritoneal sac from another.

Many viscera, notably the small intestines, appear to be within, or partially within, a "cavity." They have, however, only been pushed into position in the process of development, carrying with them folds of the peritoneum. The intestines and the other abdominal viscera, although they may be described as partially covered or even, in some cases, as entirely surrounded by this membrane, are all completely outside the sac of the peritoneum.

In normal conditions this sac contains only a little serous fluid, sufficient to keep its surfaces moist, but, owing to its intimate relations with the lymphatic vessels and its abundant vascular supply, serum and lymph may be thrown into the peritoneal space very quickly, and absorption from it may also take place with great rapidity.

The peritoneal surface is opposed everywhere to peritoneum, and if injured in any way this membrane is particularly liable to contract adhesions. Especially when a raw surface is made, in the course of an operation or otherwise, any peritoneal surface opposed to the divided tissues is very apt to become fixed by a firm union between the two. Such a union between irritated peritoneal surfaces or between a peritoneal and a raw surface takes place and becomes firm much more quickly than when two raw surfaces are concerned.

[1] 'Quain's Anatomy.'

Adhesions thus formed are frequently seen during operations some time after the patient has recovered from an abdominal section. They are, in my opinion, a result of a simple inflammatory and healing process, quite independent of the action of micro-organisms, and it is interesting to note that, however insignificant the reaction caused by an incision or injury may be, the resulting adhesions are almost invariably described, and I believe rightly so, as "inflammatory" adhesions.

The peritoneum is not alone in being particulary susceptible of adhesive inflammation. All serous and synovial membranes are readily affected in the same way. If a joint is injured and is kept quiet, its synovial surfaces are very apt to adhere, but movements prevent this. Pleuritic adhesions are very common. The serous coverings of the brain may also become adherent when inflamed, and adhesions of the iris are not infrequent.

The peritoneum is, however, so situated that it is to a great extent protected from every external injury which does not place it in contact with the outer air, or with the contents of some hollow viscus, either directly, or by continuity through damaged tissues; and the more we learn about inflammation of the peritoneum the more clear does it become that peritonitis, in a large number of cases, is produced secondarily by extension of inflammations affecting tissues adjoining this membrane.

These inflammations are generally septic in character, and it has been considered doubtful whether an aseptic peritonitis exists at all.

Mr. Pearce Gould and Dr. Collings Warren, although they divide inflammation into simple and septic varieties,[1] nevertheless begin the chapter on peritonitis in their book by stating that "peritonitis for all practical purposes may be defined as an inflammation of the peritoneum caused by the presence of bacteria and their products."[2]

Mr. Watson Cheyne and Mr. Burghard divide peritonitis

[1] 'International Text-Book on Surgery,' 1902, vol. i, p. 45.

[2] *Ibid.*, vol. ii, p. 334.

into suppurative and non-suppurative forms, and they say that the non-suppurative form [1] "may occur without the intervention of the pyogenic organism, and it is quite possible that in cases of localised peritonitic exudation no micro-organisms have penetrated into the peritoneal cavity. This pathological question, however, need not detain us here."

Sir Frederick Treves in his Lettsomian lectures on peritonitis wrote that [2] "It has now become evident that peritonitis depends almost entirely, if not entirely, upon infective processes, and that these agencies are concerned, directly or indirectly, in every form of the disease. There are those who maintain that there is no form of peritonitis which is not due to infection, and, although the data on which such an assertion is based are not entirely perfect, there is yet much presumptive evidence in favour of its accuracy."

Again, Sir Frederick Treves said: [3] "The domain of non-infective peritonitis is becoming rapidly more and more dubious," and in the same lecture he wrote that there was much "conflict of opinion" on the subject of "peritonitis due to irritants. If its existence be established, then the existence of a non-infective variety of peritonitis has to be at once acknowledged." [4] But [5] "a consideration of the whole matter leads to the conclusion that the production of peritonitis by non-infective irritants has not yet been satisfactorily proved."

Thus Sir Frederick Treves did not recognise as more than a vague possibility any peritonitis that was not septic. He, however, said that [6] "other views of the mode of death in peritonitis are held by many competent authorities," and he referred to my paper in the

[1] 'Manual of Surgical Treatment,' Part VI, Sect. i, p. 399.
[2] 'Med. Soc. Trans.,' vol. xvii, p. 140.
[3] *Ibid.*, p. 141.
[4] *Ibid.*, p. 154.
[5] *Ibid.*, p. 156.
[6] *Ibid.*, p. 132.

'Medical Society's Transactions'[1] as illustrative of such views.

It seems to me that the difference between Sir Frederick Treves' views and my own, to which he directed attention, depends primarily on the fact that he regards a conflict between the cells of the body and the invading bacteria as "a representation of the inflammatory process,"[2] whereas from my point of view the phenomena to be observed in connection with the surgery of the peritoneum may be better explained if it is recognised that every injury of sufficient but not too great severity necessarily leads to inflammatory reaction, although no micro-organisms of any kind may be present.

Peritonitis caused by Torsion of the Pedicle of an Ovarian Tumour.

There are certain not uncommon circumstances of a very obvious and definite character which were not mentioned in the Lettsomian lectures on peritonitis delivered by Sir Frederick Treves, but which require to be considered in this connection. One of the most convincing instances of acute aseptic inflammation appears to me to be found in the phenomena which usually follow firm twisting of the pedicle of an ovarian tumour.

The fact is well known that an ovarian pedicle may undergo such acute torsion that, as a consequence, the blood supply to the tumour is suddenly arrested. Slight degrees of strangulation may occur, with varying symptoms, but when the torsion is sufficiently tight the blood supply is completely shut off, and a well-defined line of demarcation arises between the healthy tissues on the proximal side of the twist and the tissues beyond it, which are deprived of their blood supply. It would appear that the veins are first affected, for it very generally, and indeed

[1] "The Physiology of Death from Traumatic Fever," 'Med. Soc. Trans.,' vol. xvi.

[2] 'Med. Soc. Trans.,' vol. xvii, pp. 126, 127.

usually, happens, if the growth be cystic, that the tumour suddenly distends, and that afterwards the fluid in its interior has a large quantity of blood mixed with it. Apparently the arteries continue to pump blood through the twisted part for a time after the softer veins have been occluded.

As a consequence of the extra pressure thus induced in the capillaries and veins, the delicate lining membrane on the inner surface of the cysts gives way, permitting the blood to escape and to mix with the ovarian fluid. After a little time the arteries also are closed, and complete arrest of the circulation through the pedicle takes place.

One of the symptoms of the twisting of a pedicle is an intense pain, commencing suddenly. The onset of pain is followed by fever, during which the temperature frequently rises to between 102° and 103° F., and it may go considerably higher. The amount of pain seems to depend on the tightness of the torsion. A small growth may give rise to very acute pain. The rise of temperature, on the other hand, may be little obvious if the strangulated growth is very small. Apparently the amount of tissue involved influences the degree of general reaction which follows, just as a large incision causes obvious increased metabolism throughout the body, although a small wound does not. Of course a large tumour affects a greater area of peritoneum in proportion to its size.

The bowels are constipated as a consequence of the presence of the strangulated mass. If obvious septic infection, with formation of pus, occurs, the danger of the condition may become extreme, but it is not usual to find any evidence of a complication of this kind. In the great majority of cases, if the woman is kept quiet, recovery follows. For a time the tumour and the parts covering it are very tender, but they gradually cease to be so. The temperature is quite normal, as a rule, well within a fortnight, and an action of the bowels may usually be obtained within a week.

If the abdomen is opened between three days and a

week after the first symptoms develop in a case in which a tight twist of the pedicle of a cystic ovarian tumour has occurred suddenly, and in which suppuration has not been induced, a tumour will be found of a dark blue-black appearance, the colour being due partly to the strangulation and partly to the blood effused into the cysts. The growth is adherent to everything it touches, but about this time the vessels in the adhesions are minute, and the connective tissue is very delicate. The adhesions can, therefore, be separated without difficulty by a sweep of the finger, and when separated they hardly bleed, and they ooze very slightly. The pedicle is, as a rule, easily tied on the proximal side of the twist, the tumour is cut away, and the patient makes a good recovery.

There can not be any doubt that in these cases an acute inflammation, a febrile reaction, and a development of adhesions are produced by the twisting of the pedicle and by the presence of the strangulated mass acting as an irritant to the peritoneum covering the parts in contact with it. If the abdomen is opened the signs of inflammation are unmistakable. There is, however, no spreading of the inflammation beyond the peritoneum in contact with the tumour.

The effects of the irritation are often slightly prolonged, evidences of disturbance not always subsiding steadily after the third day, as is usual in the case of a flesh wound under favourable circumstances. This, as in the case of the signs of irritation in a small wound over a joint that is not kept at rest, is fully accounted for by the fact that the inflamed parts can not be kept still, because every movement of the coils of intestine adjoining the tumour tends to drag upon and to irritate the delicate newly-formed tissues in the inflamed area.

If a patient is kept quiet for a few weeks after the pedicle of an ovarian tumour twists, recovery usually takes place, and if an operation for the removal of the growth is performed some months later an ovarian tumour of ordinary appearance is found, the pedicle is twisted, and generally,

if the growth is cystic, some of the cysts contain fluid which is darkened by the admixture of blood. Blood effused into an ovarian cyst seems never to be removed, probably because the inner lining of the cyst is a secreting surface.

If the pedicle is so firmly twisted that an acute febrile illness has been induced, adhesions are always found, and a part, sometimes a very large part, of the blood supply of the growth is conveyed through them. But although the tumour becomes adherent to everything it touches immediately after its pedicle becomes acutely twisted, the adhesions are rarely universal when a few weeks have elapsed. The greater part of them become absorbed when the tumour is revived by a fresh supply of blood, but sufficient adhesions always remain to insure the nourishment of the growth, although they may be found only at one or two places on its surface. The conditions observed in these cases explain also how any tightly ligatured tissues may survive.

Peritonitis due to Rupture of an Extra-Uterine Gestation.

There is another not infrequent peritoneal condition in which an internal disturbance arises, accompanied by pain and high fever, and in which there is certainly an acute inflammation, but the evidence that this is due to micro-organisms is not obvious. I refer to the circumstances developing in some cases of extra-uterine fœtation. In these, about the third month after conception, there is often an acute and painful inflammatory attack, connected with a rupture of the Fallopian tube. After a short time the symptoms may abate, and in a number of cases the pregnancy, in spite of such an attack, goes on for several months or to the full period of gestation.

A similar inflammatory attack frequently takes place in connection with the death of the fœtus (extra-uterine) at or near term. The fact that in many such cases the fœtus becomes putrid shows that when germs of putrefaction do reach the dead organism, they at once grow and develop,

This may occur at once, but septic matter sometimes gains access to the dead fœtus months or years after the parts have become quiescent. Probably some bone is pushed gradually towards a hollow viscus, and when it penetrates the mucous membrane micro-organisms are admitted and a septic inflammation is excited. Nevertheless, in a certain number of cases the inflammation, although it is around a dead fœtus well advanced in gestation, does not give rise to suppuration or to any signs of putrefaction.

Peritonitis caused by Rupture of an Extra-Uterine Fœtation in the Early Stages of its Development.

The effusion of blood into the peritoneal cavity in the early stages of the development of an extra-uterine fœtation is also frequently attended by acute pain when the rupture takes place, and this is followed by a febrile reaction. Masses of blood-clot form, and these offer favourable conditions for the growth of septic germs; but they are often absolutely free from all clinical signs of such influences, and complete absorption of the effused blood frequently takes place.[1]

[1] Since the above was written Mr. Leonard S. Dudgeon and Mr. Percy W. S. Sargent have published an exceedingly interesting and instructive record of a bacteriological study of peritoneal conditions ("Erasmus Wilson Lectures," 'Lancet,' February 25th, March 4th and 11th). They found a Staphylococcus albus "in almost every variety of peritoneal lesion" (*loc. cit.*, p. 618). This was "an organism of very low virulence" (*loc. cit.*, p. 474). It, or a similar coccus, had been "isolated from aseptic wounds" (*loc. cit.*, p. 478) in which it was found "frequently" (*loc. cit.*, p. 550). These gentlemen stated that "slight as are the pathogenic properties of the Staphylococcus albus, we are of opinion that the febrile disturbances so frequently found after effusion of blood into the peritoneal cavity are due to the presence of this organism" (*loc. cit.*, p. 474). I hope to discuss this question on a future occasion. At present I would only say that no fact stated in these lectures seems to me inconsistent with the views I have advanced, although the idea which seems to underlie the argument of the authors, namely, that micro-organisms are necessary for the production of inflammation and fever—that the tissues resent nothing but the action of micro-organisms—is in my opinion altogether untenable.

Sometimes, however, a considerable mass remains for a time, and if the abdomen is opened for its removal, the Fallopian tube is found with more or less blood-clot around it, and a recognisable embryo may or may not be discovered. There may be no evidence of putrefactive changes.

The blood may come from a rupture of the tube, but, without rupture, blood in varying quantity and the ovum also may escape from the fimbriated end. The abnormal parts become matted together and adherent to neighbouring structures. A blood-clot may be found, well defined and surrounded by a capsule.

I have already described how, in my opinion, a capsule is formed around the clot in these cases, and I cannot do better than repeat what I have previously written on this subject:[1]

"It is well known that adhesions readily take place between healthy peritoneum and any raw surface to which it is exposed. When peritoneum is exposed to blood it throws out serum which, with the blood, becomes organised into a sort of membrane which may be of considerable thickness and strength. This forms a capsule round the blood, and the enclosed portion is usually of a syrup-like consistence or in the form of a dark clot. The capsule adheres to the peritoneum which has helped to form it, sometimes slightly, but sometimes very firmly. At the point of rupture of the tube or at its open mouth a limiting membrane does not form unless the rupture is very small. I have seen an encapsuled clot forming a kind of cap to the open end of the tube as if it had been blown out like a soap bubble. It was only lightly adherent to any peritoneum, and not more adherent round the ostium of the tube than elsewhere, so that it could be peeled off this part without difficulty, and when removed it exhibited an opening corresponding to that of the tube. When such a gap in the capsule exists at the point whence the blood escapes from the tube, it is obvious that if a fresh

[1] 'Brit. Med. Journ.,' July 13th, 1901.

hæmorrhage occurs the blood will flow into the artificial sac which has been formed, and will distend or burst it. On the other hand, when very firm adhesions form to intestines and neighbouring parts, these with the capsule may exercise a sufficient pressure to restrain or even arrest the bleeding."

It is somewhat difficult to understand why the blood-clot remains in the neighbourhood of the tube.

Much thin, red fluid may, however, be found flooding the sac of the peritoneum when the abdomen is opened in some of these cases, and in similar cases after a time nothing but a circumscribed clot remains. Recently, I removed a mass consisting of clot, Fallopian tube, and placenta from a patient seven days after the first symptom of rupture was observed. Within thirty hours before I operated there were signs of another fairly severe hæmorrhage, and when the abdomen was opened a considerable quantity of red serous fluid was found free in the cavity, in addition to the mass of adherent clot in the pelvis around the tube. Blood is a viscid fluid and probably it does not flow freely amongst the intestines. It would seem that the serum separates and flows over the peritoneal surfaces more quickly, the thicker parts of the blood remaining around the source of the hæmorrhage. The serous fluid is easily absorbed by osmotic action, but a clot can only be removed slowly, by a process of gradual assimilation. If the patient survives the hæmorrhage, and if septic mischief does not occur, the adherent peritoneum generally accomplishes this, but frequently an organised membrane is first formed around the clot, and this membrane seems sometimes to be absorbed very slowly.

The conditions to which I have drawn attention, namely, the presence of a strangulated ovarian tumour, a dead fœtus of advanced development, completely or partially enclosed by its membranes, and a collection of blood in the peritoneal space are all examples of circumstances in which, as it appears to me, the evidence shows that an acute aseptic peritonitis is likely to arise.

In all of these conditions, suppuration from bacterial infection may occur, and then the clinical history is altogether altered. In the case of a dead fœtus septic infection not infrequently develops. In connection with a twisted ovarian tumour or a blood effusion, this is a rarer complication. There are, however, many cases in which a fœtus of advanced development is preserved in an aseptic condition within the body for years. A case is recorded in the 'Obstetrical Society's Transactions,'[1] in which "a perfect fœtus," which had been carried to term, was retained for forty-three years and removed after the woman's death from a cause unconnected with the fœtation, at the age of 74.

Dr. F. W. N. Haultain has recorded a case,[2] and collected nine others, in which a fœtus was retained, in the form of a lithopædion, over 40 years. Blood-clots, also, are often found, after having existed for weeks or months, free from any evidence of putrefactive change.

There is no doubt that a severe inflammatory disturbance occurs in many of these cases, and that in the midst of the inflamed area there is a half-dead ovarian tumour, a fœtus which is often dead, or a clot of blood, all favourable centres for the development of putrefactive organisms. Yet frequently the abnormal parts might be preserved in spirits of wine for all the evidence of putridity that exists in them. If bacteria do not multiply under circumstances so favourable for their development, the proof seems complete that in the many cases in which no putrefactive change occurs the surrounding inflammation is not a septic disease, and that therefore it does not necessarily depend in any case on the presence of micro-organisms which may induce septic mischief.

The peritonitis thus arising, although acute and often sufficiently alarming, is, like the inflammation attending a simple incision, intimately associated with, and, in fact, is

[1] Vol. viii, p. 106.

[2] 'Journ. of Obstet. and Gynæcol. of the British Empire,' October, 1904.

part of, a healing process by which, in the first case, the half-dead tumour is united to adjacent tissues and is re-instated as a part of the body; in the second case the tendency to removal of the parts by the formation of adhesions and subsequent absorption is so strong that when a dead aseptic fœtus comes into contact with a peritoneal surface the two may become intimately adherent, and there can be no doubt that frequently in this way the living tissues gradually absorb the dead with the exception of the bones. In the third of the cases under consideration if the parts remain aseptic and are not operated on, the adhesions, as a rule, eventually lead to a complete absorption of the blood effused. Clearly, in all these cases there is a response to injury having as its object the removal of an abnormal condition, and the process is accompanied by well-marked local inflammatory signs and by a general febrile reaction.

Peritonitis due to Irritation of Tumours.

Without acute torsion ovarian tumours may cause peritonitis, possibly from slight injuries, and perhaps sometimes also from irritation due to twistings which become undone spontaneously.

In some cases adhesions are due to a mechanical irritation. For instance, in the case of a lady, aged 32, on whom I operated, an ovarian tumour was surrounded everywhere by firm old adhesions. The patient had suffered from occasional attacks of pain in the abdomen, which, however, were never very severe, and there was nothing in her history to indicate that there had been an inflammation likely to induce the extensive adhesions which were found. The tumour was a dermoid cystoma, and numerous spicules of hard material were projecting from its surface, which, when set free, was so rough that it might even have injured a delicate skin if rubbed against it, and I have no doubt that the friction of this on the peritoneum had been the cause of a chronic

inflammation and of the consequent development of adhesions. There is no evidence that micro-organisms are concerned in the production of adhesions in such conditions.

The absence of symptoms at all commensurate with the effects produced may be attributed to the gradual development of the irritation, so that it was not at any time comparable to more than that of a very small external incision which would heal without general disturbance and with little or no evidence of local trouble.

An aseptic peritonitis, if sufficiently intense and extensive, might induce a reaction of a dangerous degree, but the largest ovarian tumours do not readily twist. Torsion of the pedicle of an intra-abdominal tumour is most frequently observed in connection with medium-sized and small growths, and, as already pointed out, peritonitis induced by such torsion has little, if any, tendency to spread beyond those parts of the membrane in direct contact with the half-dead tumour.

Moreover the inflammation subsides as soon as the formation of a fresh blood supply for the neoplasm is attained. Hence only a limited area of the peritoneum is affected, and the period of irritation is also limited. A peritonitis involving the whole of the peritoneum, caused by the twisting of an ovarian pedicle, and followed by spontaneous recovery in the course of one or two weeks, is an unknown condition. An inflammation of the peritoneum, if it is caused by twisting of an ovarian tumour, and if it involves the whole of the peritoneal surface, or even the whole of the greater sac, must spread beyond the parts in contact with the tumour, and must be of an obviously septic character.

If it is the case, as Sir Frederick Treves teaches, that the conflict between the cells of the body and infective micro-organisms is "a representation of the inflammatory process," we must believe that the presence of a mass of tissue of any size up to that of a football, or even larger, receiving all its blood and lymph through a narrow pedicle, with the exception possibly of a small amount of lymph

obtained through the peritoneal space, may suddenly have its source of supply arrested by twisting of its pedicle, that this process gives rise to an immediate intense pain, followed by an inflammation of all the peritoneum in contact with it, and that this inflammatory reaction cannot be brought about without the presence, or, it may be said, without the assistance, of micro-organisms which stimulate the apposed surfaces to throw out lymph, by means of which fresh blood-channels may be formed for the nourishment of the growth.

The micro-organisms in the circumstances assumed would require to be of an inferior type, a kind of helot or coolie breed, working under command of the native cells which accompany them, and attacking all parts of the peritoneum in contact with the tumour, but leaving all other parts alone. These micro-organisms might either be circulating in the blood generally, or they might be introduced from the nearest surface. In the latter case they would come from the skin, from the intestine, from the uterus, or from the bladder; but however they gained access they would have to be carefully herded so that they would not interfere except on all the peritoneal covering of the tumour and on the serous membrane in contact with it. The strangulated mass of the tumour itself must not be invaded by them.

In my opinion the view that bacteria are concerned in producing the conditions under consideration cannot be supported by any scientific arguments carrying the same weight as the evidence against it. It seems to me that a more natural explanation of the phenomena may be found if we accept the view that the presence of a large mass of strangulated tissue is a source of irritation, that the leucocytes within reach of it, by virtue of their chemotaxic properties, immediately proceed towards the mass with a view to eating it up, that the disturbance connected with this process constitutes inflammation, and that a general febrile reaction is produced in proportion to the size of the area affected.

Some Peculiarities which may be observed in Serous Inflammations.

Inflammatory conditions connected with a serous membrane exhibit certain characteristics which are not so obvious elsewhere. We have seen that a healthy peritoneal surface frequently becomes adherent to a raw and therefore, according to physiologists, an inflamed tissue. It might be held, however, that the raw tissue is the only inflamed part, and that it becomes adherent to healthy peritoneum in the same way that a raw wound may throw granulations into, and become firmly fixed to, any clean dressing that is applied to it.

But in the conditions produced by the twisting of an ovarian pedicle there are two peritoneal surfaces apposed to each other which are quite free from irritation, except for the changes induced by the strangulation of the pedicle of the tumour.

As a result of this strangulation, there is a well-marked disturbance which affects the whole surface of the growth and all the parts of the peritoneum in contact with it, whilst the rest of this membrane remains healthy. The changes produced cannot be described as other than inflammatory, and they are accompanied by a well-marked fever if the tumour is of considerable size.

It is difficult to believe that the mere presence of a strangulated ovarian tumour can be an *immediate* cause of irritation. But when rupture of an extra-uterine fœtation and profuse hæmorrhage occur, there is also an immediate intense pain which is followed by an inflammatory action.

There is no reason to suppose that the giving way of a blood-vessel can cause so much pain, and there is abundant evidence in the shape of adhesions that inflammatory reaction is caused by the presence of the blood. Hence the blood seems to be a cause of irritation.

In the case of an ovarian or other tumour, with a twisted pedicle, the inflammation seems to be brought

about by the presence of the mass of dying tissue, and the effect, as regards obvious evidences of fever in the pulse and in the temperature, is roughly proportionate to the size of the growth. I think the same may be said as regards the amount of a hæmorrhage, but of course in this case both pulse and temperature may be influenced by the loss of blood from the vascular system. A great loss would increase the pulse rate and lower the temperature.

The facilities for the access of leucocytes to the peritoneal sac are great. This sac constitutes a large lymph space which communicates freely with the lymphatic system.[1] But lymph-cells "are in reality the same elements that enter the circulation with the lymph stream, and within the former are designated white blood corpuscles."[2] On the other hand, "the migration of cellular elements from the blood-vessel system into the commencement of the lymph-channels may be regarded as a normal process."[3] Moreover, according to Sir William Turner, a wide-meshed plexus of small arteries, which he named the sub- or extra-peritoneal plexus, lies in the fat outside the peritoneum.[4]

Thus the pouring of leucocytes and blood-plasma into the peritoneal sac in almost any quantity may be effected simply by an exaggeration of normal processes, and the chemotaxic properties of these cells accounts for their presence in large numbers when a strangulated mass of tissue, a dead fœtus, or a blood-clot, occupies this sac.

We have seen that the removal of effete matter is a normal function of leucocytes, and it seems certain that in the female peritoneal space, in health, the leucocytes may be called upon frequently to remove stray ova and blood-corpuscles escaping as a consequence of the rupture of Graaffian follicles. However this may be, the fact that

[1] Landois, fifth English translation, p. 363.
[2] *Ibid.*, p. 366.
[3] *Ibid.*, p. 362.
[4] 'Introduction to Human Anatomy,' 1877, p. 432.

lymph, which may rapidly develop into connective tissue, is thrown out very copiously from the surface of the peritoneum when any cause of irritation arises is indisputable. A certain amount of adhesiveness may often be observed even during the course of an operation. In some patients, if a sponge is left for a quarter of an hour in contact with the peritoneum, the latter may adhere to it with considerable tenacity. On one occasion I saw a medium-sized sponge that had been left in the cavity during twenty-four hours. After that time it was removed without any harmful effect on the patient, who made a good recovery, and no suppurative action followed, but the sponge was penetrated all round to a depth of over the eighth of an inch by granulation tissue. In another case a patient died on the third day after an abdominal section, and at the autopsy nothing abnormal was found except that a coil of intestine was adherent, over a very small area, to the pedicle of a divided broad ligament. This had fixed and bent the bowel at an acute angle so as to cause a complete obstruction and a consequent distension of the intestines above. The adhesion must have formed and become firm very soon after the abdomen was closed, for aperients given on the second day failed to disturb it.

There can be no doubt that in cases of strangulated tumour adhesions and a fresh blood-supply to the growth must form with very great rapidity. The tumour is completely and suddenly deprived of all nourishment except that which it may receive from the peritoneal space, and yet sloughing of such a tumour, under these circumstances, is, I think, a very rare, if not an unknown, condition. When it receives a fresh blood-supply, the growth continues to develop as before. There must, therefore, be either an extremely rapid formation of a fresh blood-supply, or a large tumour is capable of retaining its vitality for an appreciable time without other nourishment than that received from the lymph in the peritoneal sac. But the appearance of a tumour a few days after a tight twist has occurred indicates clearly that it is in a dying

condition, and apparently the fresh blood-supply arrives just in time to prevent complete loss of vitality.

It is important to note that when an ovarian tumour becomes strangulated adhesions cannot possibly form before the exudation of leucocytes and lymph takes place. But the changes which occur seem to be exactly comparable to those of inflammation and healing by first intention in a flesh wound, and it would appear that, as in a flesh wound, they are brought about by a physiological reaction caused by the irritating presence of the strangulated tumour. Hence it may be argued that in a flesh wound also exudation must precede union. As Lord Lister wrote, "a certain amount of inflammation, as caused by direct irritation, is essential to primary union."[1]

In the same way the changes observed in the case of a strangulated tumour are comparable to those described by Dr. T. G. Stevens in connection with the absorption of the ovum and Graafian follicle in the child, in which phagocytic action must necessarily precede the formation of cicatricial tissue. In this case the vascular tissue surrounding the follicle gradually fills in the cavity which was originally occupied by the ovum and its membrana granulosa. In like manner a considerable space may be filled up by the granulation tissue of a flesh wound. If a drainage-tube, with side holes, be left in a healthy wound, the clot which first forms in it may often be seen to be obviously undergoing organisation by a development of connective tissue through the holes, and it frequently requires considerable force to tear across the new growth uniting the organised clot in the tube and the tissue outside it. Moreover, the tissues connecting the clot with the parts outside the tube bleed on being severed, which shows that they contain vessels. It would almost appear that we might maintain that the exudation, under these circumstances, is purely a process developed with a view to the formation of union of the parts, and thus again we are led to the conclusion that the early stages of inflamma-

[1] *Vide* p. 252, *supra*.

tion and those of the process of healing are exactly the same, the cells thrown into the tissues being probably in part occupied in removing effete matter and in part in building up new tissue. In fact, in the most perfect form of primary union the phenomena of inflammation and of repair are practically one. If the leucocytes may be regarded as workmen, they remove *débris* and lay down fresh tissue by a simultaneous process, and union may be accomplished in two or three days, as soon as the inflammatory process is complete.

When a wound breaks down, or if the surfaces of a wound are necessarily far apart, or when much skin is destroyed, a gradual extension of cicatricial tissue from the healthy parts is necessary, as in the case of granulations eating into the blood-clot in a tube or eating into a sponge in the process of sponge-grafting, or into a sponge placed in the peritoneal cavity. Thus cicatrisation or repair may occupy an indefinite period.

When union does not take place by first intention it is carried out most satisfactorily under a scab. The exudation becomes dry and hard over the granulations which remain firmly attached to the scab until the epithelium gradually covers the cicatricial tissue which quickly forms underneath. There are, however, no signs of inflammation or febrile reaction after the first few days of this process, unless the parts become septic or are subjected to fresh injury. Of course, an injury of the delicate connective tissue or of the granulations may very easily take place. Healing under a scab proceeds by exactly the same process as that which takes place when the umbilical cord is thrown off. The dead cord acts as the scab. Healing under a scab is, therefore, a physiological process.

To sum up, it seems to me that all the irritations to which I have drawn attention, and which I believe to be non-infective, from that caused by the prick of a pin to that of the largest aseptic incision, or to that arising from the presence of a strangulated tumour in the abdominal cavity,

produce changes in the tissues of the same kind, and these changes are physiological consequences of the presence of tissues whose vitality has been lowered, and which are undergoing excessive degenerative change. Moreover, the extent of the local mischief varies with the amount of tissue involved.

The effects on the general system also vary with the amount of local irritation. They are imperceptible in the case of a small wound, but every large wound gives rise to increased tissue change, which is indicated by an excessive skin action and an abundant excretion of solids in the urine. A firm torsion of the pedicle of an ovarian tumour, if the growth is of any considerable size, invariably causes a rise of temperature, and often a very decided rise. Hence the general reaction also seems to vary with the extent of the mischief.

Septic Inflammation.

When a wound is quite free from micro-organisms, and is placed under favourable circumstances for healing, the apposed surfaces adhere almost immediately, and firm union is brought about later by the development of fibrous tissue which replaces the abundant cellular matrix thrown out in the process of inflammation. It is an established fact that, under favourable circumstances, when antiseptic precautions have been successfully employed, the effects of a carefully made incision, if it does not constitute too great a shock to the system, and if there is no serious complication, are free from danger.

When bacteria are introduced into a wound the inflammation in it is complicated thereby. It is known, however, that the evil effects of a living poison, if it be not too powerful, nor in too great quantity, may be neutralised by the destructive action of healthy tissues on the micro-organisms. The leucocytes which are brought to, or formed in, the irritated area, if the circumstances be favourable for healing, have power to kill and to absorb

certain micro-organisms in considerable numbers, although they may not be able to destroy an indefinite quantity.

When bacteria of sufficiently irritating power are introduced into a wound the comparatively simple processes by which immediate union takes place are impossible. The irritation caused by the injury is aggravated and prolonged, its nature is changed and an absorption of poisonous material into the blood and lymph streams may take place. Primary union is prevented and the patient's life may be endangered.

Our knowledge of micro-organisms is still far from complete, but we know that their effects vary widely, that some, such as those that cause tuberculosis and those that, in all probability, are the causes of the specific fevers, may gain access to the body without any obvious breach of continuity of the surface. In some cases, however, if not in all, the condition of the tissues affects the power of the invading force. This is certainly the case as regards the bacilli of tuberculosis and as regards those of all the fevers which confer immunity from a second attack. Other poisons, like that of tetanus, or that of hydrophobia, may be introduced through a wound, and may lead to characteristic and well-marked symptoms without exciting any irritation in the wounded tissues that can be recognised as being caused by them.

Yet another class of minute organisms has the power of producing a direct irritation of tissue.

Sometimes the obvious effects are entirely local, as when an abscess forms and simply enlarges, but heals up at once when its contents are evacuated. It used to be said that such an abscess contained "laudable" pus.

In some cases an abscess forms and the irritating cause extends to tissues in the immediate proximity of the original area of infection or at a distance from it, and it would seem that, under varying circumstances of position of the affected area, of resisting power of the individual, and of the concentration and amount of the poison, the

same organism may give rise either to a local or to a spreading irritation.

From the point of view of the surgeon, the simplest condition arising from the presence of micro-organisms is that in which suppuration is brought about by their action on a raw surface without any tendency to infection of other tissues, and only this simplest form of infective inflammation will be considered in this paper.

When micro-organisms are introduced into a wound in such numbers, and of such power, that the leucocytes are not able to absorb the effete matter of the cells damaged by the injury, and to absorb and destroy the micro-organisms also, a great effort is made to produce sufficient cells for the work. Leucocytes are thrown into, or attracted to, the tissues of the affected area in increasing numbers, and a suppurating surface either in the shape of an abscess wall or of an open wound is produced. Landois says, as I have already pointed out,[1] that if "colonies of staphylococcus (bacteria of suppuration) collect at a given part of the body, their metabolic products attract the leucocytes from the neighbouring vessels, and in this way inflammatory reaction and suppuration result."[2] This attraction of the leucocytes is attributed by Landois to the quality of chemotaxis possessed by them. But we have seen, and Landois states, that leucocytes collect in a part which is subjected to any irritation, although the latter be not septic in nature.[3]

According to this it seems obvious that when, in addition to the irritation of an injury, that of the staphylococci is added in sufficient intensity to induce pus-formation, the reaction on the part of the tissues is of exactly the same kind as that which takes place when union occurs by first intention, although it differs in degree and in results. Thus pus-formation also may be traced to physiological causes stimulated to excessive action. The results achieved

[1] P. 257, *supra.*

[2] Landois, *loc. cit.*, p. 47.

[3] *Vide* p. 254, *supra.*

are less perfect than in the case of a simple resolution or of a union by first intention, because it is necessary to throw out of the body, either into an abscess cavity or on to a free surface, the irritating micro-organisms and the *débris* of damaged cells which the tissues are unable to absorb and assimilate. With these, many leucocytes are also lost. But this throwing off of the irritating and effete material is simply a reversion to the methods of the lowest forms of animal life which normally extrude, or crawl away from, any irritating matter or remains of food which they are unable to assimilate. This method is typically exhibited in the case of the amœba, and it is interesting to note that in man the extrusion of irritating matter from the body should be accomplished so largely by means of the leucocytes, which closely resemble amœbæ in their appearance and movements. This view of the changes that take place is in complete accord with clinical experience and clinical practice, for there is no rule of surgery more well-established than that the exit of pus from the tissues should be facilitated whenever it is possible. This treatment assists nature.

In the deeper parts of an abscess wall—that is, in the parts nearest the healthy tissues—the phagocytes may be able to hold their own, but on the surface fresh leucocytes are constantly thrown off in the form of pus-cells.

The accumulating cells cause a steadily increasing pressure on the abscess wall so long as it remains unopened. Under this pressure the leucocytes and blood-plasma cannot enter freely into the tissues adjacent to the abscess cavity, and the bacteria, instead of being destroyed, extend the area of their influence. If, however, an abscess is opened and efficiently drained, the pyogenic organisms and pus are thrown off and escape, the tension is relieved, and the phagocytes in the surrounding, more healthy, tissues gradually remove all micro-organisms and *débris* so that union by granulation, or by the formation of cicatricial tissue between opposed surfaces may take place.

As soon as a simple abscess containing laudable pus is

opened and efficiently drained all evidences of extension of mischief subside and healing progresses steadily; but drainage must be thorough, as any tendency in the tissues to unite superficially causes tension in the deeper parts, so that the phagocytes cannot so easily remove the *débris* and destroy the living micro-organisms. In some cases, when the power of the tissues and that of the invading bacteria are nearly equal, the slightest obstruction to the exit of discharges or the slightest injury to the suppurating surface seems to create a balance of power in favour of the micro-organisms.

Recent researches on the subject of leucocytosis are of importance in connection with the subject of suppuration. It would seem that not only are leucocytes poured in large numbers into the affected part when suppuration occurs, but that the wastage is rapidly made up, and frequently it is more than made up, by an excessive development of white blood cells. There can be no doubt that the changes by which these developments are brought about consist of physiological processes carried on with unusual activity, proportionate to, or in excess of, the destruction of the white cells.

It appears, moreover, that in certain circumstances the multinuclear leucocytes are chiefly increased, whilst in others the mononuclear are mostly affected. Dr. Thomas Edward Holmes has performed a number of experiments to elucidate the effects of various substances injected into the tissues or into the peritoneal cavity, and he thinks that the results "bear out the suggestion that in rabbits the polynuclear leucocytes are chiefly responsible for the destruction of toxic products and living bacteria, while the mononuclear leucocytes deal chiefly with non-toxic matter and nutritive substances." [1]

Septic Peritonitis.

Septic peritonitis may arise in three ways—(1) from infection by noxious germs circulating in the blood; (2)

[1] 'Guy's Hospital Reports,' vol. lxx, p. 183.

from extension of septic irritation in adjoining tissues; (3) from direct introduction of noxious micro-organisms into the peritoneal cavity.

In this paper I propose to deal only with the last of these methods of access of septic mischief to the peritoneum, but I hope on a future occasion to show that the phenomena of infection through the first and second channels are not inconsistent with the views now advocated.

I would here point out that the word "peritonitis" is frequently used with a considerable degree of vagueness. This term may be compared with the word "dermatitis." When a patient suffers from dermatitis, the mischief may be due to a scratch, to a blister, or to any one, or to a combination of, the many causes of specific skin inflammations; the part affected may be anywhere from the crown of the head to the sole of the foot; it may involve a minute portion of the surface or a very large area, or it may be spreading rapidly or well localised. To say that dermatitis exists conveys no information on any of these points.

The area of the peritoneum has been said to approach in extent that of the skin. It is certainly very large, and to say that peritonitis exists leaves much to be inferred from a knowledge of the case, which must be otherwise obtained, if obtained at all. The simple statement that a patient has peritonitis gives no information whatever as to the cause, position, extent, or severity of the mischief. Hence, it would lead to much more clear views if the word "peritonitis" were never used without the addition of one or more descriptive adjectives, or if care were taken that the necessary information, if available, should be clearly indicated by the context.

Even when this plan is adopted the description is not always exact. For instance, a "general" peritonitis is frequently described, and in numerous cases it has been reported that patients recovered after an operation, when a general peritonitis was said to have been found. I feel

pretty confident that in some, at least, of these cases the word "general" only implied that there were no limiting adhesions and that a "diffuse," a "spreading," or a "very extensive" peritonitis would have been a more exact description of the conditions. In some cases a general—that is, universal—inflammation of the larger sac of the peritoneum may be found, whilst the lesser is unaffected.

A primary septic peritonitis caused by the introduction of noxious germs into the peritoneal cavity during an operation is now, happily, rare. Before the days of antiseptics, however, this complication was very common in abdominal surgery, and the same disease may still be seen as a result of wounds, of ruptures of various hollow viscera into the peritoneal sac, and of imperfect surgical methods.

When a general suppurative peritonitis arises as a direct consequence of an operation, or of a wound affecting the abdomen, the patient dies within three days, and after death the whole surface of the peritoneum—its larger sac at least—is found to have suppurated.

When such a peritonitis arises, the conditions are very complicated. I have elsewhere[1] pointed out that a general septic inflammation of the peritoneum gives rise to a triple pathological state. *First*, there is obviously an intense inflammation affecting a very large area, namely, the whole peritoneal surface. *Second*, as a consequence there is a complete paralysis of the muscular wall of the intestine. *Third*, septic material is absorbed into the circulation. Clinically the patient shows signs of all these conditions. The temperature and pulse steadily rise. The signs of intestinal obstruction caused by the paralysis are present, namely, meteorism, vomiting, and the absence of any passage downwards of the bowel contents. The mind is not clear and becomes progressively more clouded. Towards the end there may be acute mania.

There can, I think, be no doubt that the difference between such a peritonitis as this and the adhesive inflam-

[1] 'Med.-Chir. Trans.,' vol. lxxi, p. 58.

mation of the peritoneum usually brought about by the twisting of an ovarian pedicle is exactly the same as the difference between the inflammation in a flesh wound, which does not heal because it is poisoned, and that in an incision uniting by first intention.

There is this consideration, however, when the peritoneum is involved, that, for purposes of infection, the whole extent of its serous sac may be added to the cut surfaces of the abdominal incision. Hence a failure to secure asepsis, when the peritoneal space is exposed, is a much more important and serious matter than it is in an ordinary flesh wound, if only on account of the very large area that may be involved. On the other hand, there seems to be a special provision for the protection of the body from this great risk. It is generally believed—and clinical and experimental evidence seems to justify the statement—that the peritoneum has a power of destroying micro-organisms in excess of that of the tissue of a flesh wound, and this is fully accounted for by the very great facility with which leucocytes may be thrown into the peritoneal space.[1]

Nevertheless, as in a flesh wound so in a wound involving the peritoneum, all gradations between union by first intention and no union at all may be observed.

Infection does not necessarily extend from the abdominal incision. For instance, if an ovarian tumour is removed, the division of the broad ligament brings that part directly into the area of operation, and an abscess may arise if a not quite aseptic ligature be applied there; or suppuration may be induced if septic material gains access to, and develops in, any exposed or manipulated part of the peritoneum, even although there is no wounding of its surface.

Adhesions may first form and then an abscess may develop, just as a flesh wound may heal over a septic ligature or a septic focus of any kind, and later an abscess may be found in the deeper part of the scar-forming tissue.

Moreover, in a flesh wound, if the recently healed parts

[1] *Vide* p. 283, *supra*.

break down and the resulting cavity is not properly drained, the septic inflammation may extend from time to time, opening up more of the cicatrix, or attacking fresh tissue, or spreading along the lymphatics.

So, in the peritoneum, there may, at first, be only a small area of pus formation, but if this is not fully drained, mischief may extend, breaking down the recent adhesions which shut it off from the rest of the peritoneal cavity, and so involving a larger area, still limited, it may be, by fresh adhesions. Or poisonous influences may spread along the lymphatics producing septic mischief throughout the body, or along the imperfectly adherent peritoneal surfaces, so as to cause a diffuse septic peritonitis.

If death follows, the whole or part of the area of a wound, and the whole or part of the surface of the peritoneum may be found involved in a suppurative inflammation.

Thus the differences between the conditions arising in a case of suppurative peritonitis due to the introduction of septic material through a wound in the abdominal wall, and those in a case of adhesive peritonitis caused by the twisting of the pedicle of an ovarian tumour, when suppuration does not take place, seem to me to be parallel in every detail to the differences between a suppurating flesh wound and one that heals by first intention.

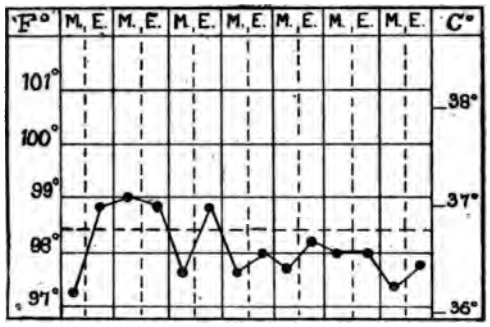
The Effects of an Inflammation on the Rest of the Body.

In the foregoing pages I have endeavoured to show that an aseptic inflammation of a large area is a physiological process not differing, except in its extent, from that produced by the rupture of a Graafian follicle or by the thrusting of a needle into the tissues, and that when a wound heals by first intention there may be no obvious local or general signs of irritation; but that in association with really large wounds, although they undergo primary union and show little or no local signs of inflammation, even if

the temperature remains low, there are always evidences of increased metabolism in the shape of profuse sweating, excessive excretion through the kidneys, and physical exhaustion, signs which indicate a condition described by Dr. Donald MacAlister as febrile. Moreover, from the evidence adduced, it seems to me that the onset of an aseptic peritonitis caused by the twisting of the pedicle of an ovarian tumour or by other causes of irritation is a well-defined, obvious, and not uncommon occurrence, and an inflammation thus induced is always associated with a distinct rise of temperature if the tumour is of a large size.

It seems to me, therefore, that the general reaction

CHART No. I.

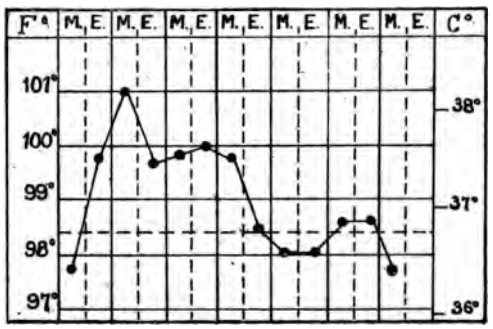


arising from a non-septic inflammation varies more or less with the extent of the mischief, there being no discoverable signs of it when the injury is slight, but well-marked indications becoming evident if the inflammation is extensive.

Moreover, if the conditions attending an operation involving the making of extensive incisions are considered, it will be noted that although union by first intention takes place, perhaps with no recognisable local disturbance, there are not only obvious signs of excessive metabolism of tissue, but, if careful records are made, a rise of temperature is usually discovered, although it may be a very slight rise indeed.

For example, Chart No. 1 shows the temperature taken in the axilla during the first week of convalescence, in the case of a lady from whom I removed the gall-bladder and the vermiform appendix. The gall-bladder was universally adherent, having been inflamed a few weeks

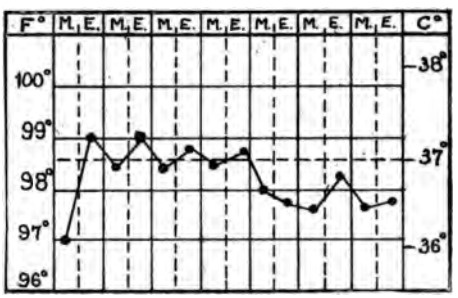
CHART No. II.



before the operation, and the vermiform appendix contained fæcal matter.

Chart No. 2 indicates the course of the temperature taken in the groin during the first six days after the

CHART No. III.



removal of a tumour of the kidney from a child under 2 years of age.[1]

Chart No. 3 is the record of the axillary temperature during the first week after an ovariotomy, when considerable adhesions were separated.

[1] 'Clin. Soc. Trans.,' 1894, 1895, and 1903.

There was no interference with union by first intention in any of these cases and the reaction occurred, although every care was taken in each instance to prevent septic infection. Such evidences of reaction are common, and it is quite certain that either a rise of temperature may occur without the presence of micro-organisms or that the precautions employed frequently fail to prevent their access to wounds.

In fact, if a rise of temperature following an operation indicates that inflammation and inflammatory fever exist, and if every inflammation is caused by micro-organisms, as many seem to believe, it appears to me that in my own practice, in that of every surgeon whose work I have had an opportunity of observing closely, and in cases publicly recorded, the antiseptic system in numerous instances has completely failed to prevent the access of micro-organisms to wounds—a conclusion which, in my opinion, is untenable, being opposed to the well-ascertained fact that micro-organisms may certainly be destroyed if suitable methods are employed.

We know that in a simple flesh wound the antiseptic treatment prevents, with absolute certainty, the onset of the dangerous inflammation associated with the presence of putrefactive micro-organisms in the tissues. It is clear, therefore, that if an elevation of temperature, following an injury carefully treated with antiseptic precautions, is due to the presence of micro-organisms, these must be of a kind which constantly resist the action of antiseptics, whereas the more powerful micro-organisms, which, if present, would most certainly produce serious inflammatory mischief, are invariably destroyed by the antiseptics. Such an explanation of the phenomena does not appear to be satisfactory.

Moreover, the means taken to prevent the access of micro-organisms to wounds may add to the effects brought about by the original injury.

Many chemical germicides, such as carbolic acid and corrosive sublimate, are irritants, and their application to the

tissues must therefore increase the inflammatory and reflex effects produced by an operation. For this reason most surgeons now use heat as much as possible for sterilising purposes, and do not allow any chemical solutions to come in contact with the tissues except those which are unirritating. This method has been called the "aseptic" system—an unfortunate name, I think, because the principles on which it is founded are fully covered by Lister's definition of antiseptic treatment as consisting of "such management of a surgical case as shall effectually prevent the occurrence of putrefaction in the part concerned."[1] The absence of sepsis is in no sense peculiar to the aseptic method. Its special feature is that, whilst aiming at the prevention of putrefaction, the surgeon also endeavours to avoid every source of irritation to the tissues. The word which would appropriately indicate both the method and the reason for its adoption is "anoxic" (non-irritating), but an anoxic method must always be simply a modification of the antiseptic system and in no way antagonistic to it as regards asepticity. There is less fever when sepsis is prevented without the use of chemical antiseptics, because the tissues are less irritated.

If we turn to a consideration of the effects of septic inflammations on the body generally, I have further pointed out[2] that the simplest of these may be regarded as physiological processes induced by the combined influences of an injury and of micro-organisms tending to destroy the vitality of the parts. In these conditions also a careful consideration of the circumstances shows that the same relationship exists as in cases of aseptic injury between the extent of a suppurating wound and the severity of the general reaction caused by it.

A severe inflammation of small size, such as that connected with an abscess in a hair-follicle, may exist, causing redness, pain, and a local swelling. As regards heat, it is certain that an area surrounded by such a free

[1] Introductory lecture, University of Edinburgh, 1869.

[2] *Vide* p. 289, *supra*.

blood-supply as obviously exists in these cases must be warmer than the surrounding parts. There is, in fact, an intense suppurative inflammation.

If such an abscess develops on the hand of one who has recently made a post-mortem examination of a putrid body, an inflammation may quickly spread along the lymphatics, and secondary areas of suppuration may arise in connection with the nearest glands. The occurrence of such secondary infections depends chiefly on the nature of the poison, but to some extent also on the condition of the tissues. An over-worked or otherwise enfeebled man is more likely than one in good health to contract such an inflammation.

If, as frequently happens, an abscess is determined in a gland at some distance from the wound, it is obvious that micro-organisms and their germs have been absorbed into the lymphatic system in such a condition that they are, for a time, harmless or comparatively harmless but not dead. Probably they are conveyed in a non-irritating condition, as spores, within the leucocytes. If the spores develop and overcome their containing leucocytes, they may immediately be attacked by other white cells and perhaps they may be destroyed. Frequently,[1] possibly always, the number of the leucocytes in the body is increased under such circumstances, so that the chances of micro-organisms being able to live are diminished. But the passage of the lymph-cells is delayed at the glands, and if sufficient spores develop in a gland an abscess will form.

An abscess in a hair-follicle often develops, however, with acute local signs of inflammation, but without showing any evidence of a tendency to spread along the lymphatics. There is then no indication of a general infection of the system in the state of the pulse or temperature, and when the abscess bursts recovery rapidly follows. It is evident that any micro-organisms absorbed into the tissues in these circumstances have their vitality and their power of doing harm destroyed.

[1] *Vide* p. 291, *supra*.

The micro-organisms which the tissues are not able to destroy appear to be all thrown out on the inner surface of the abscess and finally on the exterior of the body.

In the same way a minute stitch abscess in a wound may develop without producing obvious evidence of constitutional disturbance, but a large boil or a large stitch abscess may give rise to an increase of temperature and pulse rate, although the parts heal promptly and the general disturbance subsides as soon as the pus escapes or is evacuated.

Again, a considerable abscess may form around a vermiform appendix or in the ischio-rectal fossa. In such conditions also an infection of other parts by the septic inflammatory action may take place, but in many cases the suppurative action is strictly localised, and only affects fresh tissue by direct extension. Under these circumstances there may be considerable fever, which subsides immediately if the pus is set free. So, in suppuration due to a septic injury, such as the entrance of a septic foreign body into the healthy knee-joint of a healthy patient, if the pus is localised, inflammatory action, accompanied by fever, may be severe and may be dangerous, and yet, if the abscess is evacuated, and if the joint is made aseptic, or if drainage is efficient, fever may rapidly subside and recovery may be complete.

The difference in the severity of the reaction seems to be in great part one of degree, corresponding to the extent of the lesion. A septic inflammation involving the whole of the greater sac of the peritoneum, the result of infection introduced at the time of the infliction of an injury, invariably causes death from the extent of the tissues involved and the consequent severity of the reaction and from certain complications that constantly arise.[1] But an extensive diffuse suppurative peritonitis may be recovered from if the pus is evacuated sufficiently early, when bowel complications do not exist, or, at least, are not persistent, and if, by cleansing or by drainage, the reaccumulation of

[1] *Vide* p. 293, *supra*.

poisonous material is prevented. A septic peritonitis of small extent, if it does not cause complications, may be cured with certainty by efficient drainage.

A study of the whole question leads me to believe that in cases of suppurative inflammation, if the disease is strictly localised—that is, if the micro-organisms absorbed into the tissues are also destroyed—the accompanying reaction shows a tendency to develop, as in the case of an aseptic inflammation, in some sort of proportion to the extent of the tissues involved. There is this difference, however, that a comparatively small septic wound causes a much greater reaction than an aseptic injury of the same extent, or even than a much larger simple incision.

The Cause of Increased Temperature.

The increase of temperature which accompanies an inflammation has been attributed to various causes. Septic contamination of a wound undoubtedly tends to produce a rise of temperature, and it seems to be a common view that after an operation such a rise necessarily indicates that a septic infection and a consequent inflammation have occurred.

But I have shown that excessive metabolism and as a rule more or less elevation of temperature follow every extensive operation even when the most careful precautions to prevent septic contamination have been taken. An increased temperature also invariably accompanies the inflammation following a tight torsion of the pedicle of a medium sized or large ovarian tumour, even although putrefaction does not take place.

There is, moreover, one form of fever which is generally believed to develop without the presence of micro-organisms.

Even some of those who maintain that all fever is due to living irritants make an exception of the case of the fever following a simple fracture. Of course, if this fever is not caused by a living irritant, whatever the

origin of it may be, it necessarily follows that the presence of micro-organisms is not essential to the production of fever.

To explain the rise of temperature following a simple fracture it has been assumed that "a hypothetic substance, pyrogen,"[1] is formed, and that this, circulating in the blood, is the cause of fever.

Those who hold this view would seem to believe that micro-organisms or their products circulating in the blood are the usual causes of fever, and that some hypothetic substance, so circulating, must be the cause of fever arising without the presence of micro-organisms. So far as I am aware, no explanation as to how this hypothetic substance induces fever has been suggested except that it is said to "act upon the heat centre," and indeed the mechanism by which micro-organisms circulating in the blood induce a febrile reaction, *how* they act upon the heat centre, seems to me to be unexplained if no other exciting cause of fever is recognised. Putrid matter circulating with the blood certainly causes fever; the transfusion of blood direct from body to body through an aseptic tube induces a rise of temperature; and many other substances which contain no living irritant when introduced into the circulation also excite a febrile reaction.

In the case of fever following the rupture of an extra-uterine fœtation in its early stages, when much blood is effused, there would appear to be abundant opportunity for the absorption of altered cells and plasma into the tissues, and a hypothetic substance, pyrogen, might easily be developed.

But in the case of an ovarian tumour with a twisted pedicle it is by no means clear that there are facilities for the development of such a substance.

In a flesh wound healing by first intention the evidence indicates that, so long as fever increases, absorption is less than is necessary and exudation into the tissues is in excess.

[1] Victor Horsley, 'Heath's Dictionary of Surgery,' vol. ii, pp. 367, 368.

I have already pointed out[1] that the immediate exudation of blood and lymph, caused by division of tissues, is, for the most part, discharged from a wound when the conditions are perfectly natural, but that when an incision is closed by sutures this discharge may collect, and, if it be not promptly absorbed, the signs of febrile reaction are likely to be well marked. The fluid, if in large quantity, causes tension in the wound, and a local condition arises which renders the necessary changes of the inflammatory process more difficult, and so tends to produce an increased local and general reaction. A wound heals most quickly when these exudations are rapidly absorbed, or escape easily on the surface of the body. It is when they are retained and are *not* absorbed that they cause a febrile reaction with greatest certainty. These considerations do not seem to support the view that absorption necessarily causes fever.

When the exudation into the interstices of the tissues, resulting from their irritation, is in excess, and seems to be the cause of febrile reaction and of local destructive processes, the deleterious effect is really due to the fact that the leucocytes are *not* able to absorb promptly the effete matter and the irritating foreign bodies that must be taken into the circulation and destroyed if union by first intention is to take place. Such union is in every way least disturbing, locally and generally, when the phagocytic cells which collect in the tissues are fully capable of rapidly absorbing and assimilating all *débris* from the damaged area and also any foreign irritating matter that may be present. It is when the cells cannot do this that more are attracted to the part and evidences of excessive exudation and pus-formation follow.

All the evidence seems to me to show that when matters are absorbed into the circulation from healthy wounds, which heal by first intention and without further complication, any irritating properties these matters may have possessed are removed by the action of the leucocytes;

[1] *Vide* p. 259, *supra*.

and that it is when they are *not* absorbed, or, being absorbed, are not assimilated, that they cause an increase of the local and reflex changes.

It is very important to draw a distinction between an absorption of micro-organisms, the vitality of which is not destroyed, and which, therefore, act as irritants throughout the body, and an absorption which involves a digestion and assimilation of the material taken up. The latter is a true absorption; the former may be regarded rather as an invasion of the tissues.

A consideration of the phenomena following an acute twisting of the pedicle of an ovarian tumour is important from this point of view. If the tumour is of fair size, the torsion of its pedicle invariably causes a considerable rise of temperature. The tumour is in the first instance cut off completely from the general circulation. It is certain that the whole mass gradually approaches a dead condition. There is, however, only a very small surface in the pedicle from which absorption is possible, and immediately after the torsion occurs there is no passage of blood or lymph through the pedicle, so that the amount of absorption of effete matter must be very slight.

There is nothing to indicate that an immediate absorption takes place from the surface of the tumour. All the local action seems to be directed to the exudation of leucocytes and the formation of cicatricial tissue between the adjoining peritoneum and the strangulated mass. Moreover, there is no more action than is sufficient to produce a fresh blood-supply for the growth, and as this is being formed the temperature rises. There can be no doubt that if the strangulated tumour did not get a fresh nutritive supply in these cases it would die, and that so long as its circulation is arrested degenerative changes must continue in it, whilst nutrition must remain in abeyance. But there is no evidence that an increase of temperature takes place on account of the absorption of degenerated matter which must occur when a fresh communication develops between the healthy and the strangulated tissues. On the

contrary, the whole of the changes which follow the twisting of the pedicle of a tumour in the abdominal cavity are directed to getting the strangulated growth back into the circulatory system, and as soon as this is accomplished the general disturbance abates.

In these cases the return to a normal temperature is not so prompt as in a well-managed flesh wound. After the blood-supply is fully re-established there are still febrile symptoms which, I believe, are due to disturbance of the adhesions formed by the primary acute inflammation. If the patient recovers, such disturbances must take place when the intestines are involved in recent adhesions.

But the ordinary rapid rise of temperature following an injury and its partial subsidence after two or three days always take place if suppuration does not occur.

Moreover, the temperature rises before the tumour is reinstated in the circulation, whilst it is dying for want of nourishment, and tends to fall when the new blood-supply is becoming established and the tumour is being revived, although at this time much accumulated *débris* must be carried into the general circulation.

It is to be noted that this accumulated *débris* is the result of normal degenerative changes and of the shutting off of nutrition, and therefore is in an easily absorbable condition.

These considerations further suggest that an exudation into the irritated tissues, rather than an absorption from them into the circulation, is associated with the febrile condition produced by the presence of a strangulated tumour.

It seems to me that a better explanation of the origin of fever than that usually given may be found, that a mechanism by which febrile reaction may be induced as a consequence of an injury is always present, and that, by a reference to this mechanism and to its normal physiological functions, a simple and rational interpretation of the phenomena of fever may be obtained.

The temperature of the body in health is remarkably steady, showing only a slight regular variation at different periods of the day. Heat is constantly being produced in the body and given off from it. "An adult produces on an average enough heat to raise the temperature of his body about 1° C. in half an hour. If no heat were given off, the body would in a short time become enormously heated—in thirty-six hours to the boiling point—provided the production of heat continued uninterrupted." [1] The amount of heat developed varies, however, in health with the amount of exercise taken, with the quantity and kind of food consumed, and to a less degree with other conditions. But however great the development may be, elimination takes place in proportion to the production, so that the balance is not disturbed. On the other hand, elimination of heat may be influenced by various agencies applied to the surface of the body and chiefly by the temperature.

A compensatory increased development of heat arises if the temperature is lowered by cold applications, and less heat is given off when the surrounding temperature is high, but neither heat nor cold appreciably changes the temperature of the body. "If marked alteration in temperature be brought about by powerful agents, namely, by vigorous abstraction of heat or by considerable addition of heat, great danger to the continuance of life results." [2]

Under all circumstances, therefore, in health, it is impossible to induce any very marked alteration of the internal body temperature, although the surface temperature may be raised or lowered considerably, and the amount of heat produced and eliminated may vary very greatly.

The degree of moisture of the skin and the state of distension of the superficial vessels might be said to have an important influence on heat elimination, but changes in the excretion of the sweat-glands and in the calibre of the

[1] Landois' 'Physiology,' 5th English edition, p. 339.

[2] Landois, *loc. cit.*, p. 382.

superficial vessels may be considered as parts of the heat-regulating processes.

It is certain, therefore, that a very powerful mechanism exists for the regulation of the body heat and that it is very delicately balanced, reacting at once to any changes induced either by thermogenesis or by thermolysis. There can be no doubt that if any cell or group of cells on a surface of the body falls below the normal temperature, unless the degree of cold is overwhelming, the result is an immediate change tending to accumulate heat either by a quicker creation or by a slower loss of it. There is no normal condition by which the temperature of any cell not on a surface (skin or mucous membrane) can be lowered without affecting the superficial parts also, but it is probable that, as the various nutritive changes take place in the body, as individual cells are nourished or decay and are replaced, each cell must have the power to indicate its condition as regards temperature to the central heat-controlling mechanism, and that the accumulated messages from different parts of the body regulate the amount of heat developed and given off.

Of course, in abnormal conditions, as when an incision is made, the temperature of internal parts may be directly raised or lowered.

If an unusual number of cells are in process of dying or in a condition of diminished vitality owing to the infliction of an injury, I think we should expect that they would indicate to the nervous centres that they are physiologically cold, that they are approaching the coldness of death, and that therefore a greater development of heat is required in the body.

There does not seem to be any good evidence that mischief extends in healthy tissues after an injurious action ceases, but when parts are so damaged that they are useless and must therefore be cast out of the body, their removal by physiological processes cannot take place in a moment, and as long as these hopelessly damaged tissues remain undealt with they must approach nearer

and nearer towards death, although still in physiological connection with the rest of the body.

Hence the intensity of the messages indicating the need for increased heat on account of the condition of these dying tissues must increase until they are separated and absorbed or cast out, and therefore the temperature rises for a time.

At first sight it may seem improbable that the tissues in an inflamed area can convey a message to the central nervous system to the effect that an increase of heat is necessary, because when on the surface of the body they are obviously warmer than the surrounding parts.

But on consideration it becomes clear that the increased heat is an effect of the irritation, one of the first changes produced by the inflammatory process being the production of this increased heat in the inflamed part, even if there be no rise of temperature of the body generally. In the case of a small aseptic or septic injury to the hand or other part at a distance from the main mass of the body, one of the earliest results is that the surrounding vessels dilate and a more free blood-supply is brought to the affected and surrounding areas.

This increases the local temperature, not above the temperature of the body generally, but so as to make the surface temperature around the irritated area more nearly the same as that of the central parts. I have shown that when a very extensive injury is inflicted the development of heat is also greatly increased and that frequently the temperature of the whole body is raised, even if the wound remains aseptic.

There are certain clinical facts which support the idea that fever is due to a local physiological coldness of the damaged tissues. The initial rigor which ushers in so many inflammatory conditions simulates exactly the effects of intense cold on the healthy body. The fact that the rigor does not always precede an inflammatory illness is fully explained by the view that a depressing influence often comes on gradually and a reaction gathers strength

with it, so that the chilly stage does not exist. It is only acute and fairly extensive inflammatory conditions that begin with a rigor. When a patient recovers consciousness after a severe operation shiverings and rigors may occur, but methods to counteract this tendency are generally adopted.

There are indications that the processes necessary for the removal of all tissues damaged by an injury occupy from two to three days. After this time fever usually begins to abate if there is no repetition of the injury and if resolution takes place. If an abscess forms—that is to say, if the tissues are not able to absorb the damaged parts together with the irritating micro-organisms which induce pus formation—it is generally on the second or third day that their failure to do so becomes obvious. The question as to whether a slough is to form as a consequence of an acute injury is also generally determined about the third day after the damage is done. If sloughing takes place, the temperature runs highest just before the death of the affected part occurs.

When recovery takes place or when a dying area is defined and becomes separated the temperature and other evidences of constitutional disturbance usually subside, and this may occur although the dead tissue is not, and cannot be, thrown off. I recently operated on a patient[1] in whose case the *central* part of a uterine fibroid tumour had died. When I removed the tumour, which measured some four inches in diameter, the white dead tissue in its centre was found to be surrounded everywhere by about half an inch of healthy vascular fibroid growth; the dead and the living tissues were in continuity, and possibly absorption of the former might have taken place after a time if the patient had been kept quiet long enough.

The first time I saw this patient was seven weeks after her first confinement, and she then had a uterine fibroma, which was extremely tender to touch and whenever she moved, or when the bowels and bladder

[1] 'Obstet. Soc. Trans.,' vol. xlvi.

were evacuated; but when she was quite still she was free from pain, and the temperature was practically normal. I have no doubt that, if absolute quietude of the parts could have been secured, there would have been no rise of temperature. The conditions seemed to indicate that in this case there was a formation of an aseptic slough soon after delivery. The patient stated that at that time she was very ill and had a high temperature.

This is a very important point, namely, that the presence of dead tissue in the body does not necessarily cause an inflammation. If such tissues are aseptic, or if suppuration is established around them and the pus escapes freely, they only cause injury by mechanical irritation. When the parts are kept quite quiet so that the dead tissue does not hurt mechanically either by pressure or by dragging on delicate tissues, it does not induce obvious inflammatory action.

But adhesions between the dead and the living tissues take place before the processes of absorption can be carried out. So in the case of a strangulated tumour in the abdomen, adhesions between the living and the dying must form before the tumour can be revived. In all these cases fever abates when the processes tending to recovery are well established.

A stimulus to heat production arising from a particular tissue as a consequence of its vitality being lowered would not be expected to cease to act because the temperature was raised. Unless and until the damaged tissues were revived or absorbed or extruded, they would continue to indicate that a physiological coldness existed and that more heat was required.

Thus there is a mechanism known to exist by which, as a consequence of a local devitalisation of tissue, an increase of action may be expected throughout those parts of the body which are subject to rapid changes, notably the muscular and fatty tissues and those concerned in blood-formation and blood-destruction.

This mechanism is constantly set in action by normal

stimuli, indicating that increased tissue changes are necessary, and it seems to me rational to expect that abnormal stimuli, such as those due to a partial devitalisation of a particular area, should also induce increased heat-production.

It does not follow, however, that the temperature must rise because there is a local physiological coldness. In opposition to the tendency to elevation of temperature there would immediately be brought into play the forces of the heat-regulating mechanism. Hence, as long as the lowered vitality of the injured tissues continued there would be two forces acting against each other, and the result would depend upon the strength of the abnormal stimulus as compared with that of the forces tending to maintain normal conditions. Thus in some cases there would be fever with rise of temperature, in others there would be increased metabolism without rise of temperature, a condition which Dr. Donald MacAlister described as *febris sine febre*.[1]

The normal temperature is easily maintained when the irritation affects a small area, but I have shown that an irritation involving a large extent of tissue usually raises the temperature, and sometimes to a very considerable degree. From those considerations it may be concluded that the obvious febrile process accompanying an extensive simple inflammation merges into normal physiological conditions, or into excessive tissue change in accordance with the severity and extent of the stimulus, just as I have endeavoured to show that local inflammatory changes merge into healthy physiological conditions, or may lead to a casting off of the damaged tissue.

Moreover, it seems to me that the mechanism by which substances circulating in the blood cause a rise of temperature has not been satisfactorily explained.

It is said that substances, sometimes hypothetic, so circulating raise the temperature by acting in some unknown way on a not quite defined heat-regulating centre. But that their effects on the tissues generally may be

[1] Gulstonian Lecture, 1887, 'Brit. Med. Journ.,' vol. i, p. 670.

ignored in this relationship seems to me to be at least a very speculative conclusion. We know that many, if not all, of those foreign matters which cause fever when circulating in the blood are locally harmful by acting as irritants. Those which have this local power must, when introduced into the blood-stream, produce a widespread irritation of tissue, or perhaps only of the blood-discs, and this irritation would presumably diminish to a slight extent the vitality of the cellular élements throughout the body, or of the blood-discs, and so would give rise to that physiological coldness which necessarily stimulates heat-production and heat-conservation in the state of health, and to which, when produced locally by an injury, I have attributed the increased temperature of fever. In the case of fever induced by direct transfusion of blood, it seems certain that a number of cells, damaged by contact with the tube used, as well as being of alien origin, must be introduced into the circulation. Such damaged cells would be rapidly destroyed by normal processes, and, according to the theory I have suggested, their presence would fully account for the transient fever which follows their introduction into the system.

If we consider the febrile phenomena of ague, we find that the first stage is characterised by an intense chilliness which is comparable to that of a rigor or to the effects of severe cold applied in health. It is clear that there is an actual physical coldness of tissue widespread throughout the body. After a little while reaction sets in, and a well-marked rise of temperature follows. Why the action ceases is not known, but it is quite certain that the irritating effect of the poison acts suddenly, and is only temporary, although there seems to be reason for believing that the malarial poison may circulate in the blood when no symptoms are recognisable. The "malarial parasite, in large numbers, has been found present in the blood of children who appear perfectly healthy."[1] This is a problem of immunity.

[1] Professor Sims Woodhead, 'Med.-Chir. Trans.,' vol. lxxxiv, p. 290.

From these considerations it would appear that if the fever of inflammation is due to a physiological coldness of an injured part, that of ague and that caused by irritants circulating with the blood-stream are produced by a similar action affecting the cellular elements generally, or perhaps only some of them.

Thus, whether the exciting cause is a localised injury or is an irritant circulating in the blood, it is possible to explain the phenomena of fever by a mechanism the constituent parts of which are known to exist, and to have definite functions in health.

If the view which I have set forth is correct, fever, like inflammation, is a physiological process. The phenomena characteristic of it, although not always perceptible, must be induced by the smallest incision and by the presence of minute quantities of irritants circulating in the tissues, as well as by the largest injuries and by the absorption of full doses of septic material. Fever merges, on the one hand, through conditions of exaggerated physiological reaction, from the healthy state; and on the other hand, if the exciting cause is sufficiently powerful or prolonged in its activity, it creates such an excessive reaction throughout the body that death ensues.

This view of the case seems at least to offer a rational explanation of the phenomena observed. The view that fever is always caused by septic mischief or by some hypothetic substance circulating in the blood leaves the mode of action of these substances unexplained; and moreover this view can only be adopted by assuming that the active changes, whatever they are, that lead to the healing of a wound cannot have any direct or reflex effect on the amount of heat production.

The fact that the state of the vessels throughout the body and in an irritated area is influenced by local stimuli has been long recognised, and it seems to me that these stimuli are obviously the cause also of many phenomena connected with the development of heat, whether it be produced in proportion to or in excess of its elimination. In

fact, the phenomena of inflammation and of fever, whether resolution, suppuration, or sloughing, or death of the whole body takes place, may all be traced to physiological processes acting in excess, and the natural effects of which are fairly well known.

As Sir Frederick Treves pointed out, the views which I hold on this subject are obviously at variance with his teaching. He compared the conflict between the cells of the body and the invading bacteria to a battle, and he said that this conflict is "a representation of the inflammatory process."

The comparison of the action of the cells of the animal body and of micro-organisms introduced into a wound to a fight between soldiers of hostile camps is an apt one; but when such a conflict is described as "a representation of the inflammatory process" the statement does not seem to be in accordance with the teaching of physiologists, or to explain such conditions as those found in connection with the twisting of the pedicle of an ovarian growth. I think that the suggestion that during the process of inflammation the human body is subjected to attack from outside, as one nation may be set upon by another, may, however, be made into a fairly complete illustration of the inflammatory process. There are more ways than by invasion by which one nation may attack another. The shelling of a seaport town when the invader is not able to effect a landing would represent an aseptic injury. But such an assault might create as much local and general excitement in a country and necessity for repairs in the town attacked as an actual invasion would. The landing of an army might represent a septic infection, and an armed encampment on an enemy's soil would be comparable to an abscess. If the invading force could spread over the country, an extension of poison in the tissues would be illustrated, and secondary camps might fairly be compared to pyæmic abscesses. The phenomena of leucocytosis are comparable to the creation of new battalions in cases of emergency, and the latest investi-

gations seem to show that the leucocytes have varying functions, some destroying the invading micro-organisms, whilst others remove waste products, just as an army of soldiers to repel an invasion might be required, or an army of scavengers to remove *débris*, or an army of workers to repair damage done. Any territory which held out against the enemy would represent the healthy parts sometimes seen in a sloughing wound. These may die slowly, may suddenly be involved in the sloughing process, or may form a focus from which healing may commence and extend, just as a fortress may be starved out, taken by assault, or retained by the garrison until help comes.

A secret introduction of a hostile party into a country and a sudden attack from within, which was frequently attempted in less civilised times, may be comparable to the invasion of the human body by germs of the exanthemata, malaria, etc., which it is to be hoped may also one day be relics of uncivilised and insanitary ages.

But great disaster, intense excitement, and an urgent necessity for immediate repair of injuries may occur to a country in time of peace. Such a condition as that brought about in the human body by the twisting of the pedicle of an ovarian tumour, by the rupture of an extra-uterine fœtation, or by the fracture of a bone may well be likened to what is termed, in legal phraseology, an "act of God," such as an earthquake or the eruption of a volcano.

An occurrence of this kind creates a disturbance and a necessity for activity in repairing mischief, in proportion to the amount and importance of the damage done as compared with the extent of the country affected. A small island may altogether disappear, or the fate of Herculaneum and Pompeii may be reproduced.

As in the case of an earthquake or of a volcanic eruption, so in the case of a patient with an ovarian tumour the pedicle of which has become twisted, there is no evidence of an invasion by a living enemy. Obviously

a country harassed by some great natural calamity might become an easy prey to a powerful neighbour, and so septic mischief may attack the subject of a fractured limb or of a strangulated abdominal tumour.

Great natural catastrophes and a bombardment, when no hostile party is landed, represent the physiologist's view of an aseptic injury, whilst an actual invasion represents a septic infection. The immediate slaughter of a landing party may be compared to the destruction of septic micro-organisms by healthy wounded tissues, and such an occurrence illustrates the impossibility of drawing a hard and fast line between cases in which a country is invaded and those in which there is no invasion, or between septic and aseptic inflammations.

This comparison of inflammation to an attack from without, and especially that part of it which refers to a direct invasion, strongly supports my view that inflammation merges into normal conditions, and, on the other hand, may destroy the body if the extent of the irritation be too great.

The commotion produced by a bombardment would vary with the extent of the mischief done; but however great the injury inflicted, if further molestation ceased, repair would be effected in a methodical manner after a period of excitement had passed, and this is what happens in the case of an aseptic wound.

Obviously the invasion of a powerful country by one man would create no serious disturbance, and even that by a hundred would hardly be recognised. But if the invaders were multiplied sufficiently a condition comparable to an appreciable injury would arise, and the disturbance, whether local or general, would increase in proportion to the number of the invaders, just as I have maintained in the preceding pages that the results of a septic irritation are proportionate to the amount and intensity of the poison.

If, however, the processes following an injury are regarded as physiological in origin, it must follow that they

are liable to modification by nervous influences, and thus it is easy to understand and explain the difference of severity of the inflammatory reaction shown in individuals subjected to apparently the same injuries, when union of the wounds takes place by first intention.

Some surgeons seem to attribute the differences in all cases to a greater or less success in avoiding septic infection. Septic mischief has, of course, a very marked and harmful effect whenever it occurs. But there cannot be a doubt that mental conditions influence the pulse and temperature during convalescence from an operation, even when the wound pursues a perfectly healthy course throughout.

A piece of news communicated to a patient a few days after an operation, whether it be sad or joyful, if it affects the patient closely, will often make its mark on the temperature-chart of a perfect convalescence. So a death in a hospital may be traced on the charts of many patients in the same ward. Such effects cannot be understood if the existence of septic mischief is held to be a complete, and the only explanation of the development of fever.

The great susceptibility to a short sharp inflammatory reaction in children is also fully explained by the activity of the processes of nutrition and the irritability of the nervous system in growing animals.

The fact that excitable women sometimes show a marked reaction in the temperature and pulse-rate after surgical treatment, and sometimes very little under apparently the same conditions, is in accord with the well-known fact that it is practically impossible to gauge the amount of nervous control which such individuals will display under particular circumstances.

Women of nervous type often seem to be unduly excited by trifling annoyances, whereas they frequently walk to an operating-table, for instance, when they know that their life is to be placed in immediate jeopardy, with every sign of fear or excitement completely concealed. Hence it is to be expected that the amount of their involuntary control may be liable to great variations.

It seems to me that there is always a personal element to be reckoned with in studying the effects of an injury, and whether inflammation and fever give rise to visible changes around an incision, and to obvious alterations in the pulse and temperature, or only indicate that some sort of action is taking place by the union of the parts, with or without an obvious increased excretion of effete products, depends, in my opinion, on the extent and severity of the damage done and on the nervous irritability of the individual.

According to the views set forth in the foregoing pages a simple inflammation is due to an irritation which is not caused by living organisms, or which is complicated by the presence of septic infective agents acting so feebly that the germs are at once destroyed and prompt resolution is not interfered with by them. All other inflammations should be regarded as septic.[1] It is not possible to differentiate more exactly between aseptic and other inflammations because they "merge insensibly one into the other."[2]

The view that inflammation is not necessarily an infective process is not only more in accord with physiological teaching, but it is clinically much more convenient than the view that inflammation is always caused by living germs. Inflammations brought about by, or aggravated by, the presence of micro-organisms have many varying symptoms, according to the nature of the living causes producing them. It is, therefore, convenient that the word "inflammation" should be retained to describe those local changes *necessarily* following an injury, even although there may often be little or perhaps even no clinical evidence of their existence. When such local changes are complicated by the presence of infective agents, unless the latter are promptly destroyed by the tissues, the term

[1] Inflammations due to constitutional causes such as gout are not considered here. They obviously depend on a chronic or oft-repeated irritation.

[2] Adami, Allbutt's 'System of Medicine,' vol. i, p. 129.

"septic inflammation" describes the condition, whatever the particular septic agent and its effects may be.

It is to be hoped that as our knowledge of the life-histories of the various pathogenic bacteria increases every septic inflammation and its symptoms will be differentiated and named, in accordance with its special exciting cause, although it is to be feared that mixed infections will continue to be common, and that an exact differential diagnosis may not always be possible, or may only be made by means of a microscopic examination, or a cultivation investigation, after an operation, or after death.

In conclusion, it seems to me (*a*) that an obvious and definite aseptic peritonitis is a not uncommon condition; (*b*) that aseptic inflammation may be described as consisting of the local physiological changes, in and around damaged tissues, which are brought about by an injury and which increase in activity for not more than three days after the injurious action ceases,—the object of this increased physiological activity being the removal by absorption, without obvious loss of tissue, or the demarcation, with a view to separation, of those parts which have been so damaged that their period of usefulness to the animal economy has ended,—but the result in some cases, being a revival of tissues which have been deprived of their blood-supply; (*c*) that septic inflammation may be described as consisting of the local physiological changes, in and around damaged parts, which are brought about by an injury and by the presence of irritating micro-organisms acting on the damaged and adjacent tissues, or which are brought about by the action of such micro-organisms on undamaged tissues,—these changes continuing and varying in activity in proportion to the duration and intensity of the irritation,—their objects, which are not always attained, being the removal by absorption or by extrusion of the noxious micro-organisms, and the removal by absorption, without obvious loss of tissue, or the demarcation, with a view to separation and extrusion, of those parts which have been

so altered that neither their absorption nor their recovery is possible.

More shortly, inflammation, whether aseptic or septic, consists of the series of phenomena necessary for the removal, or for attempting the removal, of effete and irritating matter from a damaged area by the physiological processes of absorption, of extrusion, of demarcation, and of revival, or by one or more of these.

In defining inflammation, the idea that a destructive or an impaired action is a part of this process must be carefully excluded.

Inflammatory fever may be described as a process of general physiological increased activity which accompanies an inflammation and is reflexly induced by the state of partial devitalisation of tissue in the injured area.

Fever due to, or complicated by, irritants circulating with the blood is excited in exactly the same way by a widespread irritation and partial devitalisation of tissue.

In all circumstances when the damaged tissues are physiologically removed, whether by absorption or by extrusion, or by demarcation, or when they are revived, if no fresh source of irritation arises, the local and general signs of inflammation cease, and healing, if there is a wound which has not already closed, progresses steadily.

If there be a solution of continuity of tissue in association with an injury, the inflammatory changes are those by which repair also is initiated. The completion of this process may, however, occupy an indefinite time, especially if the mechanical separation of tissues physiologically marked off is difficult.

I would reiterate that I am following the teaching of Lister when I maintain that inflammation is not necessarily an infective process.

I would also add that there is nothing in the views expressed in the foregoing pages that is inconsistent with the fullest appreciation of the enormous importance of bacteriological science. I do think, however, that in pursuit of this science the importance of the natural pro-

cesses taking place in the living healthy body should not be under-estimated. There seem to be not a few who believe that no local or general reaction ever follows any injury, so long as no micro-organisms are permitted to enter a wound. The idea that the human body resents only the irritation of living organisms seems to me as probable as would be the belief that a foreign navy might bombard the port of London, and that nothing would happen except that the inhabitants would clear away the *débris* and build up what was knocked down, without excitement here or elsewhere.

DISCUSSION.

Mr. ALBAN DORAN referred to the question of twisted ovarian pedicle and tubo-gestation. Couvelaire had shown that tubal pregnancy was not one of the results of a previous salpingitis. The trifling inflammatory changes in a tubal sac were, on the contrary, produced by the products of conception, which were certainly not septic. But early rupture of a tubal sac and tubal abortion were followed by pain and pyrexia, although there was no sepsis. These phenomena, he thought, supported the doctrine enunciated in the paper.

Mr. L. DUDGEON considered that few people would describe inflammation as a physiological process, but, on the other hand, he thought it would be better to drop such terms as "physiological" and "pathological" when dealing with inflammation. If a simple incision was made under strict aseptic precautions there was an increase of leucocytes, and the finely granular polynuclear cells were increased in number both relatively and absolutely. The same resulted if a sterile saline solution was injected into the peritoneum of guinea-pigs within fifteen minutes; this could hardly be considered physiological. Many aseptic wounds contained staphylococci. Cocci in the tissues did not mean suppuration, as some observers suggested. The finding of the so-called sterile exudate of peritonitis was often the result of faulty technique. Pieces of the omentum cultured showed micro-organisms, chiefly the *Staphylococcus albus*. The pyrexia after ruptured ectopic gestation had been attributed to the absorption of fibrin ferment, but the blood-clot contained the white staphylococcus. But he had not found this organism to give rise to suppuration when injected intra-peritoneally or subcutaneously into guinea-pigs. The same organism was found in twisted ovarian pedicle, and most varieties of peritonitis. He asked what evidence there was that the processes described in the paper were really of aseptic origin. Had bacteriological investigation been made?

Sir LAUDER BRUNTON said that he was of opinion that the production of "ferments" played an important part in inflammation. He said that many "vital processes" were now recognised to be due to the action of ferments, and instanced the processes of digestion in the alimentary canal and the action of yeast in the formation of alcohol. When white corpuscles are injured plasmase is excreted, which causes coagulation of blood, and also produces a ferment which can digest fibrin. He thought that the local production of "ferments" and their circulation in the blood was a likely cause of the rise of temperature from inflammation.

Dr. G. E. HERMAN said that non-septic peritonitis was a usual thing; for in cases of abdominal section which had run a normal

course, and in which for some reason it was necessary to reopen the abdomen within a period of a few weeks, adhesions were always found in the peritoneum. This was so in every case that he had either seen or read of. He believed that local peritonitis was an invariable sequel of abdominal section.

Professor CLIFFORD ALLBUTT (who had been invited to take part in the discussion, but could not be present, had written to Mr. MacAlister as follows): "In the paper itself I am much interested, and I have speculatively entertained like opinions; but I think two classes of witnesses only will be really useful in this question—(1) those who as surgeons are continually inspecting the very parts; (2) bacteriological pathologists. We physicians cannot have anything worth the saying. Anyhow, I feel sure I have not."

Dr. DONALD MACALISTER (who had been invited to take part in the discussion, but could not be present, had written to Mr. MacAlister as follows): "Mr. Malcolm seems to me to be on the right track, but I am so pressed this week that I have not time to give his suggestive and well thought-out paper the study it deserves. I wish I could be present at the discussion."

Mr. MALCOLM, in reply to Mr. Dudgeon's question as to whether the leucocytosis following an aseptic incision or the injection of sterilised fluids into the blood-stream could be described as a physiological process, said that this condition certainly appeared to him to be due to an increase of changes which were normal. He disclaimed the assertion that all micro-organisms gave rise to pus; indeed, he had asserted in his paper that micro-organisms which usually gave rise to pus when in large numbers might be destroyed by the tissues in small quantity. He pointed out that Professor Walsh had found the *Staphylococcus albus* in aseptic wounds, and that Mr. Dudgeon described it as "an organism of very low virulence." Moreover, it was described as producing a serous exudation in guinea-pigs, but never suppuration and never death; whereas, in connection with an ovarian tumour with a twisted pedicle, there was certainly no serous exudation, but all the changes were directed to a rapid formation of adhesions between the tumour and the surrounding parts. Hence if the *Staphylococcus albus* developed in this position, it could only be present to be rapidly incorporated with the adhesions; and if this coccus was the cause of the inflammatory reaction it was necessary to believe that a dying mass of tissue, perhaps as large as a football, in the peritoneal sac was not in any way a cause of irritation. Mr. Malcolm thought Sir Lauder Brunton's interesting remarks on ferment development supported his views by showing the great changes which the tissues were capable of effecting, and he was glad of the support of Dr. Herman in his opinion that an aseptic peritonitis was a common occurrence.

THE INFLUENCE OF POSTURE ON THE NORMAL CARDIAC SOUNDS AND ON THE NORMAL CARDIAC DULNESS

BY

DR. WILLIAM GORDON

Received February 8th—Read November 14th, 1905

THE changes in cardiac murmurs which occur on change of posture are so pronounced as to suggest the inquiry whether alteration of position also affects the normal heart-sounds. Careful observation of normal hearts will soon convince anyone that change of position does affect the normal heart-sounds, sometimes slightly, sometimes markedly. The change produced is a change in the character of both sounds. It will generally be found that, in the upright position, the first sound is sharper, whilst the second sound is duller, than in the recumbent position, so that the two sounds are much more like each other in the upright position than they are in the recumbent. Indeed, it may be fairly said that the "lub-dup" of the text-books is, in most cases, a true description only of the sounds when the body is recumbent, and that "lup-lup" more exactly describes them when the body is erect.

How can these differences be explained? I have shown elsewhere [1] that the changes in cardiac murmurs produced by change of position can be explained partly by the action of gravity on the intra-cardiac currents, partly by the flattening of the chest which occurs, as I have pointed out, when the patient lies on his back.

As the changes now referred to are changes in the *character* of the sounds, differences in the depth of the chest cannot be held to account for them, and the question reduces itself to this: "Can the action of gravity account for the changes?"

If the position of the valves of the heart in the upright and recumbent positions are considered it becomes obvious that, when the first sound is produced, a weight of blood is resting on the mitral and tricuspid valves if the person examined be *recumbent*, but that if the person be erect, no such weight rests on these valves. Also it is obvious that, when the second sound is produced, a weight of blood is resting on the aortic and pulmonary valves, if the person be *erect*, but that if he be recumbent, no such weight rests on these valves. Therefore the question resolves itself into this (since the first sound is admittedly in part valvular): "Does a valvular sound vary according as a fluid weight does or does not rest on the valves producing it?" The following experiment shows that it does:

A glass tube A, 3 cm. in diameter, has one end open and the other drawn out to a neck. A membrane, B, of inelastic waterproof material is stretched not quite tightly over the broad end. The neck is connected with a ball-syringe, C,[2] by a short length of rubber tubing, D. The whole apparatus is filled with water, so that a slight sudden pressure on C makes B suddenly tense, and thus produces a sound. It will be found that when A is held, as in Fig.

[1] 'Brit. Med. Journ.,' March 15th, 1902, "Posture and Heart-murmurs."

[2] The ball-syringe is kept base upwards in both experiments to prevent any air bubbles it may contain from getting into the tube A.

2, with B upwards, *i. e.* with no weight of fluid on B, this sound is sharper than when A is held with B downwards,

FIG. 1.

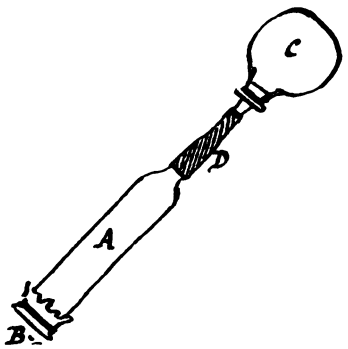
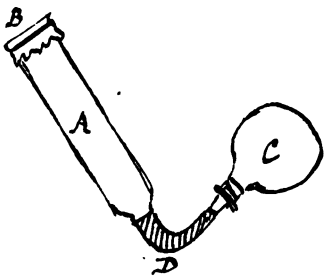


FIG. 2.



as in Fig. 1, *i. e.* with the weight of the water in A resting on B.

FIG. 3.

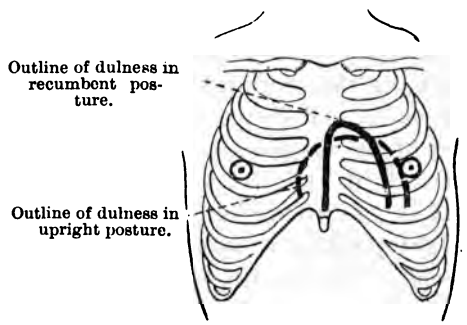


Diagram to illustrate the change in the limits of cardiac dulness with change of position.

The observed changes in the normal heart-sounds produced by change of posture may therefore be reasonably explained, at least in part, by the different relations of the valves to the weight of blood in contact with them in the different positions.

Posture also affects the deep cardiac dulness. In the erect position the cardiac dulness drops nearly a rib's breadth (on an average) further from the clavicle than in the recumbent position, and (in the average adult) becomes about three-quarters of an inch wider from side to side at the level of the fifth costal cartilage, the increase being greater to the right than to the left, that to the left being about one-third of an inch. The accompanying table, of thirty-six consecutive unselected cases with normal hearts, illustrates these changes.

It will be seen that in several cases the upper limit does not alter, and that in three cases it alters in the reverse direction to the usual one. The change, however, in the width of dulness is strikingly constant, so much so that it seems curious that it has not been observed before. [The same change in width of dulness is even more striking in disease. Thus, in a case of hypertrophy and dilatation due to combined aortic and mitral disease, I have found the dulness on recumbency only five inches wide, whilst in the erect position it was actually eight inches wide.]

How are these changes to be explained? I think in this way. On assuming the erect position the heart tends to fall lower in the chest, and, owing to the forward slant of the anterior part of the diaphragm, to also fall forward against the front wall of the body. Thus the cardiac dulness should tend to sink somewhat lower, and to widen out when the upright position is assumed, which is just what usually happens. [In disease, where the weight of the heart is increased, this drop on change to the erect posture may be very marked, the apex being sometimes found to beat, when the patient stands or sits, in a lower space than when he lies on his back.]

In a much smaller number of cases, however, the upper limit of dulness actually rises, instead of falling. If this is due to the heart being anatomically more firmly held up than is usual, and to its upper part coming forward into contact with the chest-wall when the person stands, it

might be reasonably expected that the dulness in those cases would widen less than usual, and this is actually found to be the case in the very few examples included in my table, in each of which the widening was only one quarter of an inch.

Whether the explanations I have offered of these changes in cardiac physical signs produced by change of posture be correct or no, I think that the importance of the changes themselves will be considered sufficient to justify me in bringing them to the notice of the Society.

Thirty-six Unselected Cases with Normal Hearts.

Sex.	Age.	In hospital for—	Changes on rising from recumbent to erect posture in—		
			Width of dulness.	Height of dulness.†	Depth of chest.*
M.	7	Circumcision	+ ¾ inch	−1 rib, 1 space	+ ¼ inch
F.	7	Accident	+ ¼ „	−1 „ 1 „	+ ⅛ „
M.	10	Accident	+ 1¼ „	− ½ „	+ ⅜ „
M.	13	Accident	+ ⅜ „	−1 „ 2 „	+ ⅛ „
M.	13	Hypospadias	+ ¼ „	+1 „	+ ⅜ „
F.	14	Flat-foot	No change	No change	+ ⅜ „
M.	15	Accident	+ ⅜ inch	− ⅛ inch	No change
M.	15	Accident	+1 „	−1 rib, 1 space	+ ⅛ inch
F.	16	Housemaids' knee	+ ¾ „	− ½ „ 1 „	+ ⅞ „
F.	16	?	+ 1¼ „	− ½ „	+ ⅛ „
F.	16	Lateral curvature	+ ⅜ „	No change	+ ⅛ „
M.	17	Accident	+ ⅜ „	No change	+ ⅜ „
M.	17	Accident	+ 1¼ „	−1 rib	+ ⅜ „
M.	17	Varicocele	+1 „	−1 „	+ ⅛ „
M.	17	Hammer-toe	+ ⅜ „	− ½ „	+1 „
M.	18	Hernia	+1 „	−1 „	+ ⅝ „
M.	18	Accident	+ ⅝ „	− ½ „	+1 „
M.	18	Varicose veins	+ 1¼ „	No change	+ 1⅛ „
F.	18	?	+1 „	No change	+ ⅛ „
F.	19	Synovitis, knee	+ ¾ „	−1 rib, ½ space	+ ⅛ „
M.	20	Varicose veins	+ ⅜ „	−1 „	+ ⅛ „
F.	21	Synovitis, knee	+ ⅜ „	− ½ „	+ ⅜ „
F.	22	Phlebitis	+ ⅝ „	?	+ ⅞ „
F.	23	Hip disease	+ ¼ „	+ ½ rib, 1 space	+ ¼ „
M.	24	Varicocele	+ ¼ „	+ ½ „	+ ¼ „
F.	24	Tubercular glands	+1 „	−1 „	+ ⅝ „
F.	26	? Appendicitis	+1 „	−1 „ 1 space	+ ½ „
M.	29	Perinæal abscess	+ ½ „	No change	+ ¼ „
M.	30	Sebaceous cyst	+1 „	−1 rib	+ ⅞ „
M.	30	? Carcinoma, penis	+ ¾ „	− ½ „	+ ½ „
M.	31	Varicose ulcer	+1 „	− ½ „ 1 space	No change
M.	33	Tubercular knee	+ ½ „	−1 „ 1 „	+ 1 1/16 inch
M.	34	Talipes	+1 „	− ½ „	+1 „
F.	35	Ulcer of leg	+ 1⅛ „	−1 „ 1 space	+ ⅜ „
F.	36	"Uterine"	+1 „	?	+ ⅛ „
M.	43	Tubercular ankle	+ ½ „	− ⅛ inch	+1 „

* *i. e.* Antero-posterior diameter measured at nipple level.

† *i. e.* Nearness of upper limit of dulness to clavicle.

\+ Indicates nearer to clavicle.

− Means further from clavicle.

DISCUSSION.

Mr. STEPHEN PAGET said he was able to confirm the changes in the percussion note demonstrated at the meeting by Dr. Gordon in the case of the heart of a healthy person first in the erect posture and then recumbent.

Dr. NEWTON PITT thought there could be no doubt that there was a difference in the cardiac dulness in the erect and recumbent attitude. In regard to the sounds, he thought that, inasmuch as the fluid pressure within the ventricle was equal in all directions, the position of the valve, whether vertical or horizontal, was immaterial; what was material, so far as gravity was concerned, was the head of blood above the valve.

Dr. T. J. HORDER thought the influence of ventrical pressure must be so much greater than the effect of gravity that it was hardly conceivable that the force of gravity could effect any appreciable alteration on the cardiac sound.

Dr. W. GORDON in reply pointed out:

1. That gravity did not act equally in all directions in a fluid.

2. That at the moment of closure of the auriculo-ventricular valves the blood in the ventricle was not continuous with the blood in the vessels.

3. That in the diseased heart the changes produced in the murmurs at the different valves by change of posture could not be explained unless it were admitted that gravity affected the intra-cardiac conditions, and that, if gravity could affect conditions in the diseased heart, it was reasonable to think that it could also affect conditions in the normal heart.

He regretted that the discussion had not dealt with the *facts* he had brought forward, but only with his explanation of them. The facts were more important than the explanation.

INFLUENZAL ENDOCARDITIS

WITH AN ACCOUNT OF TWO CASES IN WHICH THE INFLUENZA BACILLUS WAS REPEATEDLY CULTIVATED FROM THE BLOOD DURING LIFE

BY

THOMAS J. HORDER, M.D., M.R.C.P.

Received June 19th—Read November 14th, 1905

Introduction.

In the study of influenza, tardy convalescence and the existence of a variety of troublesome sequels have always attracted attention. Of late, however, one of the most striking features in connection with the disease has been the occurrence of prolonged attacks of the fever, suggesting the continued operation of the causal organism in the tissues rather than a mere delay in the recovery of these from an infection lasting only a few days. In these prolonged attacks there is often no bacteriological evidence forthcoming to prove what organ forms the nidus of the bacillus. But in still a third series of prolonged cases definite complications are now known to be directly due to the action of the organism: otitis media, pleurisy, pneumonia, pericarditis, meningitis, cerebral abscess, arthritis —in each of these the influenza bacillus has been isolated from the seat of the lesion. It would now appear that a

true influenzal septicæmia may occur, to add to the terror of the disease already known. This event is probably uncommon, although instances may be found to be more numerous as observations are extended.

It is true that Canon, studying cases of influenza shortly after the discovery of the causal bacillus by Pfeïffer, asserted that the organism was to be found in the blood-stream in nearly all patients examined; but these results were not confirmed by later observers. Canon constantly found a short bacillus in coverslip preparations made direct from the blood of patients suffering from the disease, and was able to cultivate this bacillus in sugar agar. Exhaustive researches on similar lines by Pfuhl, Pfeïffer and Beck, and Klein and Andrewes failed to demonstrate that the bacillus invaded the blood in ordinary cases of the disease, or showed that its presence was only occasional, and that it then occurred in very small numbers. Thus, out of forty-three cases examined by Klein and Andrewes, cover-glass specimens showed a small bacillus, which might possibly be the influenza bacillus, in six cases only, and doubtful growth was obtained in only one of these six cases. These authors conclude that "any bacilli of influenza that may gain access to the circulation lose here their vitality and are present in the blood only as dead bacilli." The conclusion is probably true, therefore, that in ordinary attacks of influenza nothing of the nature of a septicæmia is present.

The two cases about to be described appear to be undoubted instances of influenzal septicæmia. Both were patients suffering from chronic endocarditis, the septicæmia therefore being of the endocardial type. The influenza bacillus was cultivated from the blood during life in one case upon four different occasions, in the other case upon two different occasions. In each cultivation the influenza bacillus was the only organism obtained. Both cases were fatal. In the first the diagnosis was arrived at by means of the blood-culture as long a time as six weeks before death; in the second case the nature of the disease was discovered in the same manner five weeks before death.

Post mortem the diagnosis was verified in both cases; the endocardial vegetations gave a growth of influenza bacilli, and sections through the endocardium at the seat of the disease showed this same organism invading the tissues deeply and in large masses. Neither in the cultures nor in the sections nor in cover-glass specimens made direct from the vegetations could any other organism be demonstrated.

I can discover no other record of a case of influenza endocarditis having been diagnosed by blood-culture during life. There are, however, records of two cases in which the organism was cultivated from the endocardium after death. These two cases were described by L. Jehle, in 1899. One case yielded a pure culture of the bacillus, the other gave a few pneumococci in addition. Two other cases are to be found in the literature in which coverslip preparations made from the vegetations on the heart valves showed the presence of an organism which was probably the influenza bacillus, but the bacillus was not cultivated. The first of these was published by Austin in 1899, the second, of special interest, from the fact that the endocarditis was grafted upon a heart which was the seat of congenital defects, was recorded by F. Schlagenhaufer in 1901. In Schlagenhaufer's case the endocarditis involved the orifice of a patent ductus arteriosus. This susceptibility of congenitally defective hearts to infective endocarditis is illustrated in one of my own cases, in which the aortic valve consisted of two large cusps.

In the two cases I shall describe the organism obtained ante and post mortem had all the characters of the influenza bacillus as described by Pfeïffer. A short non-motile bacillus, with rounded ends, tending to show considerable variation in size and shape; bipolar staining common, suggesting, when marked, a diplococcus; Gram's stain[1] quickly and constantly lost; staining by ordinary dyes feeble, but by dilute carbol-fuchsin (1 in 10) very good. Growth only

[1] Aniline gentian violet, one minute; Gram's iodine, four minutes; alcohol, until no more colour comes away.

occurred with certainty in the presence of blood; a first subculture without blood might grow on agar, on glycerine-agar, or in broth, but rarely a second subculture, unless blood were added; no growth at all occurred on gelatin. The bacillus was a strict aerobe; no growth was obtained in an atmosphere deprived of oxygen. Growth on blood-agar appeared during the first 48 hours as minute, discrete, translucent, dew-drop-like colonies, raised and sharply outlined, often escaping attention at first unless carefully looked for by reflected light, so that shadows were produced (Fig. 4). Growth only occurred at a temperature near that of the body. The ordinary animals of the laboratory were immune to the organism; no pathogenic effects were obtainable in mice, guinea-pigs or rabbits, whether the inoculation were made subcutaneously, intra-peritoneally, or, in the case of rabbits, intra-venously.

The organism obtained in the two cases now dealt with was, for a specimen of influenza bacillus, exceptionally vigorous. The growth obtained in the original blood-cultures on solid media gave colonies which were sometimes of large size (2 mm.), well raised and almost opaque. (Such giant colonies, as compared with the colonies more commonly seen, I have also met with in the case of the gonococcus, streptococcus, and pneumococcus, when cultivated directly from the blood-stream during life in cases of septicæmia. Indeed, it would seem that the classical descriptions of the colonies formed by these bacteria must be considerably modified when dealing with the organism obtained from living blood.) The colonies were noticed to be viscid in consistency, the platinum point bringing away the organism in a stringy mass which only made a uniform emulsion on the coverslip after much rubbing up in the drop of water used to prepare the film. If the growth in the condensation fluid were used to make the films, this same feature was noticed. The first subcultures grew well, especially upon glycerin agar, yielding good-sized colonies which were again rather opaque. A second subculture was sometimes obtained without the addition of blood. Another instance

of the vitality of the particular specimen was the fact that a culture (first subculture) was revived after thirty days by the addition of a little blood. This is a much longer time than is stated to be possible by Pfeïffer and others. Cultures thus revived, however, and all subcultures after the second, always consisted of small translucent colonies such as are known to be typical of the influenza bacillus when obtained from sputum during life or from bronchial secretion post mortem. On several occasions a first subculture grew in melted gelatin. In broth the usual appearance was that of a powdery deposit at the bottom of the tube.

A striking morphological feature of the organism was the occurrence of long bacilli, measuring several μ in length, resembling the threads seen in some typhoid cultures (Fig. 6). These long bacilli were not seen in the original blood-cultures, but only in subcultures. These long forms of the bacillus are figured by Albrecht and Ghon in a recent and valuable contribution dealing with the morphology of the influenza bacillus. There was noticed to be a greater tendency to definitely bacillary forms in the subcultures than in the original cultures. The organism was never seen to grow in chains. As the blood-culture yielded a very abundant growth of the organism it was possible to inoculate animals with enormous numbers of the bacilli. This, together with the exceptional vitality of the particular organism obtained, makes the negative effect of the animal inoculations a striking confirmation of all previous observations upon the pathogenicity of the influenza bacillus.

I may add that Dr. Klein and Dr. Andrewes were good enough to examine critically several of the films and cultures; they confirmed the view that the organism was the influenza bacillus. A couple of films were also sent to Prof. Pfeïffer, who kindly endorsed this opinion.

Case 1.

Walter B—, aged 31, a draper's assistant, was admitted to St. Bartholomew's Hospital under the care of Dr. Gee on May 14th, 1904.

(1) *Clinical.*

Past history.—Thirteen years previously the patient suffered from an attack of influenza followed by rheumatic fever; the illness lasted three months. He went back to work, but was told he had a "weak heart." Seven years previously he kept his bed for three weeks, feeling generally run down. Four years previously there was another attack

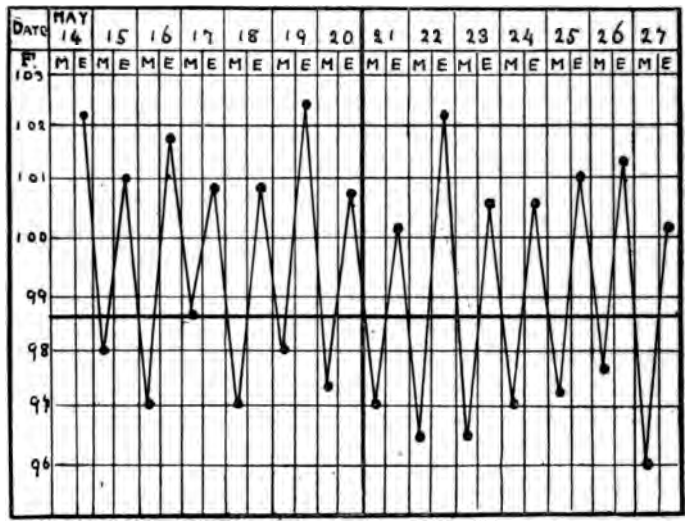


Chart I.—Influenzal endocarditis. Case 1. Temperatures during the first two weeks of observation; quotidian intermittent fever.

of (?) acute rheumatism lasting for ten weeks; at this time he was told that his heart was enlarged. From this date the patient kept at work until ten weeks before admission, when he began to ail again with weakness, sweating at night, and complaining of slight pain over the heart. For four weeks he had been unable to work and had lost weight. These symptoms continued until the day of admission, when he was suddenly seized with severe pain between the shoulders, extending to the neck and head.

Note of condition on admission.—Patient is a fairly

healthy-looking man, with flushed face. Temperature 102°; pulse 104, jerking in character; respirations 24. The bowels are constipated; the urine contains a cloud of albumen, specific gravity 1020, amount natural. The tongue is slightly furred. There is marked systolic pulsation of the carotid arteries. The lungs yield no physical signs of disease. Examination of the heart shows the usual signs of aortic regurgitation, with hypertrophy of the left ventricle. There is no œdema. The spleen is not palpable.

Course of the disease.—On May 21st pulsatile pulmonary murmurs were heard; these disappeared a week later. The fever was quotidian intermittent in type, rising to 101°–102° in the evening and falling to 97°–98° in the morning. (See chart 1.)

The condition remained unchanged, with the exception of increasing loss of flesh and colour, until June 13th, when the patient suddenly developed left hemiplegia, involving the limbs, face, and tongue; there was lateral deviation of the face to the right, and conjugate deviation of the eyes to the right. There was also left hemianæsthesia. There was no loss of consciousness. Sweating was profuse, there was severe headache, and the temperature rose to 103° twelve hours after the attack. On June 29th œdema of the face and feet was noticed. The patient was much thinner. On July 4th there was a sudden attack of right hemiplegia: the patient was delirious, the temperature rose to 104°, and on July 6th death occurred.

No change was noticed in the character of the aortic diastolic murmur during the time the patient was under observation.

(2) *Leucocyte Count.*

On May 31st the white cells numbered 18,400, and on July 2nd they numbered 14,900. The differential leucocyte count showed nothing unusual: the increase was in the polymorphonuclear cells.

(3) *Blood-Culture.*

This was undertaken upon four different occasions. In each instance the same technique was employed. One c.c. of sterile sodium citrate (0·5 per cent.) was drawn up into a 5 c.c. sterilised glass syringe, and a vein at the bend of the elbow was then punctured, after careful sterilisation of the skin. The syringe was then allowed to fill from the vein. The 4 c.c. of blood thus obtained were used to inoculate broth and sloped agar-agar tubes. Different dilutions of the blood and broth were made: a little blood with much broth, so as to dilute thoroughly any anti-bodies which might be present, and much blood with little broth, so as to be more sure of obtaining growth of any organism which might be present in only small numbers. These different dilutions were made on account of theory; in the actual results it was found that no difference obtained in the two sets of culture-tubes. After a preliminary roll of the inoculated tubes they were kept absolutely still in the warm incubator (37° C.), and shaking was carefully avoided during later examination. Previous experience in blood-cultures had shown that in this way it was possible to obtain a loose, colourless, jelly-like clot, which remained suspended in the broth and formed an excellent nidus for the development of any colonies that might appear; the blood-pigment usually sank to the bottom of the tube in the course of the first twenty-four hours (see Fig. 1).

First culture, May 26th.—On the second day small colonies were seen in the clot of the broth tubes, and near the mixture of blood and condensation fluid of the agar tubes. The colonies in broth were opaque and white; on agar they were also opaque, circular, well raised, with clear outlines (Fig. 3). The growth in broth was much more abundant than on the agar surface. There were about nine to ten colonies in each 1 c.c. of blood. The colonies in broth and in the agar condensation fluid were tough and stringy, difficulty being experienced in making uniform films from them. The surface colonies on agar

were also somewhat viscid, but yielded good films. The organism was a very short bacillus, about 1 μ in length, non-motile, staining feebly with Loeffler's methylene blue, rather better with dilute carbol-thionin, but very well with dilute carbol-fuchsin (one in ten). Gram's stain[1] was readily lost. Some of the bacilli showed a degree of bipolar staining; others resembled cocci somewhat. The individual members never grew in true chains (Fig. 5). The resemblance to *B. influenzæ* was morphologically so close that, in conjunction with the above-named cultural and staining features, the opinion was arrived at that this was the organism which had been isolated. Subcultures confirmed this view. Growth was very scanty upon ordinary agar, better upon glycerin agar. The colonies were very small, quite transparent at first, becoming slightly opaque after four or five days. In broth, during the second twenty-four hours, slight turbidity occurred, with a powdery deposit at the bottom of the tube. Second cultures either grew very feebly or not at all. The addition of a little blood to the medium, however, caused again a fairly vigorous growth. No growth was obtained on gelatin in the cool incubator (22° C.), but there was some growth in melted gelatin (37° C.) at the first sub-culture. No pathogenic effects were obtained on animals. Two mice were inoculated with 1 c.c. each of the original growth in broth, one subcutaneously, the other intra-peritoneally. Two rabbits were inoculated with 4 c.c. of the original broth culture, one intra-peritoneally, the other intra-venously. All four animals were alive and well a month later.

Second culture, June 7th.—The blood was spread over the surface of four large agar plates. Only one colony appeared, on the third day. This colony yielded a small bacillus in all respects similar to that previously obtained. This method of culture was evidently ill adapted to the growth of the organism.

[1] Anilin gentian violet, one minute; Gram's iodine, four minutes alcohol, until no more colour comes away.

Third culture, June 20th.—In twenty-four hours minute white colonies appeared in three broth tubes; no growth was obtained on agar slopes nor on three agar plates. The colonies in broth grew rapidly and on examination yielded a bacillus with characters as before described. The rabbit previously inoculated intravenously was again given by the same channel the greater part of a broth tube containing a large number of the original colonies. The animal was alive and well two months afterwards (August 27th).

Fourth culture, July 2nd.—Copious growth occurred in four broth tubes and in the blood and condensation fluid of two sloped agar tubes. Similar growth was obtained on two glycerin agar tubes, but none on a solid serum tube, nor in milk. Glucose broth, however, showed good growth on the third day. One c.c. of the patient's blood was injected directly into the peritoneum of a guinea-pig, but without leading to any pathogenic effect. No growth was obtained in anaerobic cultures. The number of colonies which developed in the broth at this, the fourth culture, was very great. It was calculated that they exceeded one hundred per c.c. of blood (Fig. 2).

An attempt was made to imitate the patient's disease in two rabbits. These were first inoculated with dead cultures of *B. coli communis* intravenously. Large quantities of the original blood-broth cultures were then injected into the animals' veins—one rabbit receiving the whole of a 10 c.c. broth tube, containing an enormous number of colonies of the organism. Neither of these animals, however, developed any symptoms of disease; they were both alive and well three months after the experiment. On being then killed the heart of each was found to be quite natural.

(4) *Treatment.*

As soon as the result of the blood-cultures was known, the patient was given quinine, besides stimulants and a liberal diet, but without any effect. Salicylates had already been administered. Sodium sulphocarbolate was then

tried in full doses, and this also was unsuccessful. The patient was then given mercury in the form of the liq. hydrarg. perchlor. in drachm doses thrice daily. But no good result followed.

(5) *Post-mortem Examination.*

This was made thirty hours after death. A few petechiæ were seen about the neck and shoulders.

The brain showed some flattening of the convolutions of the right hemisphere. On section there was considerable softening of the cortex and centrum ovale on the right side, the colour being paler than natural. The right middle cerebral artery was found to be plugged by an embolus which had lodged at the first point of branching of the vessel. There was no evidence of organisation of the clot.

The lungs were engorged and œdematous. There were no infarcts and no areas of consolidation. There were old pleural adhesions on the left side.

The intestines contained two or three small hæmorrhages.

The spleen weighed 10 oz., was large and firm, but contained no infarcts. Sections showed congestion only.

The kidneys weighed 12 oz. together; the surface and the cortex were mottled and pale. There were no infarcts. Sections examined by the microscope showed no special changes.

The heart weighed 23 oz. It was very large, the left ventricle being considerably hypertrophied; its walls measured 30 mm. in thickness. The interventricular septum was also very thick, measuring 28 mm. The aorta was stout and large, its diameter just above the sinuses of Valsalva measuring 45 mm. These changes in the organ were obviously due to old-standing incompetence of the aortic orifice, which was formed by two valves only, lying anteriorly and posteriorly, both much thickened and of unusual size; they measured 45 mm. in length at their free edge. There was no recent aortic endocarditis. The *mitral cusps* were thickened, but were also free from recent endo-

carditis. At a point on the wall of the left auricle, just above the base of the anterior mitral cusp, was situated a single mass of newly-formed tissue, very slightly pedunculated, firmly attached to the endocardium, dark red in colour, smooth, and rounded in outline. It measured about 12 mm. in diameter. On examining the anterior of the two aortic flaps it was seen that the mass of new tissue had penetrated the substance of the auricular wall and had produced a patch of small granulations which appeared at the base of this aortic cusp, some distance from its free margin. These points are shown in the illustration (Figs. 7 and 8).

Bacteriological examination.—The *heart's blood* proved to be sterile on agar, glycerin agar, and in broth. Rubbings from the vegetations on the aortic cusp showed large numbers of small non-Gram-staining bacilli morphologically resembling the influenza bacillus. No Gram-staining organisms were present. Cultures from the vegetations on blood-agar plates showed typical colonies of *B. influenzæ*, with a few contaminations (yeasts). Cultures from the spleen were sterile on blood-agar and in blood-broth.

Case 2.

Frederick Stanley T—, aged 13, was admitted to the Great Northern Hospital under the care of Dr. Clifford Beale on November 8th, 1904, suffering from abdominal pain and fever.

(1) *Clinical.*

Past history.—Apart from being troubled with nocturnal enuresis the boy, though a delicate child, had had no previous illness. Twelve months before admission, however, upon the occasion of his being circumcised, the doctor had said the boy's heart was weak and that he should not lift any heavy weights. Three weeks before admission he had been attending school. At this time he began to ail, the most noticeable thing being a tendency to vomiting after meals. This, with listlessness and abdo-

minal pains, constituted his illness. There had been no acute symptoms noticed.

Note of condition on admission.—The boy is a somewhat anæmic thin lad, highly nervous. The sole physical signs of disease are pyrexia (100°–101°) and evidence of mitral disease: a loud rough systolic murmur heard at the heart's apex and conducted into the axilla. The pulse is 104, regular. The spleen is not palpable. There is no œdema nor albuminuria.

Course of the disease.—The vomiting occurred once or twice during the week after admission, but then ceased, as

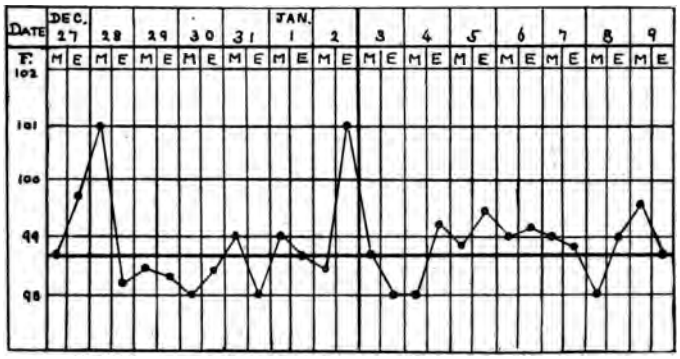


CHART II.—Influenzal endocarditis. Case 2. Temperatures during eighth and ninth weeks of observation, showing afebrile periods.

did the abdominal pain. The temperature remained irregularly raised. A month after admission (December 3rd) the systolic murmur became musical in character, but it lost this feature a week later. The musical quality reappeared ten days afterwards, again to disappear in five days' time. The general condition altered but slightly; on the whole the boy was thinner and rather more anæmic. But he was not very ill—he was able to take part in the Christmas festivities of the ward. Twice more the musical character of the heart murmur came and went. These alterations in the character of the heart murmur discounted any idea of improvement which the period of quiescence of the fever at this time might otherwise have

supported (see Chart II). Six weeks after admission (January 17th) the temperature was noticed to have a higher range (98°–103°), and there was a slight rigor, followed by vomiting (see Chart III). The anæmia was now a striking feature. A second rigor occurred a week later and the patient became more ill. Albuminuria occurred for the first time, and was considerable in amount; a few renal casts were also present, but no blood. There was a third rigor eight weeks after admission (January 30th),

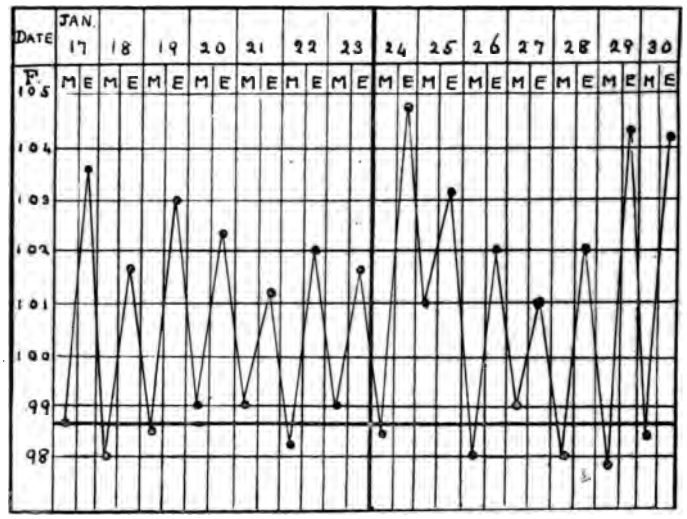


CHART III.—Influenzal endocarditis. Case 2. Temperatures during eleventh and twelfth weeks of observation, showing quotidian intermittent fever.

and the temperature rose to 104°; œdema of the legs appeared, and the urine became scanty. Some delirium was present, with great weakness, and the patient died on February 6th, nine weeks after admission and three months after the onset of his illness.

(2) *Leucocyte Count.*

On January 17th the number of leucocytes present in the blood was 22,400 per c.mm.

(3) *Blood-Culture.*

This was undertaken upon two occasions. The technique was that described under Case 1.

First culture (January 2nd, 1905).—Growth appeared on the second day in four broth tubes and on two sloped agar tubes, the colonies quickly becoming large and opaque in the broth tubes. They were very numerous. On the agar slopes the colonies were also very numerous close to the condensation fluid, running together into a semi-translucent layer of growth; the condensation fluid itself was crowded with colonies. A few colonies appeared upon the general surface of the sloped medium. The cultures resembled those obtained in the previous case in every respect. The growth was pure, and consisted of an organism similar in all its characters to that described under Case 1.

Second culture (January 28th).—Again there was a very copious growth in all six tubes, the colonies being even more numerous, at least 100 per c.c. of blood. The growth was again pure.

(4) *Treatment.*

At first a similar line of treatment was adopted as in the former case; the mercury was administered in full doses. Here again, however, no good resulted. On February 1st the boy was inoculated with freshly-drawn normal horse's serum with the hope that this might provide the complement which his own blood perhaps lacked. The serum was given subcutaneously in doses of 20 c.c. The first dose appeared to prevent the high rise of temperature which was daily occurring at this time. But after the second injection on the following day the temperature rose again, 104°, and subsequent doses of serum, though repeated each day for a week, did not prevent the high fever.

(5) *Post-mortem Examination.*

This was made twelve hours after death. The only organs presenting any pathological change were the heart, spleen, and kidneys.

The heart weighed 8½ oz. Both sides were somewhat dilated, and the left side was hypertrophied. The myocardium was pale, and showed granular degeneration under the microscope. The mitral valve was thickened and somewhat stenosed, these changes being evidently of some considerable duration. Sprouting from the posterior aspect of the fused mitral cusps was a single mass of rounded "vegetation" obstructing the orifice in such a way as to readily suggest that this was the cause of the musical systolic murmur which had been a clinical feature of the case. The whole mass was about 10 mm. in diameter. Its surface was smooth. There was no destruction of tissue, neither of the valve nor of any other part of the heart (Fig. 9).

The heart's blood was sterile on cultivation. A piece of the "*vegetation*," rubbed over the surface of two glycerin agar plates, yielded, besides air contaminations, numerous colonies of *Bacillus influenzæ*, which were sub-cultivated on blood agar. Films made direct from the "*vegetation*" yielded large numbers of minute non-Gram staining bacilli, having all the characters of *B. influenzæ*. No Gram-staining organisms were found in the films.

A section taken through the endocardium at the site of the vegetation showed a layer of fibrin beneath which lay dense masses of organisms. Deeper than these masses, in the loose endocardial connective tissue, there were seen other groups of organisms, less crowded together, and therefore more easily studied. They were short bacilli, often seen to be diplococcal in form, and here and there some of the thread-like bacilli already described were plainly seen. The depth to which the organisms had penetrated the tissue was very striking. None of the organisms present took Gram's stain (Fig. 10).

The spleen weighed 5 oz.; there was extensive old perisplenitis, and three or four old infarcts, white and sunken, the largest of which occupied about a quarter of the whole organ. There was no general enlargement of the organ. Cultivations from the splenic pulp yielded no growth of any

organism, nor did sections of the spleen show any on microscopic examination.

The kidneys weighed 12 oz. They were large and pale, the surface mottled, the cortex swollen and very pale. Several old infarcts were present. The microscope showed very little change in the general kidney substance. There was some recent infiltration of the cortical interstitial tissue. The cells of the convoluted tubules showed a considerable degree of granular degeneration.

Conclusion.

There seems no doubt that in the two cases here dealt with a condition of influenzal septicæmia was present. They therefore, as already stated, form a striking contrast to the ordinary cases of influenza, in which, despite the earlier assertions of Canon, it is now agreed that the bacillus does not invade the general blood-stream. The focus of the disease was, in both cases, the endocardium. Henceforth, to the already rich flora of endocarditis must be added Pfeiffer's influenza bacillus.

The illness of both patients began somewhat insidiously; there was no initial disease which bore any obvious resemblance to the common features of an influenzal attack. In this respect the cases are analogous to the more chronic cases of streptococcus endocarditis. Both cases ran a prolonged course; one lasted three months, the other lasted four months. In both instances the influenzal infection was grafted upon an endocardium which had been damaged by previous attacks of rheumatism.

The clinical picture presented by the patients differed in no essential points from that seen in the majority of cases of chronic malignant endocarditis. The terminal symptoms were in one case due to cerebral embolism, in the other case due to nephritis. Both of these conditions are of common occurrence as terminal events in malignant endocarditis.

A point of some considerable interest is the fact that

in each case *a well-marked leucocytosis* was present. In the adult case the highest count was 18,400; in the case of the boy the highest count was 22,400. So that, whatever may obtain in ordinary attacks of influenza—and it seems certain that these cases usually present no leucocytosis—it would appear that influenzal septicæmia leads to considerable increase in leucocytes.

Turning to the morbid anatomy of the cases, it was noticeable that there was little or no tendency to destruction of tissue in the heart, as is often seen in endocarditis due to pyogenic organisms, but rather to the formation of new masses of material of considerable size, firm and rounded. In the heart first described the situation of the single large sessile mass on the wall of the left auricle suggests a direct infection of the endocardium at this spot by organisms arriving in the pulmonary blood-stream. The presence of a congenital valvular defect in one of the hearts—two aortic cusps—furnishes an illustration of the special tendency to infective endocarditis which this condition confers upon the subject of such malformation.

As to the frequency of the disease here dealt with, future observations can alone show whether the discovery of these two cases within six months of each other constitutes a mere coincidence or whether, as I think is more likely, the condition is really not a rare one. Malignant endocarditis is quite a common disease. It sometimes happens that cultures made from the blood and vegetations post mortem fail to reveal the nature of the organism present. It may be that some of these cases are of influenzal origin; for, judging from the two instances here recorded, the bacillus dies very rapidly in the blood after death, even when present in the circulation in enormous numbers a few days before death. And cultures from the vegetations on the valves or heart wall would often prove sterile unless the media used contain fresh blood—a precaution not often adopted in routine post-mortem work at present. I have recently seen two post-mortem examinations in cases of malignant endocarditis, where the heart's

blood and vegetations both proved sterile on cultivation, and rubbings and sections of the vegetations showed no Gram-staining organisms present, but a minute bacillus whose morphological characters were those of the influenza bacillus. It is not unlikely, again, that some of the cases of infective endocarditis thought to be due to streptococci are in reality influenzal. The coverslip preparations made from the vegetations in the two cases here recorded gave a strong superficial resemblance to a short streptococcus. To employ Gram-staining in every instance is the safeguard against such an error.

In considering the question of the treatment of patients suffering from influenzal endocarditis we find ourselves faced with a problem of great difficulty. The various means which are at our disposal of indirectly raising the patient's resistance must of course be employed here, as in all other cases of septicæmia. But, left to his own resources, the patient would seem to be doomed from the day on which the diagnosis of influenza endocarditis is made. And yet the physician is at present helpless to battle with the disease in any direct manner. Experience shows that chemical antiseptics, whether given by the mouth, subcutaneously, or intra-venously, are disappointing in the treatment of septicæmia. Even the hopes that have been so largely entertained in recent years with regard to the use of bactericidal sera in cases of pyogenic septicæmia must be abandoned here. For the causal microbe is so strict a parasite that no certain pathogenic effects have yet been obtained by animal inoculation. No actively immunised serum can therefore be expected at present. Therapeutics have not yet arrived at a stage which admits the employment of serum of human beings recently convalescent from attacks of influenza. If faced with another case of the kind described, I should try direct inoculation of the patient with dead cultures of the organism, with the hope that by a process of vaccination the infection might be combated by increased resistance on the part of the patient.

I have to thank Dr. Gee and my colleague Dr. Clifford Beale for permission to make use of the clinical notes of the cases as well as for their kind encouragement in the pathological investigations connected therewith.

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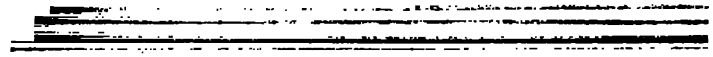
DISCUSSION.

Dr. HERBERT S. FRENCH remarked that leucocytosis was not the rule in cases of infective endocarditis. About 12,000 was the average number in most cases in hospital. He asked what was the probable route by which the influenza bacilli got into the patient. The cases suggested the question whether influenzal patients should be brought into a ward with patients suffering from chronic valvular disease.

Dr. NEWTON PITT wished to emphasise the fact that the causal influence of the influenza bacillus in producing septicæmia had probably been often overlooked because a syringeful of blood had not been examined, the organism being missed when only a few drops of blood were taken. Dr. Horder's method of suspending a mass of blood-clot in the middle of a tube of broth was a very efficient and successful one.

Dr. HORDER, in reply, said that in one of the cases a possible source of infection was suggested by the position of the vegetation in the wall of the auricle away from the valve, and that it was by the lung. He agreed that the fact of leucocytosis in both patients was not to have been anticipated; it was not the rule in cases of chronic infective endocarditis.



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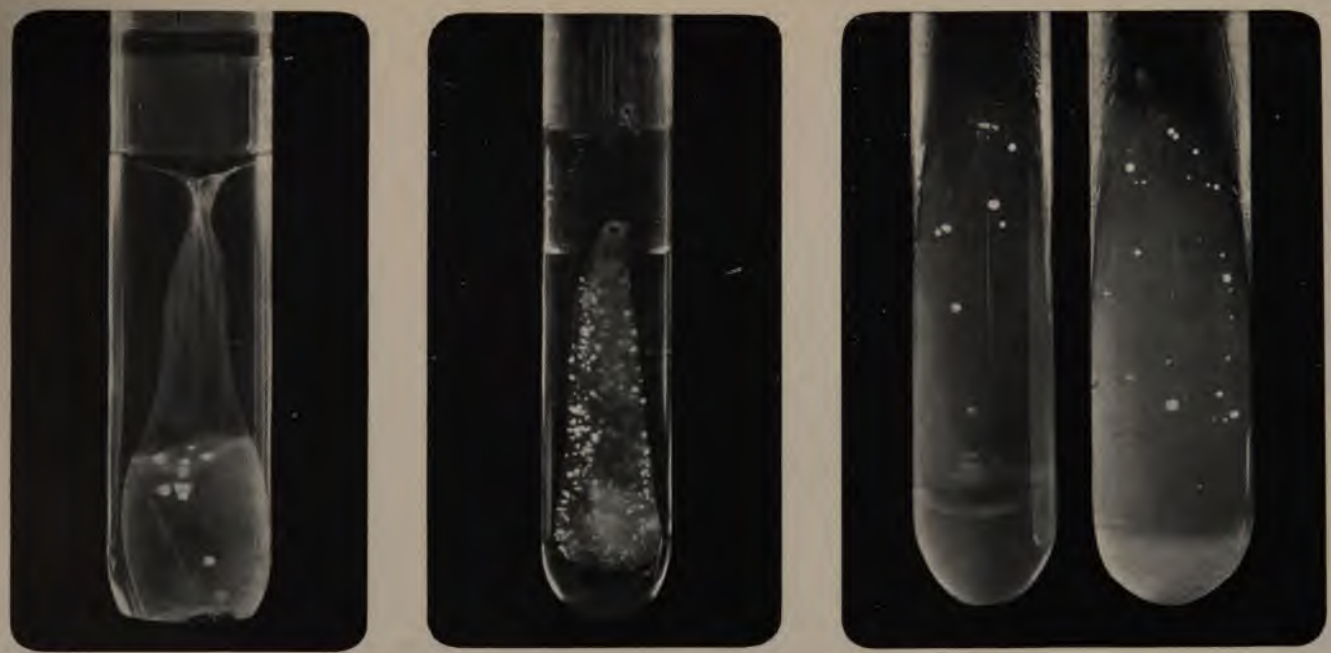

FIG. 1.—Broth tube from first blood-culture in Case 1. Forty-eight hours. × 1.
FIG. 2.—Broth tube from fourth blood-culture in Case 1. Forty-eight hours. × 1. The second blood-culture in Case 2 gave a similar appearance.
FIG. 3.—Two agar-slope tubes from first blood-culture in Case 1. Third day. × 1. The general surface of the slope has been re-inoculated from the condensation fluid after twenty-four hours.

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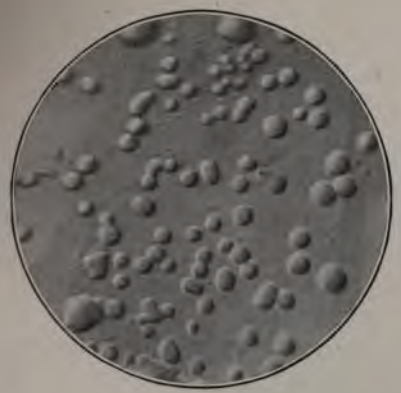
FIG. 4.



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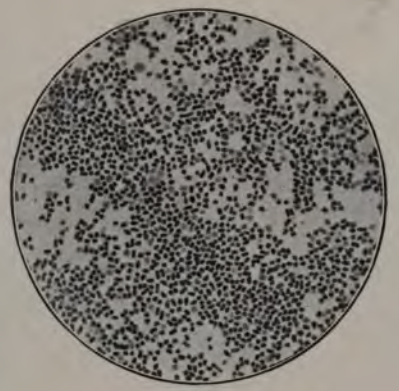

FIG. 6.

FIG. 4.—Colonies of *B. influenzæ*, fourth day. Subculture on glycerine-agar from original blood-broth tube in Case 1. × 40.
FIG. 5.—*B. influenzæ*. Film made direct from blood-culture tube in Case 2. Forty-eight hours. × 1000.
FIG. 6.—*B. influenzæ*. Film made from colony shown in Fig. 4. × 1000.

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Fig. 1. Fig. 2. Fig. 3.

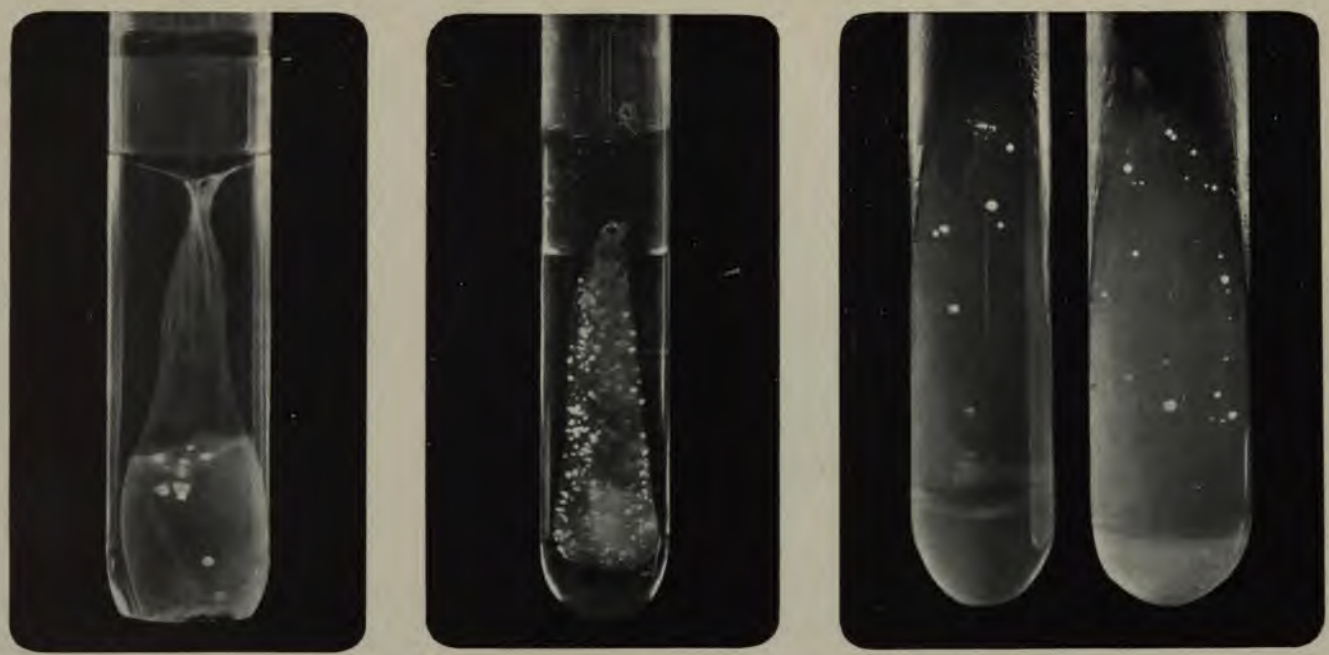

Fig. 1.—Broth tube from first blood-culture in Case 1. Forty-eight hours. × 1.
Fig. 2.—Broth tube from fourth blood-culture in Case 1. Forty-eight hours. × 1. The second blood-culture in Case 2 gave a similar appearance.
Fig. 3.—Two agar-slope tubes from first blood-culture in Case 1. Third day. × 1. The general surface of the slope has been re-inoculated from the condensation fluid after twenty-four hours.

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FIG. 4.

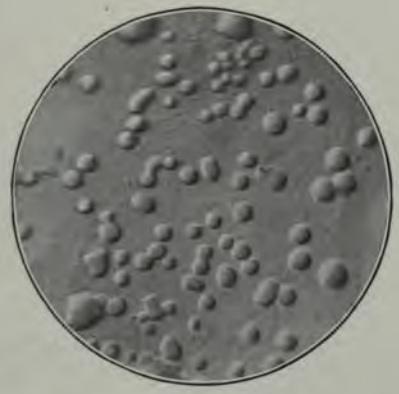
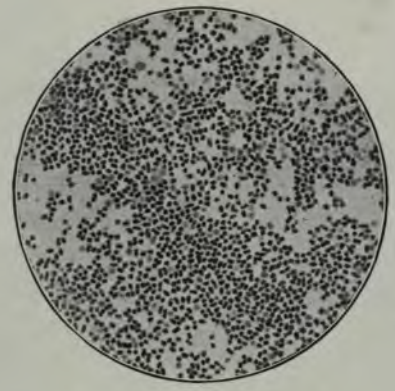


FIG. 5.



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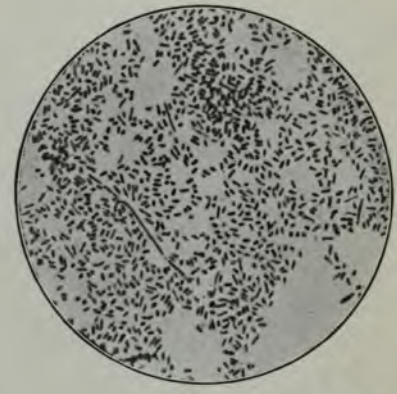

FIG. 4.—Colonies of *B. influenzæ*, fourth day. Subculture on glycerine-agar from original blood-broth tube in Case 1. × 40.
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Fig. 7.

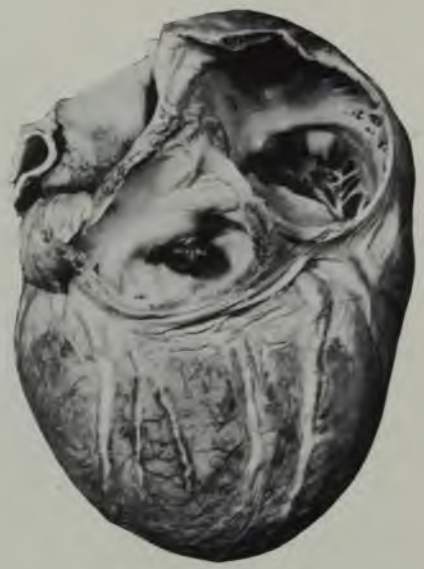

Fig. 8.

Fig. 7.—Heart from Case 1, showing single sessile mass on wall of left auricle. × ½.

Fig. 8.—Heart from Case 1, showing patch of "vegetations" beneath abnormal aortic cusp. × ½.

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THE EFFECTS OF VIOLET INFUSION ON MALIGNANT GROWTHS

AN INTERIM REPORT

BY

DR. WILLIAM GORDON

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On March 18th I published in the 'Lancet' a case of presumable malignant disease which disappeared during treatment with violet infusion. Since then, by the kindness of my colleagues and other medical men, I have been enabled to collect a considerable number of cases, some of which came under my own observation, the rest being watched and described for me by other people. The publication of these cases at the present time will, I hope, serve two useful purposes. Firstly, it will show the desirability of further inquiry into the action of the infusion, and may help to indicate the direction such an inquiry should take. Secondly, it will tend to correct the mistaken statements which have unfortunately been circulated in the Press.

I need scarcely say that I do not propose to discuss here the question of a "cure for cancer." No sensible person acquainted with medicine talks of a "cure" for malignant disease after only a few months of observation.

But the results I have to record are remarkable, and will probably be held to justify my bringing them forward. In considering them it should be remembered (1) that the majority of the cases were already very advanced when submitted to treatment, and (2) that differences in the nature of the growths, in the organs affected, in the patient's constitution, as well as—not improbably—in the varieties of plants chosen, the soils they grew in, the way the leaves were used, and possibly even the season in which they were picked, may have helped to determine the differences in the effects.

I shall begin by re-stating the case which first drew my attention seriously to the infusion.

CASE 1. *Disappearance of a presumably malignant growth in the mouth; recurrence ten months later.*—A gardener, aged 53, consulted me on November 8th, 1904, for what I thought, and still think, was cancer of the tongue. He had been a healthy man, had had no venereal disease, and his wife had had no still-births or miscarriages. One sister had died, and another was said to be dying, of cancer. Six months before I saw him he thought a sharp edge of tooth had hurt the left side of his tongue, and after a time he began to have pain which ran up to his left ear. Later still he had difficulty in opening his mouth. Two hæmorrhages, one of a pint, occurred just before he came to me. There had never been any discharge of pus. He had lost a stone in weight. I found him unable to open his mouth more widely than just to admit my finger, or to protrude his tongue except just beyond the teeth. Salivation was excessive, and the breath very offensive. There was a deep ragged ulcer on the left side of the tongue opposite the last molar teeth, with hard raised edges, very tender, bleeding on examination, and surrounded with much induration, which spread to the gum and anterior pillar of the fauces. He had severe pain at night, which sometimes was agonising, radiating to the ear. I could feel no enlarged glands. I diagnosed

cancer of the tongue, and sent him at once to a surgeon. He saw four surgeons, all men well qualified to form a correct opinion. All four diagnosed cancer, and an immediate extensive operation was advised. A microscopical examination was not made, because no occasion for it then existed. No one questioned the need for operation. No one imagined he would get well without one. However, he refused to be operated on, and treated himself at home with violet infusion, beginning it on November 10th. By January 23rd, 1905, *i. e.* in about ten weeks, he was so much better that his employers sent him to me to show himself. The change was extraordinary. He looked well, and had gained 32 lbs. in weight. The pain had become trifling, he could open his mouth well, and protrude his tongue almost naturally; the ulcer was much smaller, the hardness less, the surrounding infiltration greatly reduced, and there was no longer any tenderness or inclination to bleed. He said that during the first week of the treatment the pain had been worse, but that after that it rapidly became less. On February 20th, the treatment having been continued meanwhile, I found practically nothing left of the ulcer but a local loss of substance in the side of the tongue and a narrow hard scar. There was only occasional slight pain. Since then he kept in excellent health, the scar remaining the same, and the pain having ceased, until December.

He then discovered a small growth on the anterior pillar of the fauces at the left side, a little way behind the seat of the former ulcer. It was, however, painless. I saw him on January 16th of this year. The growth is small, is ulcerating and indurated, but there is little surrounding inflammation; no glands can be felt in the neck. He says he is using the violet infusion as before, and that the growth is no larger than when he found it a month ago. At that time I understand he was still taking the infusion. He is a great smoker, and although warned to give up tobacco, has not done so. Whether

this has tended to cause recurrence is a matter for conjecture. I hope I may be able to induce him to have the growth removed or at least a part of it for microscopical examination.

The second case which came to my knowledge was also not microscoped, for the same reason as the first case. No doubt existed as to the nature of the disease when the question of operation was raised, and no recovery apart from operation seemed possible. But, in spite of the absence of microscopical confirmation, it will probably be conceded that this case is a very important one. Syphilis of the tongue is a common enough disease, and may sometimes closely simulate cancer, but syphilitic ulceration of the cervix uteri resembling cancer is a very rare disease, and, considering the very careful examination which was carried out in this case, it is scarcely conceivable that an error in diagnosis has been made. It should be noted, in passing, that Case 1 presented no features justifying the diagnosis of gumma.

CASE 2. *Disappearance of a presumably malignant growth of the cervix uteri* (under the care of Dr. Bird, of Sidmouth).—Mrs. M—, aged 52, began to suffer in January, 1903, from uterine pain and discharge. She had previously enjoyed good health. Her periods had ceased at forty-nine. She had had twelve children and one miscarriage between the tenth and eleventh child. There had been no still-births. Eight children, including her eldest, are alive and well "so far as she knows." Early in 1903 she had a severe uterine hæmorrhage, and this was repeated later in the year. Dr. Bird examined her in September, 1903, and found a condition which he diagnosed as malignant ulceration of the cervix. The discharge was then sanguineous and offensive, and digital examination caused bleeding. The glands were enlarged in the left groin. The patient had lost flesh, and looked cachectic, her appetite was bad, and there was frequent

sickness. As she was bleeding when he saw her, Dr. Bird put her on an ergot mixture, and ordered hot creolin injections each night. When she was fit to travel he sent her to the Great Northern Central Hospital, under the care of Dr. G. F. Blacker, who has kindly sent us the note dictated at the time, and allowed me to mention his name. The note was as follows:

"Examined under an anæsthetic.

"*Nil* in abdomen.

"*Per vaginam.*—Cervix (vaginal portion) has almost disappeared, and there is an ulcer invading it and the posterior wall of the vagina. The tissue of the ulcer breaks down readily and bleeds easily. It is evidently a malignant ulcer. The anterior lip of the cervix is still comparatively intact. Vagina has undergone some senile changes. Uterus appears fairly movable.

"*Per rectum.*—Thickening felt in right utero-sacral ligament, and the ligament is shortened. Left utero-sacral ligament is also thickened and shortened. Growth can apparently be traced out from cervix into the utero-sacral ligaments.

"Considered inoperable therefore."

The patient returned home, and, soon after, about the end of October, 1903, on the advice of a lady in Sidmouth, began to treat herself with violet infusion under Dr. Bird's supervision. Every day about thirty fresh violet leaves were washed with cold water, placed in a jug, and a pint of boiling water was poured on them. After twenty minutes the water was poured off, and taken internally in the next twenty-four hours. At the same time, by Dr. Bird's advice, she used hot creolin vaginal injections (a drachm to the pint) each night and took a drachm of Scott's Emulsion thrice daily after food.

In a week "she felt better," in two months the discharge ceased to be sanguineous, in six months all pain had left her. She went on with the treatment up to last January with occasional breaks of a month. During the breaks she said she missed her medicine. No unpleasant symptoms

were caused. No considerable hæmorrhage occurred again. No slough seems to have come away.

On March 21st last I saw her with Dr. Bird. I found her a healthy-looking woman without a trace of cachexia, fairly well nourished, but easily tired, although stronger than she had been during her illness. She had no pain or bleeding, the slight vaginal discharge was not at all offensive (creolin injections still used), her feet, which used to swell, no longer did so, and she was never sick. Her pulse was good, a little tense perhaps. The abdomen was thin and wrinkled, but no pelvic growth could be made out by palpation. There were no abnormally large glands in either groin.

Per vaginam.—The cervix had vanished, being replaced by a dimple from which cicatricial bands radiated; nothing could be felt resembling a growth or an ulcer. There was no trace of fœtor, and ordinary examination caused no bleeding. More forcible examination did cause slight bleeding.

Per rectum.—The womb was difficult to make out, seeming curiously contracted. No infiltration or growth could be felt anywhere.

On August 1st Dr. Bird kindly sent me this note:—"When I last examined patient it was about four months ago with Dr. Gordon of Exeter. Ten days after our visit patient took her violet leaf infusion for a month and then left it off until July 15th, when she began again for another month. In fact she is now taking one large breakfast-cupful once a day. About a month after she was seen by Dr. Gordon and myself, the vaginal discharge ceased and she has had none since. Patient is much stronger than when I first examined her and is able to do all the housework herself; appetite good; no sickness; bowels regular.

"On examination, August 1st, 1905, nothing detected on abdominal examination. No glands felt to be enlarged in either groin. *Per vaginam.*—No os uteri to be felt, in fact the end of the vaginal canal feels exactly as if a

successful hysterectomy had been performed, the body of the uterus not being detected." The douche had been discontinued for some time.

On January 12th Dr. Bird found her in just the same condition as on August 1st. She had discontinued the infusion at the beginning of September, but there has been no return of symptoms, and she thinks that she has put on weight.

The doubt about the nature of these two cases arises solely from the fact of the disappearance of the disease. The next case, however, in which the growth greatly diminished, is one in which the diagnosis was supported by microscopical examination.

CASE 3. *Great temporary diminution in size of an epithelioma of the tongue* (under the care of Dr. Rake, of Fordingbridge, near Salisbury).—G. C—, a gardener, aged 63, began to complain of soreness of his tongue in January, 1905. He had had a patch of leucoplakia on the left side of his tongue for seven years, and about two years ago had had a "well-marked syphilitic eruption" of copper-coloured spots on the right arm. Dr. Rake diagnosed cancer of the tongue, and sent him to Salisbury Infirmary where the diagnosis was confirmed and immediate operation advised. Dr. Rake saw him afterwards on March 16th. He was then pale and ill-looking, the speech was thick, the breath highly offensive, and there was a hard lump in the left side of the tongue about its middle, just in front of the patch of leucoplakia, covering an area the size of a shilling, with infiltration of the floor of the mouth, rising to a level with the teeth, and fixing the tongue. There were also some glands below the jaw on the left side. The patient refused operation.

When Case 1 appeared in the 'Lancet' of March 18th, Dr. Rake intended suggesting the trial of violet infusion as operation was refused, but the patient had already begun it. Since there was nothing more to be done for him Dr. Rake did not see him again till April 23rd, *i. e.* about

four weeks later, when he found him "most extraordinarily improved." During the first week of the violet treatment the pain, which had been moderate, became much worse, but afterwards was greatly relieved. The offensiveness of the breath had soon got less. Dr. Rake found that the hardness in the tongue was less and the tongue more movable, that there was more freedom and clearness of speech, less salivation, that the submaxillary glands were smaller and softer, and that the man's appearance had altered markedly for the better, all signs of cachexia having disappeared. On May 9th Dr. Rake removed a piece of the growth for microscopical examination. This was examined by my colleague Dr. Solly, Medical Registrar and Pathologist to the Royal Devon and Exeter Hospital, and pronounced by him epitheliomatous. At Dr. Solly's request a section was also submitted to a distinguished London surgeon who wrote, "It is not a typical case, but I believe the disease to be epithelioma." Dr. Rake made the following note at the time of cutting the growth :—"Tongue much smaller, glands diminishing, salivation stopped. Has a little neuralgia in left submaxillary region." His subsequent notes were as follows :—"May 23rd.—The glands under the jaw are smaller and not tender; there is no salivation now, the growth is smaller and softer; the movements of the tongue are more free. Patient says that, whereas he used to be awakened every few minutes with the pain, now he can enjoy a good night's rest. He also volunteered the statement that the shooting pain which darted up behind the ascending ramus and through the ear had almost entirely disappeared. May 30th.—Tongue much better, more movable, glands softer and smaller. June 7th.—Still smaller, glands softer, very little pain. June 21st.—Tongue softer, hard nodules in places, glands smaller and softer."

On July 6th, by Dr. Rake's kind arrangement, the patient met me at Salisbury. I found him a healthy-looking man. His mouth could be opened widely and the tongue easily and fully protruded. On the left side, about

halfway along the tongue and just in front of a white patch of leucoplakia, I found a hard smooth surface about an inch in length and half an inch broad, which was all that was left of the growth already described. I could find no other growth in the mouth. There were a few small glands in the neck. The patient told me there was no cancerous family history.

On July 18th I heard from Dr. Rake that there was still a gland in the neck, that the cancerous nodule removed for microscopical examination had grown again, and that a hard nodule, the size of a buckshot, could be felt on the under surface of the tongue. On August 16th Dr. Rake wrote as follows :—" Granulating surface rather larger and more raised, hard nodule on under surface of the tongue, perhaps rather larger, complains of rather more pain, no salivation, eats and sleeps well, and moves tongue about quite freely. Whereas in March it was a most hopelessly unfavourable case for operation, the violet infusions have changed it into a very favourable case for operative interference." As the growth seemed to be threatening to increase again we now advised the patient to undergo operation. This he refused, and on November 5th I heard from Dr. Rake as follows :—" C— has gone from bad to worse. The hard lump behind the original sore has broken down, and the cancer is going at an alarming rate. I have advised operation for the last three or four months to no effect, but he went to Salisbury last Tuesday, and they still think it might be successful if done soon. The glands are not any more affected, and his health is not so bad as at the beginning of the year. He has steadily continued the use of the violet leaves. The result is very discouraging."

On January 13th, however, Dr. Rake wrote again :— " C—'s tongue was successfully removed some four or five weeks ago. There is still the gland in the neck which Dr. L— would like to take out, but could not do it at the time of the major operation. The man looks better. I had a terrible trouble to get him to submit to operation,

and Dr. L— said the case was very far advanced. It progressed at an alarming rate at last."

In this case the reduction, which occurred up to July, in the size of the growth was very striking, but it has been suggested that the infusion only affected inflammatory swelling, perhaps of specific origin, and that the cancer (if cancer it was) remained, minus the inflammation. This is, of course, a very reasonable suggestion, but it will not apply to the next case, in which there can be no doubt that the tissues which broke down during the administration of the infusion were cancerous, and not merely inflammatory.

CASE 4. *Breaking-down of epithelioma, re-growth, and renewed breaking down* (under the care of Mr. Russell Coombe and myself).—R. W—, a hawker, aged 45, came under the care of Mr. Russell Coombe last March at the Exeter Dispensary, when he kindly allowed me to see him. He had then an extensive growth involving the left side of the tongue, the floor of the mouth, and the jaw, appearing externally as two large red bosses on the chin. He dated it from August, 1904. There was profuse salivation and very fœtid breath. He was very cachectic. Violet infusion was given at the end of March. In two weeks the cachexia was less, but the centre of the external growth in the skin was sloughing, and looked as if "melting out"—an appearance quite new to me as well as to Mr. Coombe, whose experience of external cancer, as a consulting surgeon's, is, of course, much wider than mine. This sloughing process went on quickly, so that the appearance shown in the photograph was produced, and it seemed as if the whole cancer might be about to come away. The opening led right through the bone into the mouth, so that the movements of the tongue could be seen through it. A piece of the breaking-down tissue was microscoped by Dr. Solly, and found to be epithelioma. Thus there could be no doubt that the tissue breaking down was actually cancerous. That

the breaking down was not merely coincident with the violet treatment, but a consequence of it, seemed clear, partly from its unusual character, partly from its following so closely on the commencement of the infusion, partly from the results of an unfortunate circumstance which perhaps prevented the disappearance we began to hope for, viz. that the patient became careless and neglected his treatment. In about two weeks the growth had sprouted up again, so as almost to fill the opening made by its breaking down. I then took him into hospital, where the treatment could be fully under control, and where it was carefully carried out by Dr. Marsden, the house surgeon, and Sister Hunter. Once more the breaking-down process set in, the opening became wider, and the peripheral part of the growth began to shrink and flatten. The patient began to open his mouth more widely, to move his tongue, and almost to speak intelligibly. He had now no pain, which, before treatment, had been troublesome. The Sister pointed out to me, what I have since observed in other cases, that the sloughing took place in small round patches, about one sixth of an inch across, which became yellow with red edges, and finally fell out, leaving a shallow smooth pit. In spite, however, of persistent treatment, the growth spread at its margin and the glands became involved, so that I was obliged to discharge him as hopeless. It should be noted that this case was alcoholic, and, although there has not been the least suspicion of alcoholism in the majority of the cases which have failed to respond to the infusion, one other case, also alcoholic, was wholly unaffected by the treatment. It is possible that in alcoholic subjects the violet infusion may be less useful than in others. The importance of this case depends on the evidence it affords that violet infusion can definitely affect cancerous tissue.

Now, taking these four cases together, we have, it seems to me, a remarkable series. Two growths with all the appearance and characters of cancer disappear, and

the only doubt of their nature arises from this disappearance. One of them recurs. A third case, with the microscopical as well as the general appearance of cancer, greatly diminishes in size (although only for a time), whilst the fourth case indicates that the infusion can act definitely on actual cancerous tissue.

For clearness sake, the rest of the cases are divided into A, cases in which the growth was microscoped; and B, cases in which it was not. Each of these classes is further divided into *a*, cases in which the growth disappeared or diminished; *b*, cases in which symptoms only were relieved; and *c*, cases in which no effect could be traced. They are described as briefly as possible. Carcinoma and sarcoma are treated separately. Although it is desirable to distinguish between microscoped and unmicroscoped cases, it will scarcely be believed that in all the cases unmicroscoped, where an influence of the drug could be traced, an error in diagnosis has been made. *Most of these cases were first reported to me, not after treatment, but before it.*

CARCINOMATA.

A. Growth Microscoped.

a. Growth disappears, or diminishes, or is checked.

Case 5. *Disappearance of recurrent nodules in breast-scar* (under the care of Dr. G. S. Elliston, of Ipswich; original growth microscoped at East Suffolk Hospital).—Mrs. C—, aged 55, began violet infusion last March. Both breasts had been removed for cancer; the growth in the left had recurred four or five times. Two or three years ago five small nodules appeared, some in the scar, some in the skin above the clavicle, and grew very slowly, but with much stabbing pain. Three of these have now disappeared, and the other two are smaller and softer.

Dr. Elliston wrote on January 13th that he had been obliged to discontinue the infusion for the last ten weeks on account of pain and stiffness, which it seemed to cause. The patient, however, appears well in general health. One of the nodules has slightly enlarged again lately. The others remain the same. The infusion is to be resumed when the limbs are less stiff.

CASE 6. *Temporary diminution of late cancer of tongue* (growth microscoped by Dr. Solly).—J. C—, aged 36; no cancer in family; began violet infusion in March. He had had a cancer of the tongue then for a year and a half, he said. For nine days the pain became severe, then got much better, and the growth got much smaller. Two months later, however, a second growth appeared at the back of the tongue, and a large glandular mass below the jaw. I first saw him on July 19th. Almost the whole left side of the tongue was cancerous, a second mass was visible just behind the anterior pillar of the fauces, and there was a mass as large as a turkey's egg below the left ear, in the neck. A week's treatment with the infusion considerably lessened the size of the cancer in the left side of the tongue, but the external tumour in the neck remained the same. He began to move his tongue much more freely. The case seemed hopeless, however, and after a severe hæmorrhage from the growth (he had had these almost periodically) I allowed him to go home.

b. Symptoms relieved.

CASE 7. *Late cancer of uterus; pain and fœtor greatly reduced* (under the care of Dr. J. Miller, of Exeter, who microscoped the growth).—Mrs. C—, aged about 60, began taking a solution of violet glucoside in May. Large masses of cancer in the vagina then almost blocked its upper part. There was a very fœtid discharge. The dose given removed the pain and fœtor in about ten days without the aid of any local treatment, which she

could not tolerate. The growth, however, continued to extend. After a time the dose of ʒj, thrice daily, seemed to cause syncopal attacks, which ceased on reducing it to ʒss. This patient died last December.

CASE 8. *Late cancer of uterus; pain and fœtor greatly reduced* (under the care of Dr. Solly, who microscoped the growth).—Mrs. P—, aged about 45, began taking the infusion in April. The cervix was deeply excavated by a ragged indurated ulcer, and the body of the uterus was much enlarged, reaching halfway to the umbilicus. She was cachectic, had much pain, and a very offensive discharge. Her general condition improved, the pain got greatly less, and the fœtor almost disappeared. She died in August.

CASE 9. *Late cancer of uterus; pain and fœtor greatly reduced for a time* (under the care of Dr. Wolfe, of Heavitree, microscoped by Dr. Solly).—Mrs. V—, aged 35, no cancer in family, began the infusion early in February. In October, 1904, she was found to have inoperable cancer of the cervix. Early in January the pain became "excruciating," and large doses of morphia with local applications of 20 per cent. cocain did not control it. The discharge was very fœtid. At the end of January she could not leave her bed on account of the pain. By March 3rd, *i. e.* nearly four weeks after beginning the infusion, her general condition was much better. She said the pain had ceased a week after beginning the infusion so that she had been able to come downstairs. The discharge was at that time no longer offensive, Dr. Wolfe tells me, but this relief only lasted six weeks. Then pain and fœtor returned, and were as bad as ever when she died on June 30th. She had, however, at the time of her death stopped the infusion for two weeks, and also, I understand, for some weeks in the hot weather, as "it did not keep well."

CASE 10. *Late cancer of œsophagus. Pain and dysphagia twice removed* (under the care of my colleague Mr. Domville; growth examined by Dr. Solly).—J. C—, aged 43, no cancer in family, began the infusion on April 6th. He had had dysphagia for nine months, was emaciated, and had considerable retrosternal pain. Fluid swallowed remained down a few minutes and then returned unaltered, although a full-sized bougie passed easily into the stomach. After beginning the violet infusion the pain gradually ceased, and the food ceased to regurgitate. Soon he could swallow soft solids, and he gained a pound a week in weight. On May 15th he was allowed to leave hospital for family reasons, but was readmitted worse on June 26th. He seemed so ill that violet infusion was not given, but a bismuth and morphia mixture was prescribed. However, as the pain and dysphagia increased greatly, violet infusion was recommenced. In a few days the pain was less, and he could swallow very much better. He gradually sank and died on August 8th.

At the autopsy a very large cancer was found at the lower end of the œsophagus, involving stomach, liver, spleen, pancreas, and left kidney. It surrounded a cavity almost as large as an orange. Miliary cancer was scattered over both pleuræ and the peritoneum, in the lungs, and in the liver. The relief was remarkable on both occasions on which the infusion was given.

CASE 11. *Late cancer of mouth; pain slightly relieved for a time* (under the care of Dr. Brunton, of 16, Endsleigh Street, London; microscoped at London Throat Hospital).—Mr. G—, aged 48, took violet infusion for six weeks before his death. He had cancer of tonsil, palate, pharynx, and glands which had begun six months previously. Pain was "lessened distinctly" for about a fortnight, but then increased again.

c. No effect.

CASE 12. *Late cancer of uterus; no effect* (under the care of Dr. Orr, of 2, Bennett Street, London; had been microscoped).—The uterus had been removed, but cancer was found to have extended into the pelvis. Two months of treatment with the infusion was not of the smallest benefit.

CASE 13. *Cancer of tonsil small but inoperable; no effect* (under the care of Mr. Domville; microscoped by Dr. Solly).—In this case I have good reason to believe the treatment was not properly carried out. The patient would neither remain in hospital nor attend as an out-patient. The growth was said to be uninfluenced, but at the end of a week, before he went home, I observed that the induration was already less. On January 12th, 1906, I heard from Dr. Powne that he had not carried out the treatment. I have therefore removed the case from the table appended.

CASE 14. *Cancer of liver and peritoneum; no effect* (under the care of Dr. Abbott, of Holloway; growth microscoped "by a specialist").—Mrs. F—, aged 47, with no cancer in her family, began the infusion in March. The liver was then slightly enlarged, but not nodular, and there was some ascites. An exploratory laparotomy showed minute growths scattered over the peritoneum. It was thought that the cancer might have begun in the ovary. She had then had symptoms for two months. She was not emaciated. Five months of violet infusion produced absolutely no benefit. She died on July 15th. The liver then reached to the pelvis, and there were huge masses of growth in the abdomen.

B. Growth not Microscoped.

a. Growth disappears, or diminishes, or is checked.

Case 15. *Disappearance of presumably malignant disease of tonsil* (under the care of Dr. Boger, of Fowey).—Mrs. W—, aged 71, was found, on March 29th, by Dr. Boger to have "a large sloughing ulcer on the left tonsil with hard, irregular, indurated edges." On March 31st she saw Mr. Lucy, of Plymouth, who tells me he made this note :—"A hard red mass bulging the soft palate forwards in the region of the left tonsil, and a crateriform ulcer lined with yellow slough at the tuberosity of the left upper jaw; there were no enlarged glands." Mr. Lucy says, "Although the history suggested chronic inflammatory (post-influenzal) trouble, the hardness and fixation seemed clinically to signify carcinoma, but I had also in my mind the possibility of actinomycosis, and so I suggested the iodide,—not for a possible specific origin, as may have seemed my reason. Clinically the appearance and feel were definitely those of carcinoma." A six weeks' course of iodide of potash produced no effect. The disease spread and seemed to be rapidly extending into the pharynx. On May 4th the patient saw Mr. Bean, of Plymouth, who found a "large excavating ulcer involving the left tonsil, velum and extending down to the epiglottis, edges hard, everted, base sloughing." Although there were neither loss of weight nor glandular enlargement, Mr. Bean tells me there was no serious doubt about the disease being cancerous and told the patient that that was his opinion. On May 6th (the iodide having been discontinued) she began using violet infusion. In a week there were signs of improvement, Dr. Boger says, and by the end of July he found the affected parts "absolutely well." I heard from him on January 12th that the throat remains healthy.

Case 16. *Recurrent growth in mouth checked.*—This patient, aged 72, was kindly sent to me by Mr. Ballance,

with a recurrent growth of two weeks' duration, under the tongue, across the gum and inside the lip. It was already three quarters of an inch broad, evidently growing fast. In the four weeks I had him under observation, the cancer almost ceased to grow, began breaking down in the centre, and flattened to the level of the gum at one side. However, I learn that he has not continued to improve. His medical attendant, Dr. Hosking, who has kindly supervised his treatment, wrote me on October 30th, "as far as I can judge the treatment has arrested the rapid growth, but, so far, has not cured the disease."

Dr. Hosking wrote again on January 12th:—"I am afraid I cannot report much improvement. The violet treatment seems to have arrested the *rapidity* of the progress of the disease, but I am afraid it was too far advanced to improve. He is slowly losing weight, and there is further ulceration."

CASE 17. *Cancer of rectum; partial disappearance; recurrence* (under the care of Dr. Sydney Ringer, F.R.S.). —Mr. C—, a farmer, began the violet infusion about the middle of April. He then had a large hard mass with a deep ulcer with sharp ragged edges in the rectum. After a couple of months' treatment the mass had disappeared leaving only an ulcer the size of a shilling with several linear ulcers running from it. The whole part was then fibrous, and felt cicatricial as if healing—"certainly different, Dr. Ringer wrote, from anything I have felt before in such cases." I heard of him again from Dr. Ringer on August 17th:—"My account of C— is not so favourable. My last account was based on a careful examination, and, I think, cannot have been wrong. There is now a recrudescence, a large growth, I think, much lower down with a deep one-and-a-half-inch ragged ulcer. Notwithstanding this the symptoms are much better, very little blood or slime and no inconvenience except slight constipation easily overcome. There are no secondary growths. Indeed, in general health he is much

better. He has gained 3 lb. in weight, which he ascribes to cod-liver oil I ordered at my last visit. He feels and looks perfectly well and does his work as usual." On August 20th he had gained another 3 lb.

Dr. Ringer sent me a further note on December 30th :— " I examined C— on my visit to L— this Christmas. The local condition was much the same, the ulcer was a little larger. He has some constipation, which he overcomes with an opening pill. When constipated he has several reliefs of reddish watery matter; there is no slime or pain. His general health is excellent. He has gained nine pounds since the summer. He has reached his average weight. His appetite is good. He can do a good day's work, and feels quite well, and looks quite well."

CASE 18. *Cancer of rectum temporarily checked* (under the care of Dr. Gibson, of 6, College Terrace, N.W.).—Mrs. P—, aged 61; no cancer in family; had an indurated ulcer removed from the rectum in October, 1903, but it recurred as submucous nodules in September, 1904. Violet infusion was begun on March 25th, 1905. There were then two nodules on the right side of the rectum as large as hazel nuts, and a ridge of thickening on the left side. The patient had lost two stone in weight, had great pain and difficulty in getting the bowels to act. The X-rays were used without effect, only seeming to increase the pain. They have been used since, with the infusion, except for an interval of three weeks, during which the pain was less and the patient none the worse otherwise for their omission. She has now much less pain, and " her nights are very different from what they were," so that the morphia " has been materially lessened." The bowels are much more regular.

The growth got much smaller and softer at first, but now seems stationary. From being unable to walk, stand, or even sit, she can walk and go for drives. For a time she also put on weight at the rate of a pound a week.

Lately she has not been so well, having burned the bowel by using an injection of pure lysol by mistake.

On January 14th Dr. Gibson sent me this note:—"Since I last wrote there has appeared a large secondary growth in the liver and peritoneum, which has lately caused some ascites. As the violet treatment did not affect this in the least we gave it up two months ago."

CASE 19. *Cancer of rectum diminished* (under the care of Dr. Powne, of Crediton).—T. F—, aged 79; no cancer in family; had a hæmorrhage from the bowel in August, 1904. Dr. Powne found a rectal cancer. I saw him with Dr. Powne on April 24th. He had a large, fixed, annular, fleshy cancer, with a lumen just admitting the tip of the index finger. He began the infusion next day. On August 4th I saw him again. He said he was weaker, and I think he was thinner, but there was no cachexia. The motions had become larger in diameter, and fair-sized masses were passed. The lumen of the growth was larger, the ring thinner, and less fleshy in feeling, and quite movable up and down and from side to side. The bowel close to it felt curiously leathery. On September 6th he had not lost any more flesh apparently, had not a trace of cachexia, and the lumen was quite wide.

Early in January I again examined him. He had not lost flesh, was free from cachexia, and from pain. But he had frequent calls to stool, and the motions were occasionally blood-stained. The growth had recurred round the anus, and caused some pain on examination of the rectum. There the condition seemed much as before. He had omitted his treatment for about six weeks. I desired him to recommence it.

CASE 20. *Large recurrent growth in breast temporarily checked* (under the care of Dr. Solly).—Mrs. M— aged 70, had her right breast removed several years ago. During the latter part of last year a swelling began above the scar of the operation. She began the violet infusion

last March. At that time the growth reached from the shoulder to just across the mid-line of the manubrium, and from the clavicle to the axilla. It was fairly prominent. Her arm was greatly swollen. There was considerable pain. Since then the growth did not increase till August, and, indeed, was definitely smaller. The arm was less swollen, and the pain decidedly less severe. She appeared in better health generally. But in August the tumour recommenced growing, and she died in November with extensive secondary deposit in the thorax.

CASE 21. *Large growth in breast temporarily diminished* (under the care of Dr. Lavery, of Swindon).—Mrs. S—, aged 61; no cancer in family; first noticed a lump in the left breast in May, 1904. She was told it was cancer, and advised to have it removed. She neglected this advice, and by June 1st, 1905, the tumour had become very large. She then began taking violet infusion.

The tumour became greatly reduced in size, her general health greatly improved, and her weight increased. On August 4th I found a firm mass three inches wide and two and three quarter inches high involving the skin, retracting the nipple, and attached to deeper structures at its lower edge. Three large glands could be felt in the axilla. On the whole, I thought it right to advise her to see a surgeon with a view to operation, but she said she would not submit to it.

The skin was much irritated by the infusion.

On September 2nd the glands were smaller, the tumour the same.

On November 8th I heard from Dr. Lavery that the growth remained about the same, and that the patient was "wonderfully well in her general health."

On December 22nd she came to see me. She looked very well, had gained 10 lb. since the summer, but the growth was again considerably increasing.

I have to thank Miss Kinninmont, our Matron at the

West of England Eye Infirmary, for bringing this case to my notice.

CASE 22. *Cancer of breast apparently checked.*—Mrs. W—, aged 46, came to me on August 24th by her doctor's request. She had a cancer of the left breast of twelve months' standing. It measured three inches by two and a half inches, retracting the nipple, and being adherent both to skin and pectoral muscle. There was a fair-sized gland in the axilla, and some small glands over the clavicle. The case had been pronounced inoperable. In two months she gained 4½ lbs. in weight, and the growth became softer and a little smaller. The glands over the clavicle had got much smaller. The surgeon, who had formerly thought the case inoperable, then consented to operate, but she refused to allow it.

On January 11th Dr. Liesching wrote that her general health was good, the mass, "if anything, smaller, though not quite so movable." "It seems softer around, but this, as I said before, seems to me to be an atrophy of the breast tissue." The gland in the axilla is no larger. Some pea-sized glands can be felt over the clavicle. He concludes that "the growth has not increased, but is more distinctly to be felt owing to atrophy of breast."

CASE 23. *Cancer of breast temporarily checked* (under the care of Dr. Wolfe, of Heavitree).—Mrs. M—, aged 57; no cancer in family; noticed a very small lump in the left breast seven years ago. It began to grow and cause pain one year ago. When she began the infusion last February it was about four inches wide and three inches high, and had involved the nipple and the skin round it over an area two inches high and one inch broad. She had "agonies of pain," which often kept her awake at night. The growth ceased to extend, and the pain disappeared. I saw the patient with Dr. Wolfe on May 17th and on August 19th. On the latter date I thought she was not looking so well, and that the growth had slightly increased

in size. I learnt, however, that for six weeks she had discontinued the infusion, and that she had been nursing her husband who had died. There were no enlarged glands to be felt. I saw her again shortly before Christmas. She says she feels well, but the growth is increasing in size.

CASE 24. *Cancer of breast diminished* (for the notes I am indebted to Nurse Holmes, of the Bath Workhouse, to whom I was referred).—A woman, aged 45, was taken to the Royal United Hospital at Bath a year ago with a tumour of the breast. The surgeons said nothing could be done. Last April violet infusion was commenced. Since then the growth has become "much smaller," and the patient has gained in weight and improved in general health. This patient died in an epileptic fit suddenly this January. The growth, I am told, had steadily decreased in size.

CASE 25. *Cancer of vulva; sloughing induced* (under the care of Dr. Campbell, of Crediton).—Mrs. L—, aged 73, was seen by me with Dr. Campbell on March 18th. She had cancerous enlargement of the whole left labium, the clitoris, and about an inch of the right labium. A firm mass of infiltration and glands reached above the pubes into the left groin, and in the right groin there were several glands as large as beans.

There was great pain and fœtor. The patient was thin and cachectic. She began the infusion at once. In four days Dr. Campbell tells me the pain and discharge were reduced. By April 20th the fœtor was gone and the change in the growth was remarkable; the mass in the left labium was sloughing, and small pieces had fallen off, the mass in the left groin was fluctuating (temperature normal), and had given way at one point with the discharge of yellow turbid fluid. The glands in the right groin were also smaller. The general condition had somewhat improved. This improvement, however, was only temporary, and she died on July 11th.

b. Symptoms relieved.

CASE 26. *Tumour of tonsil and glands; pain relieved* (under the care of Dr. Todd, of Torquay).—Mr. C—, aged about 50, saw me at the end of March. He had a large fixed tumour in the tonsil and neck, which several London surgeons had seen and pronounced malignant and inoperable. The infusion failed to check the growth, but "undoubtedly eased the pain." He died early in May.

CASE 27. *Cancer of floor of mouth (small); symptoms relieved up to time of operation* (under the care of Dr. Powne, of Crediton).—A man, about 45, had a small cancer, not larger than a hazel nut, under the tongue in the middle line close to the jaw, and a number of enlarged glands in both sides of the neck. He was cachectic, and complained of soreness round the growth. There was salivation and offensive breath. Operation had been advised, and the patient was waiting for a vacancy at a hospital. In the meanwhile the infusion was given for a fortnight. At the end of that time I saw him again. The cachexia had gone, his general health improved, he had a better appetite, the soreness was less, the salivation less, the breath was no longer offensive, and the growth was less red, and perhaps smaller and more movable. His removal to hospital terminated the treatment.

CASE 28. *Cancer of stomach; temporary marked relief of pain and sickness* (under the care of Dr. Wolfe, of Heavitree).—Mrs. L—, aged 60, with no known family history of cancer, was seen by me in consultation with Dr. Wolfe on March 22nd of this year. She complained of considerable abdominal pain, worse after food, and of constant sickness. There was a large tumour projecting into the epigastric region from under the left ribs. Morphia in very considerable doses, and bismuth, had failed to

control the pain and sickness. She was put on violet infusion, and in about a week the pain and sickness entirely ceased, although no other treatment was used except a very occasional night draught of chloral. This cessation of symptoms could not have been due to any sort of "suggestion," because she did not know she had cancer and did not know what drug she was taking. Her general condition also improved, probably mostly because the pain and sickness had ceased. But the tumour remained apparently the same. This interval of relief, however, only lasted about six weeks; then pain and sickness returned, though they did not become as bad as they had been. Ascites set in about the middle of May, and several tappings were necessary before her death on August 7th. It is, perhaps, worth noting that during the latter part of her illness she stopped the abdominal fomentations made with the infusion which she had used till then. I learn from Dr. Wolfe that "during the hot weather" she stopped the infusion for a few weeks.

Case 29. *"Cuirass" cancer of both breasts; pain relieved* (under the care of Mr. Domville).—Mrs. L—, aged 49, noticed both breasts enlarged, especially the left, in June, 1903. On June 21st, 1903, the left was amputated, a month later the right. In July, 1904, the left cicatrix began to ulcerate. Violet infusion was begun on March 22nd, 1905. The disease was then very extensive and the pain considerable. At first the extension of the disease was checked, and after a week of increased pain, the pain was very greatly relieved for several months. The patient is now dead.

Case 30. *Cancer of vulva; fœtor lessened slightly* (under the care of Dr. Thomas, of Exmouth).—A woman of about seventy had a cancer of the vulva in an advanced stage. The infusion was given internally and applied externally. The fœtor was reduced, but no other influence could be traced.

c. Little or no effect.

CASE 31. *Presumable cancer of tongue retarded* (under the care of Dr. Metcalfe, of Skelmersdale).—W. M—, aged 59, no cancer in family, began the infusion five months ago. He had then an "ulcerated growth on the right side of the tongue the size of a florin, the tongue being infiltrated and fixed; there was slight enlargement of the glands of the neck." It had existed a year and a half. He was well nourished and plethoric, able to work. Since then the growth has slowly extended, the tongue has become fixed, deglutition is now more troublesome, and he is losing flesh and unable to work. Dr. Metcalfe, however, thinks the growth has been retarded. Some time ago, I should add, I advised small doses of Liquor arsenicalis in addition, but this seems to have made no difference.

CASE 32. *Malignant œsophageal stricture; no effect* (under the care of Mr. Lucy, of Plymouth).—A lady of fifty-six, on whom Mr. Lucy had performed gastrostomy on February 2nd, 1905. A thorough trial of the infusion gave no results. The patient is dead.

CASE 33. *Presumable cancer of pylorus; no effect.*—A medical man of fifty-five was operated on in November, 1904, for dilated stomach and pyloric obstruction. He began treatment about the middle of April, when he had a large tumour and fluid in the abdomen. He died on May 2nd.

CASE 34. *Cancer of pylorus; no effect* (under the care of Dr. Powne, of Crediton).—Mrs. S—, aged 45, no cancer in family, came to me on September 20th, 1904, with a pyloric cancer of six months' duration of symptoms. The tumour was so unusually movable that I could not say removal was impossible, and the friends

wished it attempted. Mr. Moynihan, of Leeds, operated, but finding removal impossible performed gastro-enterostomy, which greatly relieved her. She began violet infusion early in March. She was then extremely emaciated. Six weeks later she was rather better, having however, been worse, and passed lumps of blood by the bowel. I cannot say any effect worth speaking of was produced. Perhaps the growth was retarded. She died early in June.

CASE 35. *Cancer of rectum; no effect* (kindly sent to me by Mr. Ballance).—Mr. B—, aged 54, had probably had a rectal growth since Christmas. On June 3rd colotomy was all that was possible. He had a very large fixed growth with narrow lumen. There was marked loss of flesh and considerable albuminuria. He began the infusion on July 14th. His temperature was never normal, varying from 99° to 102°. The growth seemed to get a little softer and the lumen larger, but on the 23rd of August he was very ill indeed, with swollen ankles, fluid in abdomen, liver below umbilicus, spleen much enlarged. He died soon after. The infusion seemed to have no effect worth speaking of.

CASE 36. *Cancer of rectum; effect?* (under the care of Dr. Marshall, of 25, Caversham Road, N.W.)—Mrs. F—, aged 57, began violet treatment early in April. She herself, Dr. Marshall tells me, speaks of being much better, but Dr. Marshall is doubtful whether there is any improvement, and attributes her improvement to her "much more careful and systematic management of her health and regulation of functions that dates from the commencement of the use of the violet leaves." At one time the lumen appeared enlarged, and she has passed natural or nearly normal-sized motions. However, Dr. Marshall, who has watched the case very carefully, is sceptical of any real benefit. He writes on January 12th last, "I called to-day, and find that her condition is much as before. The bowels act comfortably without aperient.

CASE 37. *Cancer of rectum; no effect or very little.*—Mr. X—, aged 59, had had symptoms for nearly a year before violet infusion was begun at the beginning of last May. Colotomy had been performed "by an eminent surgeon" in October, 1904. The growth was very advanced. His medical adviser thinks the infusion perhaps lessened the pain, but is doubtful. No other effect was produced at all events.

CASE 38. *Cancer of uterus; no effect* (under the care of Dr. Duncan, of Lewisham).—Mrs. M—, aged 55, whose mother died of cancer, began violet infusion in March last. She had then had the disease at least six months. On 1st December, 1904, part of the growth was removed by a specialist; part was irremovable. At first the treatment caused some general improvement, but this ceased, and she has since died. There was no evidence of any effect of the drug.

CASE 39. *Cancer of uterus; little or no effect* (under the care of Dr. May, of Plymouth).—Mrs. W—, aged 50, began violet treatment about the middle of April. Abdominal hysterectomy had been performed in June, 1904, but cancer had recurred in the scar. When Dr. May wrote in April he said he thought the patient was within a very few weeks of death. She died on May 23rd. Dr. May thinks the infusion had little effect unless it was the cause of the growth becoming rounder and less ragged, and the entire cessation of bleeding. He thinks that the growth was perhaps slightly checked.

CASE 40. *Cancer of uterus; no effect* (under the care of Dr. Rice, of Steventon).—Mrs. S—, aged 62, family history of cancer, was found to have advanced uterine cancer, implicating the vagina, the cellular tissue at the sides of the pelvis, and the base of the bladder. She began the infusion in March, using wild violets, and kept it up for six weeks. Then she left it off, but began again on July 26th. She has steadily gone down hill.

CASE 41. *Cancer of uterus; "very little effect."*—Mrs. R— began the infusion at the beginning of April. There was then cancer of the uterus involving the bladder. In a month she looked and felt better, but the local condition remained the same. On July 28th I heard there was very little discharge, and no fœtor, but the growth had increased and caused constipation. She had been very ill, but, having got the bowels to act, was again "wonderfully well." I place the case, however, as the doctor's opinion seems to direct.

CASE 42. *Cancer of breast; no effect.*—Lady, aged 66. Infusion begun early in April. No good effect could be traced. She died on June 25th with recurrence in the right lung.

It is only fair to draw attention to the late stage in which the infusion was generally tried in these cases of "little or no effect," and also to slight indications in some of them of the improvements which have been so noticeable in other cases. In very advanced cases of carcinoma, so far as my experience goes, the infusion seems to have no power to arrest growth.

SARCOMATA.

A. GROWTH MICROSCOPED (none disappeared or diminished).

b. Symptoms relieved.

CASE i. *Sarcoma of uterus* (under the care of Dr. Naismith, D.S.O., of Ayr).—Mrs. ——, aged 54, began the infusion on May 27th. She then was cachectic, though stout. The uterus had been curetted and the growth microscoped by a specialist. Further operation was impossible, and she was said to be within about three months of death.

On July 19th Dr. Naismith wrote recording a steady downhill course, but on September 2nd he wrote that "undoubted improvement has set in. Not only has she already lived over the three months, but she has had no return of the awful hæmorrhages she used to have, and from the extreme weakness to which she had been reduced she can now move herself freely in bed, can read and take an interest in things, and admits that she now feels stronger and better than she has done for months." Dr. Naismith adds, "Personally, I am delighted and surprised at the whole thing."

On January 12th Dr. Naismith wrote again that the drug had been continued internally, and on tampon unremittingly, and in larger doses. He said "The general result is simply wonderful." "Up to four or five months ago she was entirely bedridden, but since then she can get out of bed, walk with very little assistance two or three times round the room, and to a sofa . . . where she stays for five or six hours." She eats well, but has considerable flatulence and insomnia. Her bowels act much better. Her complexion, which had "lost much of its deadly pallor and cachectic tint, and . . . regained a good deal of its natural rosy hue," has again begun to look worse. "She has not had a single *large* hæmorrhage such as she used to have before the violet infusion was begun." For three months there was no discharge, but now there is a little. He adds: "I am forced to the conclusion that, *cure* or *no cure*, the circumstance that my patient has survived eight or nine months, and is *in the condition I have described to you*, is due to the treatment."

B. Growth not Microscoped.

c. Little or no effect.

Case ii. *Sarcoma of base of tongue; no effect* (under the care of Dr. Mole, of Callington).—This case went from bad to worse between April 5th and July 16th, 1905.

Case iii. *Sarcoma of upper jaw and liver; no effect* (under the care of Dr. Fitzpatrick, of Ashburton).—Mrs. W— had a sarcoma of right superior maxillary bone, filling the antrum and a secondary large growth in the liver. She began the leaves at the end of April, but no improvement occurred. She died in June.

Cases iv and v were sarcomata seen by Mr. Bean, of Plymouth. They have been published elsewhere as instances of improvement, but Mr. Bean considers they ran a usual course and ended fatally.

Mode of Using the Infusion.

In most of the recorded cases the infusion has been used both locally and internally. About fifty good-sized freshly-picked garden-grown violet leaves with their stalks (the "Princess of Wales" variety was used in Case 1) are put in a jug and a pint of boiling water is poured on them. The jug is set aside in a cool place for twelve hours, say overnight, and then the green liquid is strained off. Half of this liquid is taken internally either at once or in divided doses during the day. The other half is used to make fomentations, or other local applications adapted to the seat of the cancer. This must be done daily as a regular routine for months. Even a week's discontinuance of the treatment seems sometimes to interfere with any improvement produced, although not so in Case 2.

Sometimes larger doses of the infusion or a stronger infusion have been given. Sometimes a shorter, sometimes a longer period of soakage has been used in the preparation of it. In one case a glucoside from the leaves has been used instead (*vide infra*). Large doses must be watched as they may cause unpleasant symptoms.

The local treatment of breast cancer was by fomentations or even poultices of the leaves. That of mouth cancer was by frequent gargling with the infusion. That of rectal and uterine cases was by local injections of it.

In some cases cod-liver oil and hypophosphites have been simultaneously given, apparently with advantage.

Locally the simultaneous use of antiseptics has sometimes seemed to be a help.

Some other Effects of the Infusion.

1. *Anorexia.*—This has seldom been observed, but the appetite has improved in some cases when the infusion was stopped. In other cases the infusion has seemed to increase appetite.

2. *Diarrhœa.*—This was noticed at first in a case of rectal cancer. It was probably due to changes in the cancer. It was easily controlled, and the case improved greatly.

In cases of constipation the infusion has sometimes helped the action of the bowels.

3. *Temporary increase of pain.*—This has been frequently noted. It has generally lasted a week, and has sometimes ceased suddenly.

4. *Rash.*—The external application of the infusion has after a time often caused great redness and irritation of the skin. Sometimes this has subsided. Sometimes the application had to be stopped.

5. *Shortness of breath.*—This has sometimes certainly seemed to be caused by the infusion. I have never seen it severe, but one patient taking large doses complained a good deal of it. He, however, had advanced atheroma, and although the dose was maintained the dyspnœa did not increase.

6. *Faintness.*—One patient taking large doses of the glucoside had syncopal attacks. When the glucoside was stopped they ceased. Afterwards a more moderate dose, viz. a tablespoon thrice daily of Mr. Gadd's solution caused no bad symptoms.

7. Dr. Elliston thinks the infusion caused gouty symptoms in his patient.

The Active Principle.

Mr. Gadd, of Exeter, has kindly prepared for me a solution of the glucoside of violet, and this has been tried alone in one case by Dr. Miller with apparently the same results as sometimes follow the administration of infusion. It was a very late case of cancer of the cervix uteri. Pain and fœtor were both removed without local treatment of any sort, and the general condition temporarily much improved. As the glucoside is an abundant constituent of the leaves, whilst the essential oil appears to be scanty, and the alkaloid extremely scanty in amount, it is not improbable that the glucoside may prove to be the active principle of the infusion. If so, it will greatly simplify the administration of the drug and make the dosage definite.

Conclusion.

One cannot too strongly urge the folly of adopting any doubtful treatment where surgery can cure. Invaluable time is thus too often irrevocably lost. But violet infusion may be tried after operation, to see if it can reduce the percentage of recurrences. In inoperable cases also it seems worth while using it to see if it can check progress, cause diminution or perhaps even disappearance of the growth, or at least relieve its symptoms. Microscoped cases form, naturally, the most reliable material, and on them the final decision will, of course, be based, but the limitations of microscopical diagnosis in cancer should be borne in mind, as well as the obviousness of some cancers apart from microscopical examination.

It should not be forgotten that disappearance is not necessarily cure, and cases where it occurs must be kept under observation for some years. It should also be remembered that cancer has been known, though very rarely, to disappear spontaneously; therefore a good many

cases of disappearance must be recorded before this possibility can be wholly set aside. Further, some improvement in general condition and in certain symptoms may conceivably be due to the combined forces of faith and hope. I think, however, that those who have watched a number of cases improving on this treatment will not ascribe all the gains to those agencies, and in one case, where remarkable temporary improvement occurred (Case 28), they cannot be so ascribed, because the patient neither knew she had cancer nor suspected what drug she was being given. The cases quoted, though numerous enough for publication, are not nearly numerous enough for the discussion of the frequency of this or that result. It may be found that disappearance, for instance, is a much rarer event than this collection of cases might suggest. I know one able observer who has tried the infusion in nine cases with no effect whatever.

In recording these observations I have done my best to avoid any unfair deduction. I hold no brief for the treatment I am testing.

My best thanks are due to those gentlemen who have so kindly placed their cases and comments at my disposal. Without their collaboration this paper could not have been written. I also gratefully acknowledge the increased weight which their names add to the conclusions reached. I would especially thank Dr. Sydney Ringer for the interest he has so kindly taken and for permission to use his name, and my friend, Dr. Solly, for placing his skill as a pathologist at my disposal, and for the time and trouble he has been so good as to give.

To Mr. Gadd, who made a preparation of the glucoside at my request, I offer my best thanks for his interest and help.

All that I would insist on at present is that violet infusion has some definite influence on malignant growths in certain cases, and that wide and careful investigation is

required to find out in what sort of cases this influence may be counted on, and how far it may be possible to push it.

Summary.

1. The drug *properly supervised* is not dangerous.
2. It has a definite influence on malignant growths in some cases.
3. Pain is sometimes remarkably relieved.
4. Fœtor is sometimes remarkably lessened.
5. General condition is sometimes remarkably improved.
6. Sometimes the growth is wholly unaffected.
7. Sometimes it becomes (sometimes temporarily) arrested.
8. Sometimes it becomes reduced in size. This may be only temporary.
9. If the growth is extensive the drug has seemed unable to check it.
10. After a time the drug has sometimes seemed to lose its effect.
11. Some small growths have even disappeared, but the cases of this are very few so far, and the nature of some is open to question.
12. It would be utterly unjustifiable to advise this treatment as a substitute for possible operation according to present experience.
13. It is desirable to try it after operation to ascertain if it can reduce the frequency of recurrence.
14. It is desirable to try it in inoperable cases to ascertain:
    - *a.* If it can cause disappearance of the growth.
    - *b.* If it can bring the growth within the reach of operation.
    - *c.* If it can at least alleviate symptoms.
15. It is desirable that all cases should, when possible, be microscoped when so treated.

16. It is possible that the glucoside is the chief active principle of the leaves.

Table of Cases recorded.

Organ affected.	Stage of growth.	Result.	No. of case.
CARCINOMATA.			
A. *Microscoped.*			
Tongue	? Operable	Greatly diminished and rendered easily operable; afterwards grew again, but was removed in December	3
Tongue, jaw, chin	Very late	Broke down extensively	4
Tongue, neck	Very late	Diminished temporarily	6
Tonsil, pharynx, glands	Very late	No effect almost	11
Uterus	Late	Greatly relieved	7
Uterus	Late	Greatly relieved	8
Uterus	Late	Greatly relieved for a time	9
Uterus	Very late	No effect	12
Breast	Small nodules	3 disappeared, 2 diminished	5
Œsophagus	Very late	Greatly relieved	10
Liver	Very late	No effect	14
B. *Not microscoped.*			
Tongue	? Operable	Disappeared, and recurred nearly a year later	1
Tonsil	Not late	Disappeared	15
Uterus	Inoperable	Disappeared	2
Gum	Early recurrence	Checked	16
Rectum	Large growth	Diminished and recurred	17
Rectum	Small growth	Diminished	18
Rectum	Large growth	Diminished and recurred	19
Breast	Large recurrence	Checked for a time	20
Breast	Large growth	Diminished for a time	21
Breast	Inoperable	Checked	22
Breast	Fair-sized growth	Checked for a time	23
Breast	Inoperable	Diminished	24
Vulva	Very late	Sloughed, much relieved	25
Tonsil and glands	Late	Pain relieved	26
Floor of mouth	Fairly early	Relieved till operation	27
Stomach	Late	Temporary great relief	28
Breasts	Very late recurrence	Greatly relieved	29
Vulva	Very late	Fœtor lessened	30
Tongue	Fair-sized growth	"Retarded," very little effect	31
Œsophagus	Late	No effect	32
Pylorus	Very late	No effect	33
Pylorus	Very late	No effect	34
Rectum	Very late	No effect	35

Organ affected.	Stage of growth.	Result.	No. of case.
Rectum	?	? after 9 months infusion	36
Rectum	Very late	No effect	37
Uterus	Late	No effect of importance	38
Uterus	Very late	Little, if any, effect	39
Uterus	Very late	No effect	40
Uterus and bladder	Late	Very little effect (?)	41
Breast	?	No effect	42
SARCOMATA.			
A. *Microscoped.*			
Uterus	Late	Greatly relieved; checked; bleeding stopped	i
B. *Not microscoped.*			
Tongue	?	No effect	ii
Upper jaw and liver	Very late	No effect	iii
Two other cases	?	No effect	iv, v

DISCUSSION.

Mr. A. Pearce Gould said that the question was beset with many and very special difficulties. A sharp distinction should be drawn between agents which were, apparently, able to affect the symptoms of cancer, as pain, fœtor, etc., and others which might have the power of affecting the growth itself. The discussion of cancer was that of a disease of most protean form. He thought he could parallel nearly every case in the paper from cases not submitted to any specific treatment at all, in such respects as arrest of growth, change of clinical type, rate of progress, etc. The inquiry was one of extreme difficulty. In reference to Cases 1 and 2, there was great doubt if Case 1 was really one of cancer of the tongue, chiefly on account of there having been no enlarged glands in so advanced a case; in the second case, that in which the uterus was involved, it was a remarkable point that so extensive a growth should have left the anterior lip of the surface intact. Cases occurred in which it was hardly possible to diagnose malignant disease from clinical symptoms alone. As to Case 3, it would have added much to the value of the record if the tongue, which had been excised, had been afterwards examined microscopically. If it were a case of epithelioma of the tongue, it was a very unusual one. There might be diseases which the profession looked upon as cancer, but which were not cancerous, as formerly was the case with actinomycosis. At the Middlesex Hospital violet infusion had been tried without any appreciable effect, except in one case, which certainly improved while the agent was given, but the improvement did not continue. The case was one of cancer of the breast, with a sloughing ulcer. The growth diminished in size and the ulcer cleared. Real, although temporary, improvement frequently followed the adoption of any new line of treatment. He considered, however, that there was something in the infusion of violet leaves which did sometimes seem to have a transitory beneficial effect. But the influence, if any, was very slight.

Dr. Norman Moore thought that every discussion connected with cancer was useful. There was no proof that the two former cases were cancerous. He agreed that the presumption should not be made that knowledge of the nature of all growths now termed cancerous was accurate and real. It was possible that certain cases reported as cured cases of cancer might have been distinct from true malignant disease. Microscopic examination alone was not a sufficient criterion. Case 19 hardly seemed a certain case of cancer of the rectum. Cases were not infrequent in which similar signs on palpation through the rectum had been met with which had

recovered. The recurrence at the anus raised suspicions of the accuracy of the diagnosis. The relief of pain, too, was susceptible of other explanation than diminution of the growth. It was remarkable how little pain many cancer patients experienced. The pain might be a mechanical, or consequential, and not an essential, effect of cancer; hence the apparent relief of pain was no evidence that violet infusion had any direct influence on cancer itself. The mental factor in such treatment was very conspicuous. Temporary improvement under careful feeding and nursing was often observed, even in cases of cancer of the œsophagus. The natural course of a case of carcinoma was one of fluctuation, intervals of days occurring in which the patient seemed improving. Hence periods of apparent improvement in the cases recorded in the paper were no evidence of the therapeutic efficacy of the agent employed.

Dr. W. BLAKE thought that in only one case recorded in the paper could the element of faith be eliminated. He had seen a case, believed to be malignant, disappear under hypnotism.

Mr. JEFFERSON FAULDER asked whether the treatment in the cases of cancer of the rectum and uterus had been applied in the form of the palliative measures of douche or lotion. He had seen much improvement under such treatment as rectal antiseptic injections. Referring to Dr. Norman Moore's speech, there were cases of cancer of the bowel which appeared to be instances of local dissemination.

Mr. STEPHEN PAGET asked if Dr. Blake had seen any improvement in external cancer under hypnotism, and Dr. Blake replied that he had not.

Dr. L. S. DUDGEON asked if Dr. Gordon had tried the effect of violet infusion on inflammatory growths. The size of cancerous growths was largely due in many cases to inflammatory changes, more especially those situated in the rectum, mouth, etc.

Dr. WILLIAM GORDON, in reply, expressed his satisfaction that Mr. Gould agreed with his view that violet infusion had some definite influence on malignant growths in certain cases. But, from his own observations, he could not help drawing the conclusion that this influence was greater than Mr. Gould's experience suggested. The effects he had described followed so closely on the giving of the infusion (although nothing else was simultaneously done which could affect the growth), that he could not think otherwise than that these effects were caused by the infusion. Moreover, although a very wide experience like Mr. Gould's might furnish an equal number of spontaneous improvements, he doubted if so small a series of cases as he had presented could have included so many marked improvements unless the treatment had had a considerable effect. Although the nature of the first two cases was open to doubt, and he had therefore not attempted

to found his argument upon them, he still was of opinion that they were cases of cancer. He was fully sensible of the great difficulties surrounding the whole question, and before coming to any conclusion had put to himself all the objections now brought forward by those who had been good enough to discuss his paper. He cordially thanked the Society for allowing him to bring the subject before them.

ACHONDROPLASIA

BY

GUTHRIE RANKIN, M.D., M.R.C.P.,

PHYSICIAN TO THE DREADNOUGHT HOSPITAL AND THE ROYAL WATERLOO HOSPITAL;

AND

ERNEST C. MACKAY, M.B., B.S.,

RESIDENT MEDICAL OFFICER, ROYAL WATERLOO HOSPITAL

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ACHONDROPLASIA, though a rare disease, is of ancient origin. Dr. George Pernet (1) has recently drawn attention to the fact that several Egyptian statues in the British Museum—notably one of the ancient god Pthah—clearly illustrate its characteristic deformities. Charcot and Richer (2) have also shown that many of the dwarfs at the Court of Philip IV who were painted by Velasquez were in all likelihood its victims.

Though apparently uncommon, it probably occurs with considerable frequency, but has failed to attract attention because most cases are either stillborn or survive birth for but a short period. Formerly the survivors were mostly regarded as examples either of cretinism or rickets, and it was not until 1860 that the condition came to be recognised as a definite pathological entity. In that year Müller (3) published a series of careful observations which went to show that the disease is one of primordial bone cartilage, and that the inhibition of the growth of the long bones, which is one of its most prominent

characteristics, is due to a disturbance of the normal arrangement in rows of the proliferating cartilage cells. In 1873 an account was given by Urtel (4) of the macroscopic and microscopic appearances presented by a still-born child, which in all details corresponded with those recorded by Müller a few years before. Earlier observers had related cases which were described under the title of "Congenital Rickets," but which, in the light of more recent knowledge, were undoubtedly examples of achondroplasia. The earliest published record dates back to 1791, when Sömmering (5) gave an account of the post-mortem appearances in a case of fœtal abnormality which he was unable to classify, but the description of which leaves no doubt as to its nature. In 1836 Busch (6) recorded another case of the disease, under the title of "Congenital Rachitis."

Among other writers who have contributed to our knowledge of achondroplasia mention may be made of Schidlowsky (7), Eberth (8), Kirchberg and Marchand (9), Kaufmann (10), Marie (11), Thomson (12), Garrod (13), Turner (14), Nathan (15), Balm and Reid (16). The term "achondroplasia," which was first suggested by Parrot in 1878, is used synonymously with the more clumsy, but also more accurately descriptive, title "chrondrodystrophia fœtalis" proposed at a later date by Kaufmann. Though it is now recognised that achondroplasia is an entirely different disorder from rickets, its close resemblance, in many particulars, to that disorder led to its being variously described as fœtal, intra-uterine, or congenital rachitis. It is also referred to by more than one author as fœtal cretinism. In 1881 Mr. Samuel G. Shattock (17) in describing the features of a fœtal skeleton which he exhibited at a meeting of the Pathological Society, said that the condition was "variously considered as distinct from and identical with that ordinarily known as rickets." Certain specimens—the limb-bones, skull, and brain—presented to the Pathological Society in 1884 by Sir Thomas Barlow (18), obviously belonged to an achondro-

plasic fœtus; and while it is admitted by the exhibitor that the appearances differ so essentially from those found in true rickets that such cases "ought to be relegated to a class of malformations depending on a very early vice of development," yet it is contended that, in accordance with the views of Virchow (20), they probably belong to a "very pronounced fœtal type of cretinism." In the second edition of Liston's 'Elements of Surgery' (19), published in 1840, there is a striking frontispiece which the author refers to in the text as a curious case of congenital rickets, and which by the kind permission of Messrs. Longmans, Green & Co. we are enabled to reproduce. This skeleton exhibits in the most graphic manner the distinctive landmarks of achondroplasia.

The external characteristics of the disease resemble rickets in so many ways that the two conditions may readily be mistaken the one for the other, especially since in children who suffer from achondroplasia there is a liability to the superimposition of rickets at the usual age for the onset of that disorder. The confusion with cretinism is also not surprising, because the physical features which accompany it are somewhat similar to those met with in achondroplasia, especially in infancy, and the few cases of the latter disorder which survive have only recently attracted sufficient attention to enable the discovery to be made that mental deficiency is not one of its accompanying phenomena. The general appearance of an achondroplasic child is characteristic. It is a dwarf, with a large head, pug-shaped nose, short and often bowed limbs, a prominent abdomen, and marked lordosis. The legs are always so short as to be out of proportion to the size of the trunk of the body, and this stunts the figure in an unsymmetrical way which is quite different to other varieties of dwarfism where the trunk and limbs are shortened in relative degree. The arms also are too short, so that the finger-tips never reach to the level of the hips as in the normal individual. The limb-bones, besides being short, are usually bent and thickened. The dis-

proportion between the trunk and extremities is readily demonstrated by measurements such as those which are furnished in the table at the end of this report. In the normal infant the umbilicus marks the central point between the crown of the head and the soles of the feet; whereas in the achondroplasic child the central point of the body is above the umbilicus, sometimes as high as the ensiform cartilage, and this relationship continues throughout life. It has been pointed out by Nathan that the dwarfism is only observed on standing; when the child is in the sitting posture its height is not far short of that of an ordinary person of the same age. The abnormal size of the head is confined to the vault of the cranium, which is unduly developed and out of proportion to the face. It equals, or may even exceed, in its circumferential measurement the length of the body, and there is decided prognathus, which is rendered more pronounced by the marked retraction of the bridge of the nose. This recession of the base of the nose is not due, as in congenital syphilis, to bone disease, but is produced, together with the prognathus and disproportionate vault, by premature synostosis of the basilar and sphenoid bones, giving rise to a deficiency in length of the base of the skull. The lips and eyelids are thickened and, from excess of subcutaneous tissues, there is an exaggeration of the natural dermal folds. The tongue is described by some observers as enlarged and protruding, but this is not a constant feature. The hair on the head and other parts of the body is abundant and healthy, while the skin is well nourished and neither harsh nor scaly. The fingers and toes are short and spatulate. The hands are odd in shape; they are fore-shortened and fat, with fingers of about equal length which taper to their extremities, and at the level of the middle phalangeal joints separate from one another. This separation, as has been pointed out by Dr. Thomson, is specially marked between the middle and ring fingers. The shortening of the long bones of the limbs is apparent at birth, but it becomes an increasingly

notable feature as the child grows. The natural curves of the shortened bones are exaggerated, and they become abnormally thickened transversely. All the epiphyses appear enlarged, and a distinctive rosary is present at the junction of the ribs with their cartilages; but it would seem that in most instances the swelling is caused by changes in the diaphyses, and that the epiphyses are actually altered in a certain proportion of cases only. In contra-distinction to the changes which take place in the cartilage-bones of the base of the skull and of the extremities, the bones that are formed in membrane and those developed from cartilage late in intra-uterine life, such as the clavicle, scapula, sternum, spinal vertebræ, etc., remain unaffected. The contrast between the semi-membranous, bossed condition of the flat bones of the skull in rickets and their normally grown, firmly developed state in achondroplasia is very striking. The mental faculties remain intact, and education is little, if at all, less difficult than in normal children. Other congenital defects not infrequently accompany achondroplasia, the most frequent being a highly vaulted palate, inguinal hernia, epicanthus, and, according to Kassowitz (21), congenital dislocation of the hip. The internal organs are normal, and no pathological changes have, so far, been found in any except the bony tissues.

Nothing is known of the etiology of the disease. Syphilis has been held responsible for this as for many other obscure disorders, but no trustworthy relationship between the two conditions has been proved. Hereditary influence has been arraigned, and consanguinity of the parents has also been accused, but the evidence is too slight to condemn either the one or the other. The sexes would seem to be about equally vulnerable, though statistics indicate a slightly increased prevalence among females.

Of the true pathology of achondroplasia little can be said. The old idea that it was closely related to congenital cretinism will not, as has been already stated, bear the

light of more recent observation. In Nathan's opinion, "the changes in the skeleton and in the subdermal tissues point very distinctly to a constitutional anomaly, which, though not exactly analogous to that of congenital cretinism, nevertheless acts upon the fœtal organism in a similar manner—that is, by disturbing the metabolism in some unknown way." The portion of the base of the skull which Virchow designated the os tribasilare is composed of the basilar process of the occipital bone and the two portions of the body of the sphenoid. In fœtal life these three portions are separated by synchondroses, which at birth are only partially ossified. The synchondrosis intersphenoidalis is ossified at birth or soon after, but the synchondrosis spheno-occipitalis remains patent until about the thirteenth year, and complete synostosis does not occur normally until between the eighteenth and twentieth years. The growth of the base of the skull depends upon the persistence of these synchondroses, premature synostosis producing abnormal shortening. According to Kaufmann premature synostosis of the os tribasilare is not the only factor which is responsible for the peculiar physiognomy of achondroplasia. There may be an accompanying shortening of the ethmoid and nasal bones as well, and also a change from normal in the angle formed at the junction of the basilar process of the occipital bone with the body of the sphenoid. The other bones of the skeleton present a variety of changes. In the long bones these occur primarily in the growing cartilage.

Kaufmann distinguishes three types:

(*a*) *Chondrodystrophia fœtalis hypoplastica*, in which the epiphysis is normal in size and consistency; there is inhibition of row formation and also inhibition of proliferation of cartilage cells.

(*b*) *Chondrodystrophia fœtalis hyperplastica*, in which the epiphysis is definitely enlarged and the consistency is variable; there is inhibition of row formation and increased proliferation of cartilage cells.

(c) *Chondrodystrophia fœtalis malica,* in which the cartilage is softened ; there is inhibition of row formation and the intercellular substance is gelatinous and very vascular.

In all these varieties the common feature is a "more or less complete inhibition of the normal row formation of the proliferating cartilage cells in the preparatory stage of ossification." All three types may be present in one individual, but one usually predominates. Despite this pathological process in the cartilage, calcification proceeds normally, periosteal bone formation is unaltered, and the bones which are formed directly from connective tissue show no abnormality. Urtel first pointed out that, in most cases, the epiphysis and diaphysis become separated by the intervention of a layer of connective tissue emanating from the periosteum. The cause of this periosteal inclusion is not clearly defined, but the most plausible explanation attributes it to an "overgrowth of the epiphysis beyond the peripheral diaphysial line, causing an involution of the periosteum, which subsequently proliferates." This periosteal invasion interferes with growth in the length of the bone, but only completely arrests it when the inclusion is extensive and undergoes ossification.

The prominent differential characteristics of achondroplasia are :

(1) A congenital origin.

(2) An abnormally large vault to the cranium.

(3) Depression of the root of the nose.

(4) Prognathus.

(5) Arrested development of the long bones of the extremities, with exaggeration of their normal curves.

(6) Normal development of the trunk.

(7) Beaded ribs and enlargement at the ends of the long bones from diaphysial and epiphysial changes.

(8) Decentralisation of the mid-point of the body, which is invariably and persistently above, and not below, the umbilicus.

(9) Characteristic wheel-spoke appearance of the hands, described by Marie as the "main-en-trident."

(10) Excess of adipose tissue.

(11) Protuberant abdomen.

(12) Lordosis.

(13) Smooth, pliable skin, with abundance of glossy hair in all the ordinary situations.

(14) Normal mental condition.

(15) A tendency to other congenital malformations, especially to high-arched palate and inguinal hernia.

The question of differential diagnosis is not difficult. The only conditions with which achondroplasia is likely to be confounded are rickets and cretinism. Its similarity to rickets has suggested to certain writers doubts as to whether there may not be some degree of relationship between the two disorders. A consideration of a few of the points in which they differ from one another will, however, show that such a relationship, if it exists, must be a distant one. In rickets the child is born healthy, in achondroplasia the characteristic deformities of the disease are present at birth. In rickets there is no premature synostosis of the os tribasilare as in achondroplasia, whereas the hypertrophic bosses and atrophic craniotabes which characterise the rickety skull are absent in achondroplasia. The stunting of the long bones, the shape of the hands, the lordosis, the sunken nose, and the abnormally high situation of the mid-point of the body are leading features of achondroplasia, just as the contracted chest, deformed ribs, curved spine, and bowed legs are unmistakable indications of rickets. Dentition and speech are not delayed in achondroplasia as they are in rickets, and the well-known constitutional phenomena which accompany the latter are absent in the former disease. The diagnosis from cretinism is obvious if the child survives infancy because, though it appears healthy when born, the cretin soon betrays evidence of mental feebleness, while, among other differentiating features, it may be noted that the thyroid gland is absent or rudimentary, the skin and hair is coarse

and thick, there are fatty pads in the supra-clavicular fossæ, the facial expression is vacant, the head hangs forward on the chest, the habits are dirty, and the patient is frequently destructive and vicious.

There is no full description of achondroplasia to be found in the text-books on medicine, and this record of the disease which is gathered from the desultory papers of writers to whom reference has been given will be found fully verified by the following account of a case recently admitted to the Royal Waterloo Hospital, under Mr. Pendlebury, for the treatment of an abscess on the right temple and subsequently transferred to one of the medical beds.

The boy's name is G. G—, and he is nine years of age. There is nothing remarkable in the family history. The mother is a healthy woman and has had a family of three boys, of whom this is the youngest. The eldest is twelve years of age, and is in all respects normal and active. The second child died of "wasting" when three years old. This child was born after a normal and unassisted labour, but was misshapen at birth. Apart from his deformities, he appears to have been from the first healthy and vigorous. His mother nursed him for one month and thereafter he was reared on milk and barley-water. In due course he was sent to school, and he has shown a degree of intelligence so much above the average for a child of his age and class that he has gained two prizes. He is still in the "infants" department and has reached the second standard, but he has been detained in that grade longer than usual from fear of his being annoyed and teased by other boys of his age on account of his diminutive size. He has never suffered from any serious illness, and is now a bright, engaging, and good-tempered child. Most children who are the subjects of achondroplasia are either prematurely or still born, and of those born alive the majority experience precarious health during infancy, though they may subsequently attain normal vigour. In this patient the period of

infancy was uneventful. The rickety symptoms which apparently complicate his achondroplasic condition may probably be ascribed to the method of his feeding when a baby. The boy is well nourished, and has a healthy, smooth skin.

When the accompanying photographs are looked at, two prominent facts at once arrest attention:

(1) The size and configuration of the head.

(2) The marked asymmetry between the body and the limbs.

The head is abnormally large and disproportionate to the size of the face. The dome of the cranium is high and the occipital region is unduly prominent. The nose is flattened and there is deep retraction of its bridge. The mouth is partially open, and there is pronounced prognathus. The tongue seems somewhat thicker than usual and its tip can just be seen between the open lips. The teeth are carious. The palate is arched and high. The voice is nasal in quality, but this is, in some measure at least, due to the existence of adenoids. Immediately below the right nostril there is a small venous nævus, and there is a rudimentary accessory auricle to the left ear. The trunk is of average size, but presents the following abnormalities: the sternum projects forwards, there is a distinct costal rosary, and a well-defined Harrison's sulcus. These features are suggestive of true rickets and indicate either that we have, in this case, to deal with a double condition, or that the two disorders, though clearly defined from one another, are yet, as has been suggested by some authorities, closely related. The abdomen is fat and protuberant, its prominence being, to a considerable extent, the consequence of the lordosis of the spine. Owing to the shortness of the legs the gait is clumsy; it lacks the rolling character of congenital dislocation of the hips which the curvature of the spine at first hints at, but which is at once negatived by examination of the joints. The umbilicus is near the intercristal line; and the mid-point of the body, when measured in the erect position,

is immediately below the tip of the ensiform cartilage. There is a general increase of subcutaneous fat, and this obesity causes an accentuation of the natural folds of the skin, which is specially noticeable round the ankle-joints. The arms are thick and short, and in extreme extension barely reach the tips of the great trochanters. All the joints are prominent. The shaft of each humerus is short, being only $\frac{5}{8}$ inch longer than the clavicle, and the extremities are large. The bones of the forearm are shortened, and there is a decided increase in the normal curve of the radius.

The hands are remarkably foreshortened, and the fingers taper towards the points and deviate from one another like the spokes of a wheel.

In the legs the features of the arms are reproduced. There is general shortening of the bones, increase in the normal curvatures, and enlargement of the extremities. The longitudinal arch of the foot is destroyed, giving rise to splayness.

The following table of measurements will be found useful for comparison.

	This case.	Normal boy of same age.
Height	2 ft. 11 in.	3 ft. 10 in.
Height sitting	2 ft. 1 in.	2 ft. 2½ in.
Weight	2 st. 3¾ lb.	3 st. 10 lbs.
Circumference of head	20⅜ in.	20¾ in.
Tip of mastoid to tip of mastoid	15 in.	14½ in.
Clavicle	4 in.	4¼ in.
Acromion to external condyle	4⅜ in.	8⅛ in.
Radius	3⅝ in.	6 in.
Olecranon to ulnar spine	4¼ in.	6¼ in.
Anterior superior spine to internal malleolus	7¼ in.	22¼ in.
Internal condyle of tibia to malleolus	5½ in.	9 in.
Chest, full expiration	20½ in.	24¾ in.

We are indebted to Messrs. Watson & Sons, of High Holborn, for the excellent skiagrams with which they have supplied us, which are reproduced here in reduced size.

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Fig. 1.—Reproduced from Liston's 'Elements of Surgery.'

FIG. 2.—G. G—, aged 9. Front view, showing characteristic facies.

FIG. 3.—G. G—, aged 9. Side view, showing lordosis and protuberant abdomen.

FIG. 2.—G. G—, aged 9. Front view, showing characteristic facies.

FIG. 3.—G. G—, aged 9. Side view, showing lordosis and protuberant abdomen.

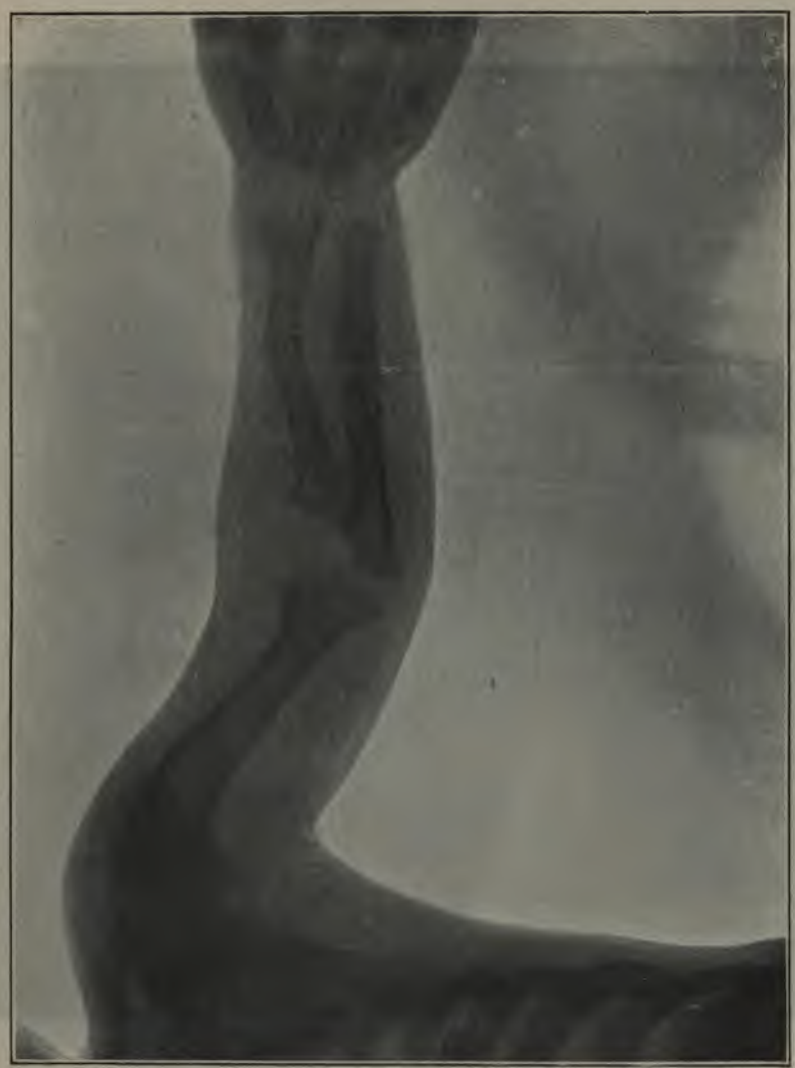

FIG. 4.—Upper limb.

FIG. 5.—"Main-en-trident."

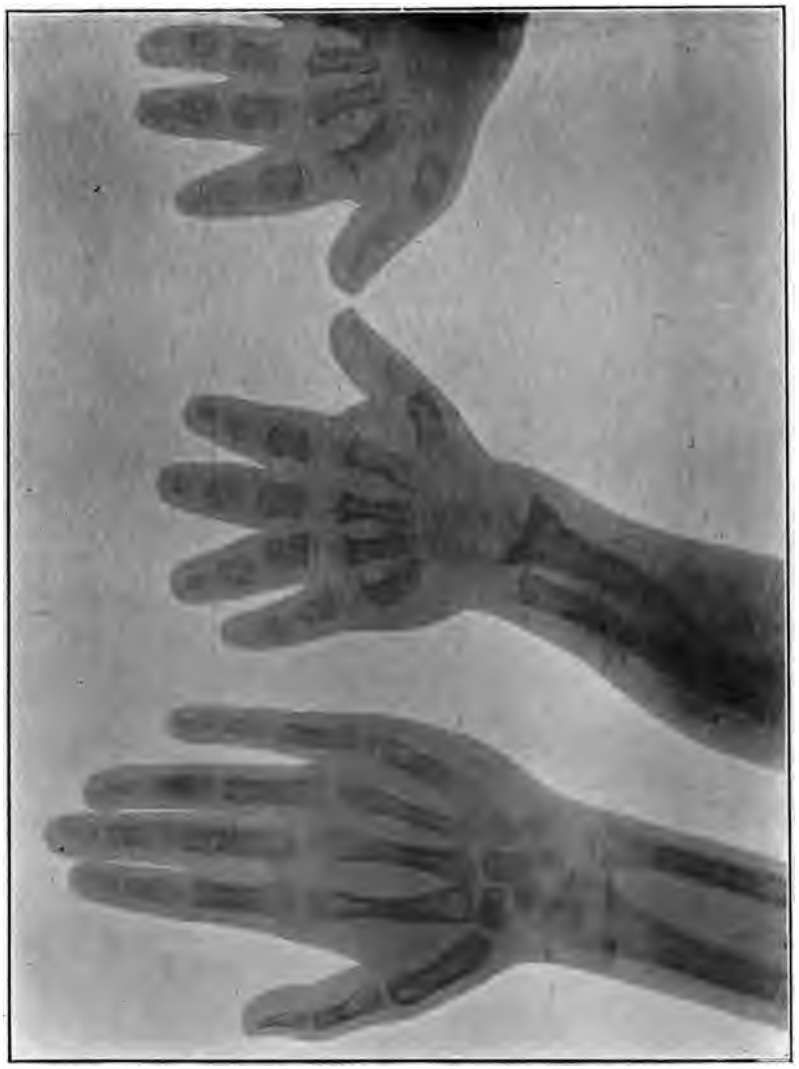

FIG. 6.—The longer hand to the left is that of a normal child of the same age

FIG. 7.—Pelvis and femora.

FIG. 8.—From a normal child of the same age.

FIG. 9.—Side view of leg and foot.

DISCUSSION.

Dr. TOOTH felt some diffidence in criticising so complete a paper, especially as he had not had the opportunity of examining a typical case before. But there was one point which he considered worthy of criticism, namely the application of the term "lordosis" to the condition of the spinal column. The profile photograph and the examination of the patient before the meeting confirmed him in his impression that the spinal column, far from showing the S-curve of lordosis, was peculiarly straight, and this feature was also well shown in the reproduction from Liston's 'Surgery.'

THE PRESIDENT said he agreed with Dr. Tooth that in the boy exhibited to the Society the spine was straight, as it was also shown in the drawing reproduced from Liston's 'Surgery.' He considered that the appearance of lordosis was given partly by the tilting forwards of the pelvis and the backward position of the hip-joints, and partly by the laxity of the abdominal muscles and the consequently protuberant belly. The boy exhibited in a marked degree the conditions characteristic of achondroplasia, to which there seemed to be added some of the symptoms of rickets. He believed the two conditions to be distinct, but there was no reason why a child born with the deformities peculiar to achondroplasia should not subsequently be affected by the change due to rickets, as, for instance, the muscular debility, and the beaded ribs and projecting sternum. From cretinism achondroplasia differed widely, as the authors of the paper had pointed out; and though it might be doubted whether the boy had the exceptional intelligence with which his mother credited him, yet it was obvious that he was by no means stupid, and that his facial expression and behaviour were those of a good-natured, amiable child. Moreover, an instance which the President had seen of achondroplasia reaching adult life confirmed the opinion of the authors that it was not characterised by mental feebleness or vicious habits. As to its causation nothing really was known; the statement of Nathan, that it was due to a constitutional anomaly disturbing the fœtal metabolism in some unknown way, did not carry them any nearer to an explanation. The photographs and skiagrams exhibited were excellently illustrative of a most interesting paper.

Mr. STEPHEN PAGET said that he had been struck by the fact that the nasal bones were loose and had not become united to the subjacent bones. Perhaps, also, they were not fully ossified. He alluded to certain cases of defective or irregular growth of the nasal bones during childhood, which might be compared to the defective or irregular growth of the epiphyses of the long bones.

Dr. RANKIN, in reply to Dr. Tooth, said he was bound to admit that the term "lordosis" was open to criticism. Both the skeleton and the photograph produced showed a straight back, but he thought the evident lordosis was to some extent variable, and that the boy at times showed a more marked degree. He was not aware of any published statistics that showed the relative proportions of survivors to stillborn. In reply to Mr. Paget, he said it was not contended that the depression of the bridge of the nose was due to disease or deformity of the nasal bones themselves; the fault was in the shortness of the base of the skull, which caused the nasal bones to be set more deeply than was usual.

THREE CASES OF MYOCLONUS

BY

FREDERICK TAYLOR, M.D.

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My first patient, Arthur N—, is a labouring man, a chaff-cutter, aged 51, who was first under my notice more than thirty years ago, was under me again as an out-patient in 1881, was in Guy's Hospital for several months in 1902 and 1903, and has again, at my request, presented himself for examination recently. On all three occasions his condition has been, I believe, materially the same. The account here presented is mainly derived from observations made two years ago.

He is a well-nourished and even muscular man, with a pronounced convergent squint and a rather puzzled and stupid expression. As he stands before one it is seen that his head is constantly being jerked by the clonic contractions of the muscles of the neck. The movements are not very extensive; they are partly productive of a backward movement of the occiput, partly of a lateral movement of the head of a quiet shaking character like the movement expressing dissent; that is, the face is displaced right, left, and right in quick succession, then a pause, and the same movement is repeated. The right sternomastoid is rather tense, and certainly contributes to

some of the movements, but there is no pronounced distortion like that which is seen of bad cases of spasmodic torticollis. The movements are much greater when he is standing than when he is lying down, and they are increased by efforts to follow objects with his eyes, and by other forms of voluntary muscular effort.

There is no obvious implication of the muscles of the arm or shoulder, nor of the face; but the speech is sometimes interrupted, or a sound is jerked out at an inappropriate time as if some of the deeper muscles of the neck, throat, or chest were in morbid operation.

As he stands he sways about a little, and this occurs both with his eyes open and with his eyes shut.

When he attempts to walk his gait is ataxic, and he is apparently in constant danger of falling. The degree of ataxia varies; sometimes he is comparatively steady, and he is sometimes even more steady when walking alone than when assisted by another person. Some of the ataxia appears to be due to a sudden rising of the body on one foot, as it were, at an inappropriate time, and though he walks with his legs somewhat apart, there is not so much of the lateral reel of cerebellar ataxy as of a forward and backward pitch.

When he lies on a bed he can move the legs much more steadily; he can raise them from the bed with the most trifling amount of swaying; or, at most, after a time, and when the leg is raised very high the swaying becomes a little more pronounced, but it is never like the ataxia that occurs when he walks, and never like what one sees in bad cases of locomotor ataxia (tabes dorsalis). While still in the recumbent position it is now seen that there is more or less constant clonic contraction of the lumbar and flank muscles. I believe the chief offenders to be the quadrati lumborum; but there are contractions in the lumbar portions of the erectores spinæ and in the lateral muscles, especially the lower fibres of the latissimus dorsi; sometimes the recti abdominis are also involved.

What happens is a sudden contraction of the muscles

concerned, followed by relaxation and then again another contraction; and this is repeated with different degrees of force in the contractions. These contractions are sufficiently powerful to shake the bed on which he lies, or the chair if he is sitting, and differ in no particular from the characteristic contractions which occur in the sternomastoid and other cervical muscles in spasmodic wryneck. They are quite sufficient to account for the slight oscillation in the legs when they are held up from the bed, or out from a chair; and I have never seen any such clonic movements in the thighs, legs, buttocks, upper part of the trunk, or arms. Frequent observations have shown that the muscular contractions are repeated at the rate of about 100 in the minute.

The muscles are generally perfectly normal in their appearance, bulk, and consistence. On one occasion the dynamometer registered 48 kilog. with the left hand and 34 with the right.

The shoulders are rounded, and there is a slight lateral curvature of the spine with a dorsal convexity to the left, and a lumbar convexity to the right: the vertebral border of the left scapula is rather prominent.

There is no modification of the sensory functions. The knee-jerks are slightly excessive, and an abortive ankle clonus can sometimes be obtained. The plantar reflex is flexor in character.

The electrical reactions of his muscles are normal. Their contractions to the Faradic current are always within the limits of the normal, and with the galvanic current K.C.C. is greater than A.C.C. He passes water normally, and the bowels are regular. There is internal strabismus of the right eye: he alternately fixes with either. Elevation of the left eyeball is slightly defective: the pupils contract to light. There is no nystagmus. He has never learnt to write or to read. He picks up small objects rather clumsily with his fingers, but can button his clothes.

His father died some years ago, from Bright's disease; and his mother and a sister are dead, from unknown causes. He has six brothers alive and in good health. He cannot

tell us of any previous illnesses. He never remembers to have walked properly, and he dates the oscillation of the head back to the age of 21, when, he says, it came on suddenly while he was chopping wood, and has never stopped since. I first saw him about this time—that is, in the year 1873 or 1874—but I have no notes of his condition then.

The notes which I made when he came to me as an out-patient in 1881 show that his condition was very similar to that which he now presents; he had then the cervical clonus, "jerking the head slightly backwards" and "frequent jerking contractions of the right erector spinæ" were visible, but I do not seem to have felt the contractions in the deeper spinal and lumbar muscles, nor in the abdominal recti, nor did I then find a satisfactory explanation of the ataxia and staggering gait.

He was in his usual work till 1892, when he had to give it up. He has never had fits nor convulsions.

Since he has been under observation in the ward his condition has remained materially the same so far as the contractions are concerned. One day it was reported by the clinical clerk that on coming to the patient there was no clonus except in the head, and an occasional twitch in the abdominal muscles; but further movements were soon developed. He walks about the ward by himself, always with well-marked ataxia, but never actually falling. He is a very quiet person, rarely speaks unless first addressed, and never reading, because he cannot; but he plays draughts and dominoes with the other patients.

Two other symptoms are frequent—namely, headache and vomiting. The headache is not confined to one spot; it has been both frontal and occipital at the same time, on another occasion "all over"; it varies in severity, and is sometimes absent. The vomiting has sometimes been a daily occurrence for several days, at night or after meals. The vomit on one occasion contained much clear fluid, some undigested food of pink colour and dark bluish-grey mucus. There is no sensation of nausea preceding the vomiting.

He remained in the hospital several months; bromide of potassium and electrical treatment were tried, but without any obvious benefit.

At my request he came to the hospital on Monday, February 27th, 1905. His condition was essentially the same, except that he looked thinner in the face. But the jerky oscillation of the head and the contractions of the lumbar and spinal muscles were the same.

After careful consideration I have come to the conclusion that this case must be classed with those to which the names paramyoclonus and myoclonus have been given.

It is admitted by all writers on this subject that the characters of the disease myoclonus cannot be confined within the limits of the case first described by Friedreich under the name paramyoclonus multiplex.[1] This patient was a man, aged 50, and the symptoms at the time of reporting were of five years' duration. The trouble consisted of sudden lightning-like contractions of the biceps, triceps, supinator longus, vastus externus, vastus internus, and rectus femoris muscles, and less frequent or less violent contractions of the adductores femoris, biceps femoris, and semitendinosus. There were no contractions elsewhere in the thigh, nor in the trunk, nor in the face. These contractions *ceased when he walked*, and were at their worst when he was quiet in bed. If he used one arm only the morbid contractions ceased in the arm in use, and were active in the unused other arm. The knee-jerks were increased. The spasms as well as the cutaneous reflexes and knee-jerk were more pronounced on the right side than the left. The skin sensibility, muscle sense, and vaso-motor and secretory phenomena were normal. They originated in, or at any rate first occurred after, a fright five years previously.

Under Friedreich's care, he was treated by galvanism; and the remarkable point about the case is that the spasms began to lessen after only a few galvanic appli-

[1] Virchow's 'Archiv,' vol. lxxxvi, 1881, p. 421.

cations, and were gone without a trace in several days; the same happened with the increased reflexes, so that these also were entirely normal within four or five weeks of the beginning of treatment.

Friedreich suggested the name paramyoclonus multiplex, the prefix "para" signifying the bilateral occurrence of the disease.

But since the publication of Friedreich's case numerous other instances of morbid muscular contractions or myoclonus have been recorded which resemble Friedreich's in essential features, if differing in less important particulars. The essential feature seems to be the rapid contraction of isolated muscles or parts of muscles in different parts of the body. In some cases the limbs are chiefly affected, in others the muscles of the trunk or face.

The contractions are generally bilateral, but do not necessarily occur at the same time in the corresponding muscles of the two sides, nor equally strongly on the two sides. The muscular contractions do not generally produce any locomotive effect upon the parts which the muscles are designed to move. They occur from 60 to 100 times in the minute, and they are quite irregular in their occurrence, so that three or four contractions may occur rapidly one after the other and then a pause may occur, then an isolated contraction, a pause, and so on. They are generally quieter when the patient is unobserved, and more active when he is subject to the observation of others.

On the other hand, in many cases, as in Friedreich's, voluntary efforts involving the affected parts stopped the contractions, which returned on the cessation of effort.

There is never any combined contraction of muscles usually associated together to produce movements such as these, which are so common in, and are characteristic of, chorea. The muscles themselves are always in good condition, have a normal bulk and nutrition and normal electrical reactions. The disease is little amenable to treatment, and generally persists. Though in Friedreich's case the movements were checked by galvanic treatment, it is on

record that the case relapsed shortly afterwards, and that the movements were present up to the time of the patient's death.

The contractions in my case answer very nearly to the above in all essential particulars. They are quick contractions in isolated muscles, or parts of muscles. Whether they deserve the epithet "lightning-like" (*Blitzähnliche*) which has been applied to so many of the German cases is open to question. Indeed, the resemblance which occurred to my mind was that they were identical with the contractions of spasmodic wryneck: and I was inclined to think my case was one of "spasmodic wryloin," or myoclonus lumbalis, and largely because it recalled to my mind the particulars of the second case which I have to record, in which lumbar contractions, occurring on one side, were associated with contractions and distortion in the neck.

The absence of torsion in the present case, and the implication of cervical, spinal, lumbar, and abdominal muscles, make such a limiting term unsuitable, and bring the case within the conception of a myoclonus multiplex.

Sir William Gowers suggests that the disease may be intermediate between senile chorea and spasmodic torticollis, but I am rather surprised that in so many of the articles I have read on the subject there is so little recognition of a resemblance between the movements of spasmodic wryneck and those of myoclonus multiplex.

I should not apply the word "lightning-like" to the contractions of wryneck. I hesitate to apply it to the contractions here. And if the lightning rapidity of contraction is an essential of myoclonus, then this case may have to stand apart from that disease-group.

In one sense, however, spasmodic wryneck is a myoclonus, equally unintelligible in its onset and pathology with myoclonus multiplex, and differing chiefly in its curious limitation and its moderate locomotive effect.

With regard to the locomotive effect of the contraction, in my case it is present to a slight degree: that is, the head is moved by contractions of cervical muscles, but to

nothing like the degree that one sees in spasmodic wry-neck. The lumbar, spinal, and abdominal contractions do not cause any obvious movements of attached parts, when he is lying down or sitting; but they are, as I believe I shall be able to show, responsible for the ataxic gait which forms the prominent feature of his case.

In their bilateral occurrence, in their frequency, and in their liability to increase under observation, they resemble other cases of myoclonus. It is not so obvious that voluntary effort in the muscles concerned checks the contractions; one cannot attempt to use the back, abdomen, or neck, for a specific purpose in the same way as one can use an arm or leg, but so far as I have seen the contractions are not stopped by effort.

I have said that at first the striking feature in his case is the ataxia which he shows in attempting to walk, and this because the contractions of lumbar, spinal, and trunk muscles cannot be observed when the patient is clothed, or are only visible in the form of the slight movements which affect the head or neck.

The majority of cases of ataxia are explained by lesions of the cord and cerebellum, which are regarded either as interfering so materially with the sensations received from the periphery as to prevent proper co-ordination, or as supplying impulses to the muscles concerned so irregularly as to account for the irregular performance of their functions.

Here it appears to me that the ataxia, both static and locomotor, has at least a partial explanation in the sharp contractions which occur repeatedly in the lumbar muscles, and which are increased both by effort and attention.

The lumbar muscles are essential factors in the act of walking. This is easily made manifest to anyone if he will place his hands deeply in his loins just above the crest of the ilium as he walks. He will feel the alternate contraction and relaxation of the quadrati and other muscles with each step.

When the weight of the body is thrown on to either foot, say the right, the lumbar muscles of the opposite side contract to assist in lifting the pelvis, and with it the whole left limb, which is then posterior, from the ground, and maintain it elevated while it is passed to the front. When, then, the left foot is placed firmly on the ground and the weight of the body is thrown on to *it* (the left foot), the (left) lumbar muscles relax, and those of the now posterior (right) limb contract in turn to raise the foot of that side from the ground.

If this simply smoothly, alternate action is constantly interrupted in a quite irregular fashion by involuntary and violent jerking action, an ataxic gait seems to be necessitated.

Such an interruption is obviously brought about by the contractions of both the lumbar, spinal, and abdominal muscles. When this patient is lying on a bed or sitting in a chair he moves his legs nearly steadily; there is no real disorder or ataxia; there is, at most, a slight tremor on prolonged effort which is equally explained by the shocks of the contracting muscles communicated through the pelvis to the innocent limbs.

This seems to me to constitute a new variety of ataxia in so far as the only muscles of locomotion which are concerned in the disorder or ataxia are the muscles which unite the whole lower limb (pelvis, femur, and tibia) to the trunk, while the muscles of the limb itself appear to be completely exempt.

This possibility accentuates the importance of the loins as elements of locomotion, and we are reminded that the spastic person with almost completely rigid legs and thighs, can still shuffle along by the lifting of each side, which he effects by the muscles concerned.

If this view of his ataxia is correct, it scarcely seems necessary to labour the differential diagnosis from other forms of ataxy in which, as far as I am aware, no such local origin of the ataxia has been suggested or shown to exist. It probably resembles the jerky ataxia of

Friedreich's disease more than anything else; but, as already stated, there is no real ataxy of the legs as such, nor of the arms.

The ataxia is stated by him to have existed as long as he can remember, whereas in Friedreich's ataxia this symptom appears after the patients have learnt to walk normally. The knee-jerks are present here, whereas in Friedreich's disease they are almost invariably absent, and there is no nystagmus.

The family characteristic is also entirely wanting; his father died of Bright's disease; his mother and sister are also dead, but he has six brothers alive and well. And even if other members of the family had been affected this would not exclude the case from the category of myoclonus, since cases of family myoclonus (*die familiäre Myoclonie*) have been described by Unverricht and others in which two or more brothers and sisters have been simultaneously concerned.

Further, there has been no progressive change in the course of more than thirty years in the direction of paralysis or rigidity, or even in the way of extension to other parts.

If, therefore, there is a spinal lesion at the bottom of it of the same nature or operating in the same way, it must be one entirely limited to the centres for the cervical, lumbar, spinal, and abdominal recti muscles.

It is certainly not *ataxic paraplegia*, for there is neither the muscular weakness nor the spastic rigidity which occurs in this disease.

The so-called *hereditary cerebellar ataxy* differs from Friedreich's ataxy, chiefly in the occasional occurrence of Argyll-Robertson pupil and of optic atrophy and the constant exaggeration of the knee-jerk; and it begins generally at a later period of life. Only in regard to the knee-jerk can this disease be said to approach more nearly to my case than does Friedreich's ataxia.

The possibility of *localised cerebellar disease* may perhaps deserve attention for a time. He complains of headaches,

and he not infrequently vomits, and there is some resemblance between the ataxia and that of cerebellar disease; but the headache and vomiting are of comparatively recent occurrence; the headache is often frontal as well as occipital; he has no optic neuritis, nor atrophy, nor nystagmus. Moreover, the duration of the locomotive symptoms during so much of his 49 years as he can remember is very much against a cerebellar lesion, of which also the myoclonus itself has not hitherto been a recognised result.

From *insular sclerosis* it differs in the absence of all the conditions characteristic of the latter; the movements are not intention tremors, but clonic contractions independent of attempts at movement; there is no nystagmus, no scanning speech; there have been no transient or temporary disorders of movement or sensation, but what has once occurred has persisted for years; there is no spasticity of any limb or muscle, there is no optic atrophy. The time-relations of the symptoms are opposed to it, and if it is conceivable that insular sclerosis might cause scattered lesions corresponding only to these symptoms, it must be a very rare coincidence.

My second case is somewhat different, and is briefly as follows:

I first saw Mr. D—, then aged 19, with Mr. Golding-Bird and Dr. C. Stirling, in 1879. Two years previously he had first suffered from cramp in the right hand, which was considered to be writer's cramp. He saw the late Dr. Hilton Fagge, was ordered potassium bromide, and was galvanised. The treatment was continued for two or three months without relief.

The affection spread after a time to the muscles of the neck. When now seen the head was forcibly drawn down towards the right shoulder, and the shoulder was elevated. He was in bed, and was restless, and unable to lie in one or other position. When he attempted to write the movements were irregular or the

result illegible; but there did not occur the more violent spasms which may occur in writer's cramp.

On another occasion the head was thrown strongly backwards, and the neck below the thyroid cartilage was curiously prominent. The muscles of the back of the neck were strongly contracted, and the sternomastoid and trapezius much less so than on previous occasions. The muscles of the forearm did not seem spontaneously affected, but attempts to write failed entirely, as above indicated. He appeared to be in great distress, was very restless, and had to occupy strained positions in order to approach any degree of comfort. He was treated again with galvanism and potassium bromide. On another occasion, six weeks later, I saw him in bed with the head drawn forcibly backwards, the sternomastoid not stretched nor contracted, the head often still, but occasionally moved by clonic convulsions. It could be forced a little forward with much effort, but on relaxing the effort, some backward jerks restored it to the old position.

His face was flushed, and the pulse was 100; and he had been excitable, and even delirious. It was stated that during sleep the head remained retracted and was subject to frequent slight jerks. A month later he was in many ways improved, could bring his head nearly into a line with his body, but only slowly, and then it was generally drawn back again with jerks into the old position. The head was slightly turned, with the face towards the left, the larynx and throat thrown strongly forward. Jerking movements of the right arm and hand were still produced when he used them.

Ten weeks later he walked with the head on one side, the face to the right and the occiput to the left; but as he sat down the muscles relaxed and he leaned his chin comfortably on his hand. On any movement the head was liable to be drawn back rather sharply. The right arm and hand were shaken from time to time by movements, chiefly of extension. The feet and legs were free from movements, and he could walk more than a mile.

On May 31st, 1880, twelve weeks after the last note, he was better, the head more frequently relaxed, and the clonic convulsions less violent. But he had noticed a new feature, namely, that he felt muscular contractions in his left flank or loin. On placing the hand on the left flank the muscles of this region could be felt spasmodically and jerkily contracting like those of the neck, and apparently the muscle chiefly concerned was the quadratus lumborum.

In January, 1882, he was still a sufferer. The most prominent spasms were those of the sternomastoid, of the back of the neck, and of the left flank. The right sternomastoid was obviously much hypertrophied, projecting as a thick curved belly when his head was at its straightest. He was much more satisfied with the position he could attain. Often the head was quite vertical, but always standing more over the left half of the body than the right; but from time to time it was twisted round, chin to the left, or drawn backwards by the powerful action of the posterior cervical muscles. The right shoulder always appeared to be elevated, but no constant muscular action was obvious, and he spoke of it as being cured. The most painful and inconvenient spasm to him was that of the left loin. This drew his left shoulder down to the left ilium, and bent him bow-like, a sort of pleurosthotonos. More closely examined, the superficial abdominal muscles seemed relaxed, and sometimes, but not always, the right erector spinæ was tense. Applying the hand deeply in the left flank, the quadratus lumborum was felt to be constantly contracting. The result of these movements was, that he was constantly writhing about, yielding to, and struggling against, and overcoming the spasms one after another. He could not sit down, as this at once brought on the flank spasm; he took all his meals standing. He could not write any letters with the right hand, but he had learned to write a little with his left.

He was treated by galvanism, potassium bromide, and arsenic. The application of some fixed support was dis-

cussed, but as the instrument maker (the late Mr. Millikin) required him to be perfectly quiet in order to fit it, and as Mr. D— objected to taking an anæsthetic for this purpose the project fell through. I heard some years afterwards that the patient was in much the same condition, but I do not think that I have seen him since the last note.

This case is one to which I have alluded in an article on "Spasmodic Torticollis" in Dr. Gibson's 'Text-book of Medicine,' vol. ii, p. 826, 1901, and it appeared to me at the time that the only explanation of it was that the lesion of wryneck usually confined to the region of the cervical muscles, or at most extending to the sphere of the facials and upper arm muscles, was in this case involving also the lumbar muscles of one side. This was truly a spasmodic wryloin, and in that very wryness, which involves a locomotive effect, differs from the majority of the cases that have been called myoclonus or paramyoclonus multiplex. In its unilateral occurrence also there is a difference; but in the character of the contractions, their persistence, their probable or almost certain independence of any recognised pathological lesions, of nerve, muscle, or central nervous system, they appear to be like those of myoclonus.

It has often occurred to me as a remarkable fact that spasmodic wryneck should be the only disease of its kind, the only disease in which a limited area of the body should suffer from constant and persistent clonic contraction of muscles, not, as we know, limited to one nerve, but limited to the nerves innervating the muscles within the given area —that is, of the neck, face, and upper arm. Such cases are common, but no corresponding affection in the muscles of the limbs or trunk elsewhere is familiarly recognised.

The present case seems to represent the extension of the nerve-lesion to other parts than those commonly involved. But the pathology of these cases is so obscure that their natural alliances must necessarily remain in doubt.

I have recently—October and November, 1904—seen a third case. I was called in consultation by Dr. A. G. Wells,

of West Kensington, to see a lady, Mrs. G—, aged 38, suffering from paralytic symptoms which are in all probability due to cancer of the spine consecutive to a mammary cancer which was removed in 1901. On my first visit I observed the tremulous condition of the arms, and was told that she had had it from her childhood, that she took no notice of it, and that it had no relation to the symptoms for which I was asked to see her. These indeed took up our attention so fully, that I was content to neglect for the time the tremor which she regarded as her own personal property. On a second visit, however, I examined it more closely, and I then found that the tremor was due to muscular contractions of the nature of myoclonus: on grasping the forearms near the elbow repeated sudden shocks of contraction were felt in the muscles arising from the internal condyle. The biceps and triceps muscles were quiet, but of course a transmitted slight shock due to the above-mentioned contractions could be appreciated. The condition was the same on both sides.

I should say that the patient had always been regarded, and was then regarded by her husband, as "nervous," and was said to have been "spoiled" as a girl. But assuming this myoclonus to have been functional, yet genuine, it would have accounted for a good deal of the appearance of nervousness, and perhaps for some of that want of confidence and absence of quiet assurance which are characteristics of many so-called "nervous" people.

The literature of myoclonus is extensive: but few cases have been published in English. Dr. Risien Russell gives a full account of the disorder in the seventh volume of Professor Clifford Allbutt's 'System of Medicine,' published in 1899, with a bibliography of fifty-four references, of which four are American but none are English; he refers, however, to two cases shown by Dr. Ferrier at the Neurological Society in 1897, and the editor mentions a case of local myoclonus in a footnote. Unverricht published a monograph on the subject in 1891.

I do not propose to discuss in any detail the nature of the disease. It is clearly one of the group of so-called functional diseases, in which no coarse organic changes are present, and presents resemblances, so far as the movements are concerned, to chorea, electric chorea, spasmodic wry-neck, convulsive tic, and certain movements in hysteria. Chorea differs in its infective origin, its curability or short duration in fatal cases: the tics and hysteria have a mental factor, which is generally absent in myoclonus.

But undoubtedly myoclonus is a veritable disease—or, rather, the term "myoclonus" must necessarily be given to a great variety of cases of intermittent convulsive contractions directly observation and experience show that such contractions occur.

The word "chorea" has been applied to confessedly different conditions and different forms of muscular contractions.

The word "myoclonus," we may suppose, was coined to distinguish the phenomena arbitrarily from ankle-clonus, in which the contractions, equally forming a myoclonus, or clonus of muscle, are induced by peripheral irritation; and from uræmic convulsions, in which the myoclonus is due to central toxic irritation.

Myoclonus remains as a term which designates any kind of spontaneous, intermittent, sudden or lightning-like, single or multiple, but in all cases inco-ordinated, contractions of muscles and large parts of muscles.

In the infinite variety of phenomena that Nature is capable of producing, both in health and disease, it is easy to see that such condition of contraction will abut closely upon hysteria, chorea, and other perhaps better defined, groups.

With a deeper knowledge of the processes taking place in motor cells, we may be able some day to discriminate all the cases other than by local distinctions derived from the muscles concerned, and we may then find out whether the cause lies always in bulbo-spinal centres, or in cervical centres, or sometimes in one group, at others in the other.

For the present I am inclined to group spasmodic wryneck with myoclonus. I am not clear how we ought to regard fibrillary muscular contractions of certain spinal disorders, and the spontaneous fibrillary contractions which occur so frequently in the palpebral muscles, but also in the limbs in practical health, and which are known to the public as "live blood."

Addendum.

In my first patient, Arthur N—, during January, 1906, fibrillary contractions were observed in the anterior crural muscles, and again in the trapezius and abdominal muscles. My third patient, Mrs. G—, died in October, 1905, of her spinal complaint, without any further development of the myoclonus. There was no post-mortem inspection.

DISCUSSION.

Dr. FARQUHAR BUZZARD alluded to the difficulty found in classifying "myoclonus" as a clinical entity. The cases he had seen corresponded rather with the type described by Friedreich, in which the contractions were "lightning-like" in character. He drew attention to a possible pathology of the condition, arguing that the muscular irritability was at least as important as the condition of the nerve-centres. It might be, as it had been suggested, that the irritability affected the fibrillary substance of the muscle, and not the sarcoplasm, as in Thomsen's disease, with its slow muscular contraction.

Dr. C. E. BEEVOR also said that the cases of myoclonus he had seen did not resemble those described in the earlier part of the paper, which he thought were like spasmodic wryneck, the spasm affecting another part than the neck. In his case the movements were more shock-like, and single muscles contracted which could not be thrown into action singly by the will. As to localisation, it was probable that the lesion was in the spinal cord, inasmuch as movements and not muscles were represented in the cerebral cortex. He alluded to the special importance of differentiating hysterical tremor from myoclonus. In regard to the third case described in the paper, that he considered a case of true paramyoclonus.

Dr. F. E. BATTEN said that he was of opinion that the term "myoclonus" should not be used for all forms of muscular contraction, but that the term should be limited to sudden clonic contraction of single muscles, or parts of muscles. The tics, for example, should be separated from myoclonus. He thought that the classification suggested by Lundborg was that which was most suitable under the present conditions of knowledge: (1) myoclonus, using the term as a symptom indicating a form of myospasm characterised by spontaneous and isolated contraction of individual muscles; (2) myoclonus multiplex; and (3) myoclonus epilepsy. In reply to Sir Dyce Duckworth, he said that he would place Dr. Taylor's first case under heading (1) and regard the myoclonus as a symptom occurring in association with a case of spasmodic tic.

Dr. FREDERICK TAYLOR, in reply, again emphasised the difficulty of strictly limiting the name of "myoclonus" to one group of cases. The case of myoclonus was like that of many other morbid conditions, in which a name was invented for the first recorded case, and subsequently other cases were observed, some like the original, but others differing in minor points sufficiently to make the application of the new term doubtful. Even from the first the clonus of Friedreich's case was different from the clonic convulsion of epilepsy and from ankle-clonus.

OBSERVATIONS ON ENDEMIC GOITRE IN THE CHITRAL AND GILGIT VALLEYS

BY

R. McCARRISON, M.B., CAPTAIN I.M.S.

AGENCY SURGEON, GILGIT, KASHMIR

(COMMUNICATED BY JAMES BERRY)

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HAVING been stationed for the past three years in two districts of Northern India in both of which endemic goitre is extremely common, I have had the opportunity of making the following observations, which I trust may be of use in helping to elucidate the obscure and difficult problem of the causation of this disease.

In recording these observations the two districts of Chitral and Gilgit will be dealt with separately.

(*A*) OBSERVATIONS IN THE CHITRAL VALLEY.

Introductory—Country, Climate, People.

Chitral lies between the parallels of latitude 35° and 37° and meridians of longitude 71° and 74°. The valley through which the Chitral River—of glacial origin—flows is narrow, being not more than one mile broad at any part. It is

bounded on either side by high hills, ranging between 10,000 and 15,000 feet. It runs due north and south. The ranges bounding the valley are intersected at intervals by narrow nullahs, or valleys, each with its mountain stream, derived from the melting of the snows above. At the mouths of these nullahs alluvial fans stretch with a gentle slope towards the river. These alluvial formations, composed as they are of a porous soil, are the only habitable portions of this mountainous country; on them we find villages and a considerable amount of cultivation.

The climate is a temperate one, never excessively hot nor excessively cold. Snow covers the ground during the winter months, usually up to the end of February. The rainfall is small.

The hills in the northern part of the valley are poorly wooded. Fuel is scarce. During the winter months the people live crowded together in small stone-built huts, of which the only ventilation is a hole in the roof. The average cubic space per individual is 200–250 cubic feet. The people are, for the most part, poor. Food is plentiful, comparatively speaking, from July to February, after which the people are obliged to live on the poorest grains, dried fruits, and the green stuffs of the spring. Their food is entirely vegetable. Flesh meat is an article of diet far beyond their means, while salt is a luxury to all except the richest families.

There are certain local beliefs as to the causation of the enlargement of the neck which are not without interest. The people say that their necks increase in size when food is scarce—that is, in the spring months after February; others that the increase takes place in the mulberry season (May, June, July), or when the water turns grey from the presence of fine sediment, or when the snows begin to melt (May, June, July). All local authorities agree as to an observed increase in May, June, and July. Curiously enough, it is only in certain villages that water is believed to cause the disease. The water of the village of Awi (see map), has a goitre-producing reputation, while it is

affirmed that Sanoghar water does not cause the disease. There is a belief in the district that goitre is not so common as it was.

(1) *Prevalence of Goitre.*

Goitre occurs all over the district; no village appears to be entirely free from it. It is, however, most prevalent in certain situations. Four villages are notoriously goitrous, namely Sanoghar, Miragram, Awi, and Morai; their situations are shown on the sketch-map. The percentage of the population suffering from the disease in these villages will be found in Table I. The figures for certain other less goitrous villages are given for the purpose of comparison.

(2) *Water Supply.*

The water supply is in all cases derived from the melting of the snows on the hills above. It comes from the nullah at the mouth of which the village stands, and is the only supply of that village. As a rule the water from the melting snows runs down the nullah as a turbulent mountain stream, taking up what matter it may on its way either in solution or suspension; in other cases it percolates into the soil and appears lower down in the form of a spring, as in the case of Awi. In the summer months the water is invariably grey from the presence of fine sediment. There are no real glaciers in the district under observation; the water is snow water rather than glacier water.

There are no wells in the villages, and, owing to the slope of the ground and the nature of the soil, water does not and cannot stagnate.

The sketch-map indicates the source of supply of the different villages mentioned in Table I. For an analysis of these waters see also Table I.

(3) *Rocks associated with Water Supplies.*

The rocks of the district are everywhere metamorphic; Gneiss and slate form the large proportion of them. Lime-

stone is less common. There are, however, in certain situations large tracts of limestone and sandstone (see diagrammatic sketch-map showing observed outcrop of these formations). Roughly speaking, it may be said that from Chitral to Baranas on the left bank of the river the prevailing rocks are schists and slates. From Baranas to Mastuj the prevailing rocks are limestones and sandstones. If the sketch-map is compared with the figures in Table I, it will be observed that the limestone areas correspond in a very striking manner with the notoriously goitrous villages. The hills behind the village of Morai are largely composed of limestone, and a reference to the table of analysis will show that the water is very markedly affected thereby. It is interesting to note that Morai occupies a more or less isolated position in respect of its goitre-producing powers, the villages on either side of it not being markedly goitrous.

The diagrammatic sketch-map showing the distribution of limestone in Chitral is taken from the 'Geological Magazine,' decade iv, vol. ix, "Fossils from the Hindu-Khoosh," by General MacMahon, F.R.S., F.G.S.

Notes on Table I.

(1) The waters were taken at different seasons of the year. The results are the averages of several analyses.

(2) All the waters were examined at the same time.

(3) The amount of fine sediment varies with the season of the year. In winter the water is perfectly clear. In summer it is grey from the presence of very fine inorganic sediment.

(4) The water of Awi comes from a spring from among limestone rocks; it contains so much lime in solution and suspension that the branches of shrubs which the water touches are coated with lime half an inch thick. The microscopical examination of the sediment of this water shows it to be composed chiefly of inorganic matter in a very fine state of division, with vegetable *débris*. The

McCarrison: Endemic Goitre in Chitral and Gilgit. Plate I.

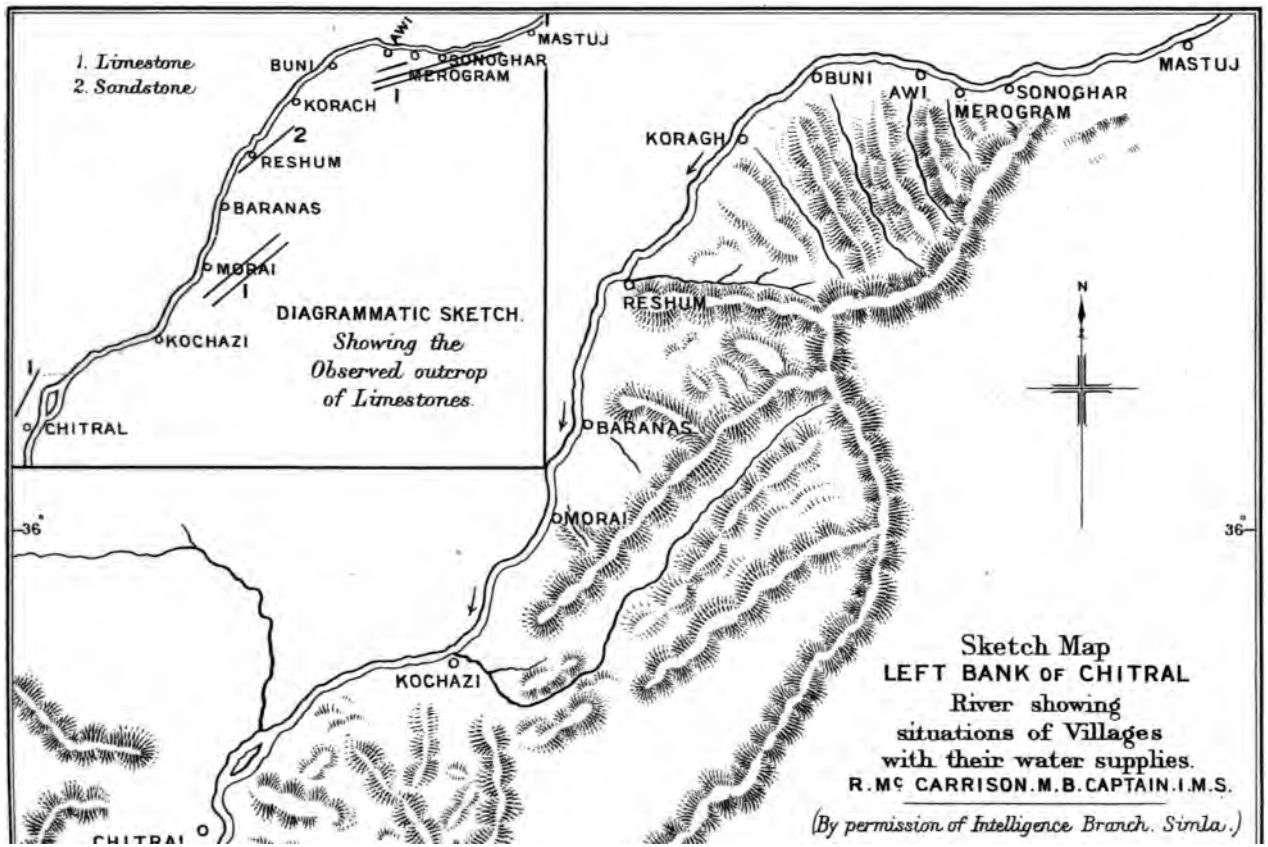


TABLE I.—*Endemic Goitre in the Chitral Valley.*

Village.	Height in feet.	Population.	Percentage goitrous.	Cretins.	Source of H_2O and associated rocks.	Qualitative analysis, grains to gallon.							Remarks.
						Total solids.	Total hardness.	Calcium.	Magnesium.	Iron.	Sulphates.	Chlorides.	
Sanoghar	7650	629	41·8	None seen	Snow water from nullah, limestone, gneiss	8·54	5·2	3·6	Present	Trace	3	*Nil*	Iron can be detected in very concentrated solution only.
Miragram	7350	275	56·5	One seen, two reported	Snow water from nullah, limestone, gneiss	5·68	3·5	3	Trace	Trace	3	Trace	Iron can be detected in very concentrated solution only.
Awi	7000	426	47	4	Spring from among limestone rocks	115·75	35·05	16 and over	Present marked	Trace	3 and over	*Nil*	Iron can be detected in very concentrated solution only; much inorganic matter in suspension.
Morai	5753	196	58	3	Snow water from nullah limestone	45·5	15·75	10	Present	Trace	3 or over	*Nil*	Iron in concentrated solution only; considerable suspended matter and vegetable *débris*.
Reshan	6480	870	10	–	Snow water, red sandstone mainly, and gneiss	11·375	9·1	3–6	Not found	Trace	3	*Nil*	Village stands on red sandstone large amount of suspended matter in H_2O.; iron in concentrated solution.
Buni	6860	1100	15	None seen	Snow water, gneiss, and some limestone	15·4	7·5	3·6	Trace	Not found	3	*Nil*	Considerable amount of suspended matter in H_2O.; inorganic and vegetable.

diatoms eucyonema and navicula are present in considerable numbers.

(5) Iron is found only when the water is evaporated to dryness and the residue re-dissolved in a small quantity of distilled water. It is present in very small amount, and is found equally in practically all the villages given in the table.

(6) The figures are based on those given by Notter and Firth ('Theory and Practice of Hygiene,' 2nd edition, p. 60), and are, of course, only approximately correct.

(4) *Conclusions from the Analysis of notoriously goitrous Waters.*

If the table of analyses is referred to, it will be observed that no definite relationship can be traced between the amount of goitre present in any one village and the amount of any single dissolved ingredient in its water supply. The amount of total solids also and the total hardness of the water seem to bear no relationship whatever to the amount of goitre in the village.

Iron is present in such small quantities that it can hardly be said to have anything to do with the production of the disease.

Nor can any relationship be established between the total amount of matter in suspension in these waters and the amount of goitre present. Awi, for example, contains by far the largest amount of inorganic matter in suspension, yet it is not the most goitrous village in the district. This remark does not, however, apply to suspended matter of any one particular variety, for it is possibly quality, not quantity, which is important.

Also in the Chitral Valley I am unable to bring forward any observation dealing with the amount of organic matter, living or dead, to be found in these waters.

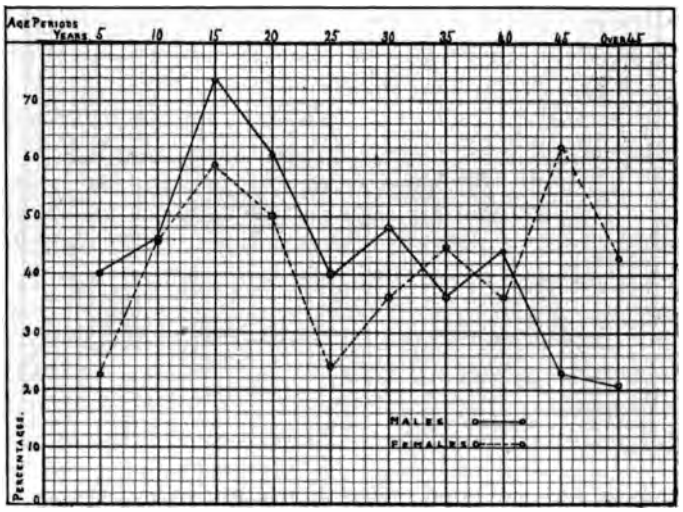
It is interesting to note that in the waters of Awi and Morai, the only two examined microscopically, the diatoms eucyonema and navicula were present in large numbers,

which fact supports the observations of Bircher on this subject.[1]

(5) *Age Incidence of Goitre.*

Two charts are appended to illustrate this observation (Charts I and II). From these it will be seen that goitre is very common in children of all ages. The swelling in children is, as a rule, slight but evident. Children at the breast are not free from the disease, as will be seen from

CHART I.



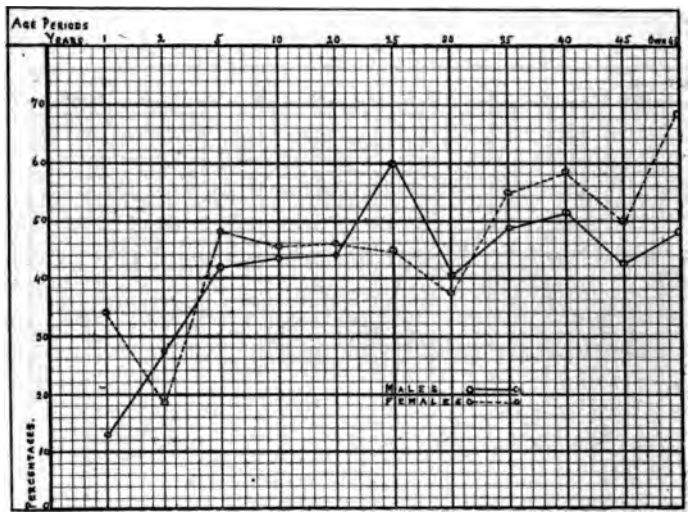
Endemic goitre in Chitral. Chart showing percentages suffering at different age periods in village of Sanoghar. Total population examined, 646; children under 15, 277; adults, 369.

the chart of Awi (Chart II); children are suckled for two years in Chitral. Twenty-three per cent. of children under one year of age who are still being suckled suffer from this disease in the village of Awi. In Miragram the percentage figure is even higher than this, reaching 61·5. In Miragram, of five female children under twelve months, four have thyroids larger than normal, while of eight male children

[1] 'The Thyroid Gland,' Berry, 1901, p. 66.

four have the gland enlarged. The mothers have in all cases been the subjects of the disease, and frequently the fathers also. What proportion of these cases is congenital, what acquired, it is difficult to determine. The fact of the high percentage of children suffering from the disease in these villages is one of great interest, and will be referred to later when these charts are compared with a similar chart for Gilgit.

CHART II.



Endemic goitre in Chitral. Chart showing percentages suffering at different age periods in village of Awi. There are no children in village, either male or female, between the ages 10 and 15 years. Total population examined, 426; children under 15, 269; adults, 157.

Other points of interest will be observed in these charts. In Sanoghar, for example, the marked rise in both males and females at the age of fifteen may bear some relation to sexual activity.

(6) *Length of Residence necessary in which to acquire the Disease.*

Seventeen individuals (two Europeans and fifteen Hin-

dustanis) resided in Sanoghar for four months; of these three, or 18 per cent., showed an increase in the size of the thyroid gland. In one case the swelling was a unilateral one about the size of a walnut. Although the fact that the swelling was a unilateral one (right-sided) detracts from the value, from an etiological point of view, of the case, still, it is worth recording. The swelling made its appearance after one month's residence in the village; the sufferer was then put on filtered water for two months, but no diminution in size having taken place, he, of his own accord, took only boiled water for the remaining month. He was certain the swelling had not increased in size, but was equally so that it had not diminished.

In the other two cases, who drank the ordinary water of the village during the whole period of their residence in Sanoghar, the gland was uniformly enlarged. The swelling was just sufficient to cause discomfort in wearing shirts, the necks of which had previously fitted well.

These men were all natives of the plains of India, who did not come from a goitrous area. They were strong, young, healthy individuals, non-commissioned officers engaged in the instruction of local levies. They lived in tents during the four months, and were not intimately associated in their daily life—sleeping, eating, etc.—with the natives of the country, a fact which points strongly to the water of Sanoghar as the vehicle of infection.[1]

In this connection also it is interesting to note that 32 per cent. of male children under one year of age of the villages of Sanoghar, Awi, and Miragram, taken together, have enlarged thyroids. These may, of course, be all congenital, but it is reasonable to suppose that some are acquired.

[1] Since this paper was written I have been informed by my friend Capt. O'Grady that during this summer (1905) two out of his ten "instructors" (young natives from the plains of India) have developed goitre after a residence of two and a half months at Sanoghar. The goitres disappeared after treatment with thyroid tabloids.

(7) *Variations in Size of a Goitre caused by leaving the District in which it was acquired.*

Symmetrical goitres diminish in size, except in old cases—that is to say, in cases of individuals past the prime of life—when the sufferer leaves the area where the disease was acquired. They again increase in size on his return to that area. This rule would appear to apply, speaking generally, even when the sufferer goes to another goitrous district and before he has had time to come under the new influence for any length of time. Of twenty young men all having enlarged thyroids who came from a different valley, also goitrous, to reside at Sanoghar, sixteen were found to have the thyroid gland diminished in size after a residence of two months, as determined by measurements, while four had the gland increased in size. Though the method of examination by measurement is subject to many errors of technique, still, the results are, I think, worth recording.

The natives of all the districts where I have made observations on goitre are well aware of this fact regarding the diminution in size of a symmetrical goitre which takes place when the sufferer leaves the area where the disease was acquired; it was first brought to my notice in the Kangra Valley (Punjab).

(8) *Experiments bearing on the Influence of boiling and filtering Waters supposed to be capable of causing the Disease (carried out in the Autumn and Winter of* 1903–1904).

(1) In the village of Awi two dogs were tied up in a house in which all the inhabitants were sufferers from the disease. The two dogs were fed alike—that is, on bread made from the flour of the country. To one boiled water was given, to the other the ordinary water of the Awi spring. The dogs were selected for me and tied up by my assistant

Khan Sahib Pir Bakhsh, in charge of the Mastuj Dispensary, on whose judgment I can rely. After fourteen days I visited Awi. The dog which was drinking only boiled water was unaffected and remained so for two months, when the experiment ceased. The other dog, drinking the water of the Awi spring, had a swelling of the thyroid as large as a new-born baby's fist. It was a uniform swelling. The gland diminished in size when I brought the dog for observation to Drosh. This experiment was carried out in the months of August and September, 1903, when the water was still turbid.

(2) This experiment was repeated in the same house on two other dogs, but with negative results. The duration of the experiment was again two months.

(3) A like experiment was carried out in the villages of Sanoghar, Miragram, and Maroi and continued for two months, but with negative results in all three cases.

(4) I have referred to the cases of the Hindustanis who developed goitre after having resided in Sanoghar for four months. In one of these, who developed a unilateral swelling of the gland, filtered water only was used for two months and afterwards boiled water for one month. The swelling did not increase in size neither did it diminish.

There is nothing in the results of these experiments which affords much help in determining the influence of boiling the water supposed to cause goitre. The first experiment suggests that boiling is beneficial, but it is just possible that it may not have been through the medium of water that the disease was acquired. The number of dogs experimented on also is too small to allow any conclusions to be drawn from the result of the experiments. In the case of the man it is regrettable that the swelling, being unilateral, was not of such a nature as to afford much help.

Conclusions from the foregoing Observations.

(1) It would seem that water is the chief vehicle by means of which this disease is conveyed.

(2) There is no evidence to prove that goitre is caused by any of the following dissolved ingredients in the water: total solids, total hardness, magnesium, lime, iron.

(3) The disease can, by susceptible individuals, be rapidly acquired in a highly goitrous locality.

(4) There is a marked association of this disease with limestone rocks.

(*B*) Observations in Gilgit and Nagar.

Gilgit lies between the parallels of latitude 35° and 37° and meridians of longitude 74° and 75°. It is only, however, with Gilgit proper, the capital of the district, and not with the whole of this district, that these observations deal. Gilgit is situated on an alluvial fan on the right bank of the Gilgit River—a tributary of the Indus. This fan is roughly ten square miles in extent and has a gentle slope from its apex, in the nullah from which it derives its water supply, to the river. On this extensive fan eight villages are situated; collectively these are known as Gilgit. The remarks which I have made as to the climate and people of Chitral apply equally to Gilgit. The valley runs east and west. The height of the fan above sea level is 5105 feet.

(1) *Water Supply.*

Appended is a rough diagrammatic sketch which shows clearly the water supply of the different villages of the Gilgit fan.

The water comes from a single source and is conveyed to the different villages in open kūls, or channels. From the diagram it will be observed that there are two main channels, an upper (2) and a lower (1). The upper channel has no villages on its banks till it joins the lower kūl, at the village of Majinpharri, marked (3). All these seven villages are situated on the banks of this lower Kūl, or are supplied by lesser channels branching from it. Each village in this way receives the drainings of the village or

McCarrison: Endemic Goitre in Chitral and Gilgit. Plate II.

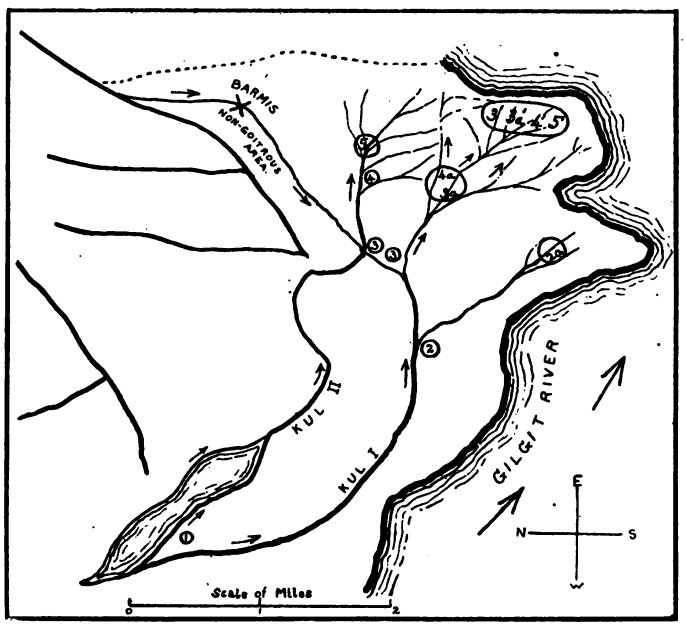
Lent by Mr. John Murray.

From Col. Durand's "Making of a Frontier," 1900.

GILGIT VALLEY: WESTERN END.

villages above it, till at the last village, Kashrote, the drinking water has been polluted by the six villages above.

The water in these open channels not only supplies the inhabitants with drinking water, but it irrigates their extensive crops, serves as an open sewer, is used for the cleansing of their bodies, household utensils, and wearing



Diagrammatic sketch of Gilgit water supply. 1, Basin; 2, Umphris; 2*a*, Damyal; 3, Maginpharri; 4 and 5, Kyk; 3*a*, 4*a*, Sonyar; 3′, 3*a*′, 4′, 5′, Kashrote.

apparel. It can readily be imagined, therefore, that considerable organic impurities find their way down to the lower villages; yet, being fed as these channels are by a purer supply, little organic impurity can be detected by qualitative tests.

The water is, during the winter months, at its source clear and sparkling, but at the village of Kashrote (see diagrammatic sketch of water supply and plate of "Gilgit Valley: Western End") invariably grey from the presence of fine sediment and impurities derived from the villages

and lands irrigated by it. During the summer months when the snows are melting it is, of course, much worse.

If the sketch of the Gilgit water supply is referred to, it will be observed that a spring (the Barmis spring) joins the supply already described at (3), Majinpharri. This spring does not produce goitre; it is the supply of all the European residents and their servants; there is also a small village on its banks, amongst the inhabitants of which there is no single case of the disease. It is a very pure water, springs from among rocks, and I have been unable to trace any case of the disease due to the drinking of its water. This is a point of very considerable importance, showing as it does that the other water supply is the vehicle by means of which goitre is produced in the inhabitants of Gilgit. The analysis of this water of Barmis will be found in the table of analyses of Gilgit waters (Table III).

(2) *Associated Rocks.*

A considerable outcrop of limestone occurs in the nullah from which Gilgit derives its water supply.

(3) *Prevalence of Goitre in the Villages of Gilgit.*

In considering this point the villages are dealt with in order, from that highest on the water supply to that lowest (see sketch of water supply). The figures are given in the following table:

TABLE II.

Village.	Population.	Houses.	Infected houses.	Per cent. of infected houses.	Per cent. of persons infected in infected houses.	Per cent. of total population goitrous.
(1) Basin . .	93	15	9	60	21·2	11·8
(2) Umpharis .	385	66	42	63·6	28·3	20
(3) Damyal .	181	30	20	66·6	30·3	18·8
(4) Majunpharri	718	108	68	63·2	24·2	20
(5, 6) Kyk .	229	33	23	71·5	30	26·9
(7) Sonyar .	458	63	52	82·5	30	24·5
(8) Kashrote .	128	24	21	87	36	45·6

McCarrison: Endemic Goitre in Chitral and Gilgit. Plate III.

Lent by Mr. John Murray.] [*From Col. Durand's "Making of a Frontier," 1900.*

THE GILGIT VALLEY FROM THE EAST.

From this table it is seen that:

(1) The percentage of infected houses goes on steadily increasing from Basin to Kashrote.

(2) The percentage of infected individuals in these infected houses also shows a steady increase towards Kashrote.

(3) The percentage of the total population suffering from the disease shows also a steady increase towards Kashrote.

(4) Although the increase in the percentage of infected houses and of infected individuals in these houses is a steady one, this increase is not observed between Umphiris and Maginpharri. This may be accounted for by the facts that at Maginpharri (see sketch of water supply) the main supply is joined by the purer supply from kūl 2, which has no village on its banks, and is, therefore, freer from pollution than kūl 1, and, perhaps, also to the fact that it is here also that the Barmis spring—a water which is known not to produce goitre—joins the main channel. The volume of water from the Barmis spring is not great, but it may possibly have a slight influence in diluting the more or less polluted waters of the main channel.

(5) It will be observed that at Damyal and Sonyar a slight fall occurs in the percentage of the total population suffering from goitre as compared with the village above. This is due to the fact that these two villages are an exception to the general rule that females suffer more than males, a rule which holds good for the other six villages under observation. The percentage of adult males suffering from goitre in Damyal is 30·5, while of females it is only 21. In Sonyar the percentage of males suffering is 43·5, while of females it is 29.

Although this steady increase in the percentage cases of goitre is observed to occur, the increase is confined entirely to individuals over the age of fifteen years. It is not observed in children, so much so that were children under fifteen years removed from the calculation, the increase would appear more regular and striking. This is a point of very considerable interest and possibly importance.

It appears to me also noteworthy that although 45·6 per cent. of the total population in Kashrote are sufferers from the disease, 13 per cent. of the houses in the village should be entirely free from it, when it is remembered that it is by means of the water that the disease is conveyed. One would almost expect to find that there would be at least one individual in every house a sufferer, were the disease caused by such means as dissolved ingredients, or even by such mechanical means as inorganic matter in suspension.

TABLE III.—*Analyses of Gilgit Waters.*

	Total solids, parts per 100,000.	Total hardness, grs. to gal.	Calcium, grs. to gal.	Magnes., grs. to gal.	Iron, grs. to gal.	Sulphates, grs. to gal.	Chlorides, grs. to gal.	Free, NH^3.	Organic matter.	Other metals, lead, copper, zinc.
Gilgit supply	30 21 grs. to gal.	7·143	6	Trace	Trace	3	*Nil*	*Nil*	See Note 2	*Nil*
Barmis supply	19 13·3 grs. to gal.	9	8–10	Trace	Trace	3 or over	*Nil*	*Nil*	*Nil*	*Nil*

Notes on Table of Analyses.

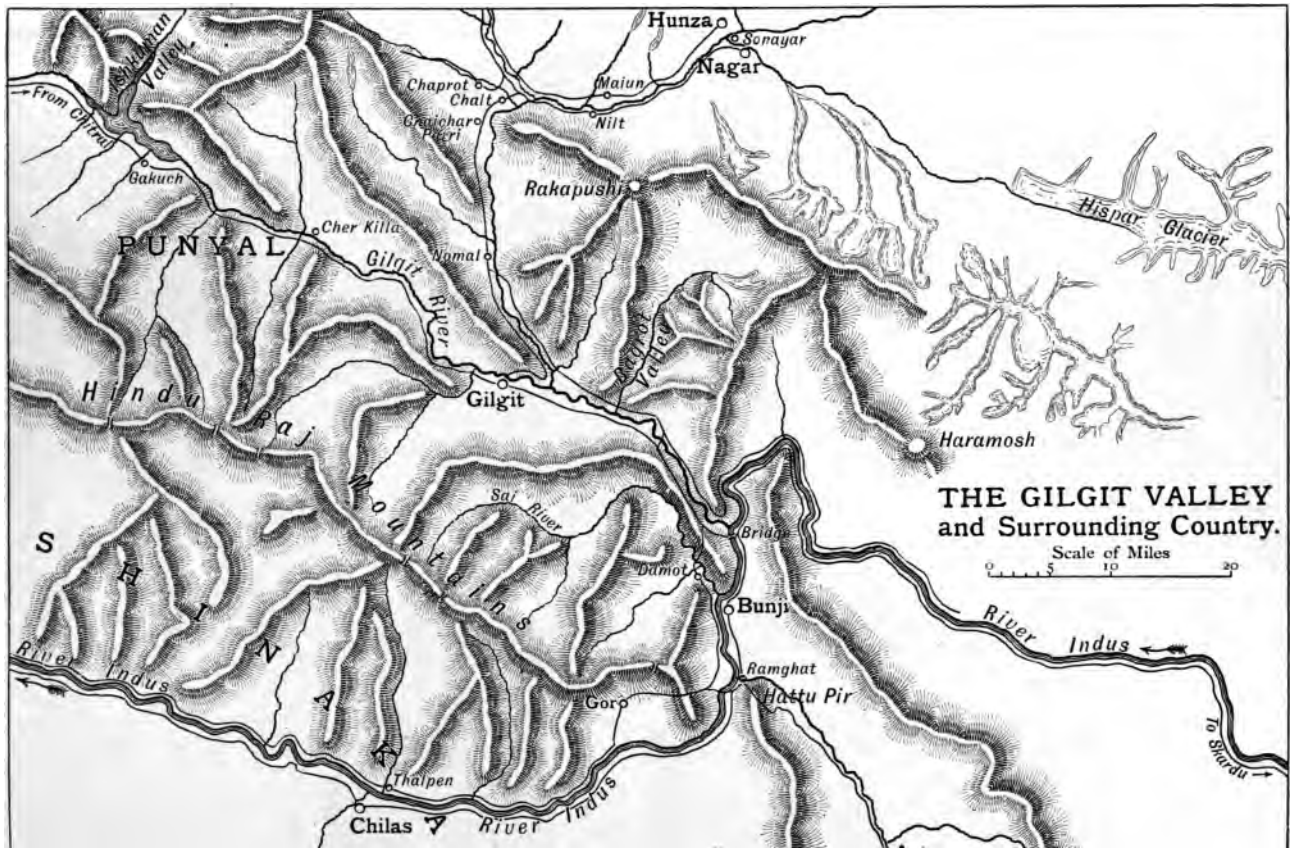
(1) Iron is found only in concentrated solution.

(2) In the water of Kashrote a faint coloration is observed with Nessler's reagent, but organic matter cannot be detected by the gold or silver tests, a fact to be explained, I think, by the continual replacing of the water by a purer supply from above.

(3) As no difference could be observed in any of the waters of the eight villages of Gilgit, it was thought unnecessary to note separately the analysis of the waters of each village.

The analysis of the Barmis spring is given for the purpose of comparison.

McCarrison: Endemic Goitre in Chitral and Gilgit. Plate IV.



(5) *Microscopical Examination of Gilgit Waters.*

By the naked eye one difference between the water of Basin and the same water when it reaches Kashrote is at once noticeable; this is the large amount of suspended matter in the waters lower down the channels as compared with those higher up. The water was examined at different points—

(*a*) At its source (Basin). The water is clear; on standing for twenty-four hours a few flocculi are seen at the bottom of the vessel in which the water is contained. Examination of deposit under a magnification of 600 diameters after decanting shows:

(1) Small amount of mineral matter, sand or clay particles.

(2) Small amount of amorphous matter.

(3) Small amount of vegetable *débris*.

(4) Minute motile organisms, not to be differentiated by the power used.

(5) The flocculi consist of masses of diatoms joined together by some material, the nature of which is not evident; attached to the mass of diatoms are particles of sand and vegetable *débris*. By far the greater proportion of these diatoms are eucyonema. The following were also identified, though in small numbers: Navicula viridis, amphora, cymbella, cocconema, Navicula gracilis, Navicula rhyncocephera, gamphonema, fragilaria, epithemia, pleurosigma. Of these naviculæ are most common after eucyonema. Broadly speaking, therefore, the chief characteristic of the water is the presence of large numbers of diatoms having a boat-shaped or spindle-shaped outline. These organisms were identified by means of the description of them in Whipple's 'Microscopy of Drinking Water.'

(*b*) At its termination (Kashrote). The water is turbid and contains a large amount of sediment on standing. Examined under a magnification of 600 diameters shows:

(1) Large amount of mineral matter in a very fine state of subdivision.

(2) Much vegetable *débris*.

(3) Considerable amount of amorphous matter.

(4) Single flagellated protozoa, etc.

(5) Contains large numbers of diatoms of the varieties mentioned above but chiefly eucyonema. It appeared to me, however, that diatoms were present in fewer numbers than in the water at its source.

(*c*) Barmis spring. The deposit is almost *nil*; on examination a few particles of sand and clay are observed with a very little vegetable *débris*. Diatoms are very few; those observed were: (*a*) Navicula viridis; (*b*) one resembling in shape and size Tabillaria flocculosa, girdle view (Whipple's 'Microscopy of Drinking Water').

The only differences, then, between the waters of Basin and Kashrote, as revealed by a magnification of 600 diameters, are the presence in the latter water of:

(1) Much greater amount of mineral and dead organic matter in suspension, also of amorphous matter in suspension.

(2) Fewer diatoms apparently.

(3) More impurities, owing to pollution.

(6) *Deductions from the above Examinations.*

Having considered now the analysis of the waters of Gilgit and their microscopy, it will be interesting to consider how far these help us in determining what the factors are which are at work in causing this increase in the prevalence of the disease as we approach Kashrote.

There appear to be three possibilities:

(1) An increase in the amount of dissolved ingredient.

(2) An increase in the amount of matter in suspension in the water, organic or inorganic.

(3) An increased pollution of the water and a consequent increase in the numbers of its micro-organisms.

With regard to the first of these the table of analysis

shows that neither total solids, total hardness, calcium, magnesium, or iron, show any increase whatever. These have at one time or another been credited with the production of goître. There is no evidence from these analyses to show that such is the case. The first possibility may, I think, be put out of court.

With regard to the second—namely an increase in the amount of matter in suspension. This matter may be:

(*a*) Organic: (1) dead, (2) living—bacteria, diatoms, other organisms.

(*b*) Inorganic: fine mineral matter.

While it would appear evident that the water became polluted on its way to Kashrote, still, organic matter was not readily detected, as I have already pointed out. As a causal factor of the disease, the fact of the greater impurity of the water may, for the present at least, be put aside. How far it is of importance in favouring the action of the real causal factor is another matter.

There remains, therefore, only suspended matter to be considered; for living organic matter, such as bacteria, diatoms, and other organisms, is "suspended matter." Later I shall return to the final analysis of this subject.

(7) *Experiments dealing with the Influence of boiling and filtering the Gilgit Water* (*February—June*, 1905).

(1) Five puppies, age varying between three and six months, were confined in netted wire pens on land supplied by the Barmis spring. They were fed liberally on Kashrote water; all their food was prepared with it. The puppies were well fed and healthy. This experiment was continued for one hundred and thirty days. Result negative. No enlargement of the gland could be detected.

(2) Five puppies as above were fed on boiled Kashrote water, under precisely similar conditions to those in the first experiment. The result was negative. The experiment lasted one hundred and thirty days.

(3) Five puppies as above were fed on filtered water of

Kashrote for one hundred and five days with negative results.

(4) Five puppies six months old were taken from a house in Kashrote in which 50 per cent. of the inhabitants were goitrous. There was no enlargement of the gland in any of them.

(8) *Experiment having for its Object the Determination of the Capability of suspended Matter in Gilgit Water of causing Goitre* (*February—June*, 1905).

(1) Five young puppies, aged three to six months, were fed on the residue after the filtration of four quarts of Kashrote water. The water was collected daily and was purposely made muddy while it was being collected. The residue after filtration was collected, mixed with milk, and the mixture given to the puppies while still hungry. They were confined in netted wire pens, and were well fed and healthy. The experiment lasted one hundred and five days. The results were negative.

(9) *Age Incidence of Goitre in four of the Villages of Gilgit.*

The appended chart is of considerable interest, contrasting as it does so markedly with the charts of Chitral villages. From it it is found that females suffer somewhat more than do males (Chart III).

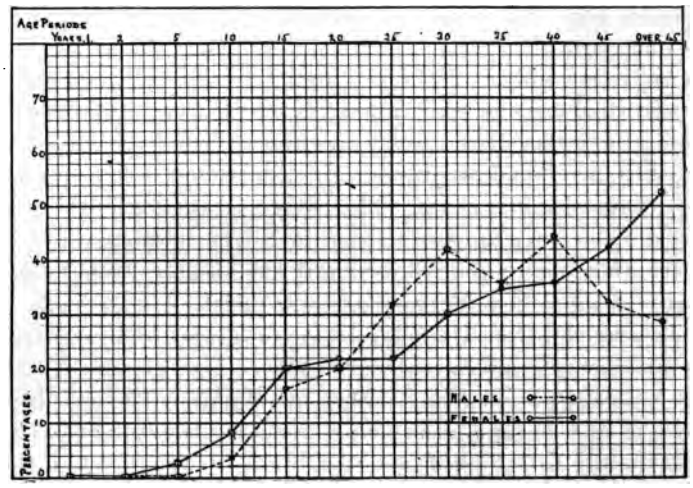
(10) *Goitre in Nagar.*

In the village of Nagar goitre was unknown six years ago. Nagar is a small State situated up one of the many side valleys on the left bank of the Gilgit River. It will be remembered as the scene of a smart frontier rising in 1893. It was after this year that the little State of Nagar began to be opened up; previously, jealous of its independence and at war with its immediate neighbours, it was careful to exclude foreigners. During recent years intercourse with the

outside world has become more free, but still there is a decided prejudice against the settling of foreigners in this little hill State.

Some five years ago certain cases of goitre were introduced from without, and since then the disease has begun to gain a footing. It may be as well to indicate clearly that there can be no doubt about the fact that goitre was

CHART III.



Endemic goitre in Gilgit. Chart showing percentages suffering at different age periods in villages of Majinpharri, Kyk, Sonyar, and Kashrote, taken together. Total population examined, 1533; children under 15, males 375, females 330; adults, males 447, females 381.

quite unknown six years ago. The fact that it has gained a footing in his territory is a matter of very considerable anxiety to the present rajah, and through his help I was enabled to go into the matter with great care. All the important men of the State, the Rajah himself, councillors, priests, etc., assure me that no case of goitre ever originated in Nagar till within the last six years.

There is a family at present at Nagar which consists of nine souls; of these three came from Gilgit some years ago,

all suffering from goitre. Two, the father and the mother, have no goitres; the father came from Gilgit. The remaining four individuals have never been outside Nagar. Three are high-caste Mohammedan girls (16, 15, and 10 years of age), which makes the statement the more likely to be accurate. The fourth individual is a boy aged 12; he has never been outside Nagar. All these four have developed goitre lately, about two years ago. This family live in the same house—that is, the same room—eat out of the same vessels, etc. It is to be observed that these, the first victims, are all young.

Another family consists of a man, his wife, and son, aged 2, and the man's brother, aged 20. The man brought goitre with him from outside five years ago. Two years later his brother developed the disease, though he had not been outside Nagar for five years. The little boy, aged 2, developed the disease one year ago; the wife is free from it.

Another man, aged 23, brought the disease from Gilgit one year ago; it is increasing in size here.

Twelve children, all under 10 years of age, were brought to me having marked enlargements of the gland. There are no other cases of the disease in Nagar. The children were from different houses scattered over the village. The first family to which I referred lives at the head of the spring which supplies the village with drinking water.

(11) *Water Supply of Nagar and spread of Goitre.*

The village supply consists of a spring which comes out of the hills; it is not the only supply of the village. The cases I have referred to all drank from this water. This spring is said to have been in existence from time immemorial; the chemical composition of its water has presumably not altered. The conditions of life of the people are the same. The only added factor in the case is the introduction of the disease from without. That it is spreading there can be no doubt, and that the course of the spread is a typically epidemic one is equally evident. It is easy to

understand why the disease should not have reached Nagar earlier, as it is only within recent years that the communications of Nagar with the outside world have become free.

It appears also evident that it is by means of the spring-water that the disease is now spreading, for the twelve children are residents of that part of Nagar supplied by the spring, and their homes are scattered here and there among the houses of the as yet unaffected inhabitants. Further, the fact that the first family referred to lives at the head of the spring is of importance, and also that no cases of this disease were observed where water from other sources only is drunk—that is, in the distant parts of the village where the nullah water or the river water is used.

It seems likely, therefore, that some poison—goitre-producing in its powers—has been introduced into a water supply which happened to be a suitable one for the conveyance of this disease. For the analysis of the Nagar spring see Table IV.

The cases of the two families mentioned are of very great interest, pointing as they do to the possibility of the disease being capable of spreading by other means than water. It will be remembered that of nine individuals three had the disease and four acquired it in a locality where it was previously unknown. It is possible that it was due to an infection of the water by these three that four other inhabitants of the same house developed the disease, but in that case why should there be such a high percentage of infected individuals in this infected house as compared with other houses in the village? Although the figures in the second family are smaller, it is a no less striking case of the possibility of infection by means other than water.

This case of Nagar can not be explained by any theory which attributes to dissolved ingredients in a water goitre-producing properties; nor can inorganic matters in suspension account for this outbreak, for it cannot be supposed that from causes in the water which have existed from time immemorial a disease should suddenly spring. There is, to my mind, only one explanation—

namely the introduction of an organism into the water supply.

The course of the disease in Nagar is that of a typical infectious disease. Presumably the organism is of slow growth, which may account for the slowness of its spread and for the long-drawn-out nature of an epidemic of this disease. One sees that a series of single cases introduces the epidemic, that the goitre-producing poison requires a suitable soil in which to develop, cases of the disease to originate it, a suitable vehicle in which to spread, and susceptible individuals to acquire it. The fact that the disease requires a calcareous soil is not peculiar. Other diseases of an infectious nature are equally peculiar in their requirements. Malaria flourishes best in marshy districts, where the mosquito, on which it is dependent for its existence as a disease, can live. It is not, therefore, to be wondered at that the micro-organism of goitre—if such there be—requires a calcareous soil to enable it to flourish.

TABLE IV.—*Analysis of Nagar Spring.*

Water.	Total solids, parts per 100,000	Total hardness, grs. to gal.	Calcium, grs. to gal.	Magnes., grs. to gal.	Iron, grs. to gal.	Sulphates, grs. to gal.	Chlorides, grs. to gal.	Suspended matter.
Nagar Spring	168	51·5	16 and over	Very plenti-ful	Trace	3 and over	1	Very slight.

Notes.

(1) Water clear, strong taste of magnesium.

(2) Deposits slight, examination under 600 diameters showed little sand and clay particles, vegetable *débris*, fungi, diatoms apparently absent.

(3) The water is so hard that it is impossible to wash in it. Soup made from it resembles in taste a weak solution of Epsom salts.

Boiled water is never used by the natives of Nagar,

even for culinary purposes. The *sole* food of the people besides fruit is chupatties (flat cakes of unleavened bread baked before an open fire.)

The case of Nagar appears to me to throw a very considerable light on the differences observed in the age incidence curves of the disease in Gilgit and Chitral. From Nagar we learn that when the disease is epidemic the most susceptible individuals are children. Now, although a steady increase in the percentages of goitrous individuals occurred between Basin and Kashrote, children were seen not to participate in this increase. These facts taken together appear to me to justify the belief that the disease is subsiding in Gilgit, and that the factors formerly at work in producing it are ceasing to operate among the indigenous inhabitants. The disease is dying a natural death owing to the fact that the new generation is not readily acquiring it.

Final Conclusions.

There is considerable evidence to show that it is to the increase of a something in the water supply of Gilgit—a something which is capable in its unassisted state of producing 11·8 per cent. of goitre—between the villages of Basin and Kashrote that the increase in the prevalence of goitre in the latter village is due. That this something exists in a state of suspension in the water appears to be fairly evident. It is possibly one of two things, inorganic matter or micro-organisms.

To my mind the balance of evidence is in favour of the view that it is to micro-organisms that the increase is due between Basin and Kashrote, and that micro-organisms are the causal factor in the disease. The most striking case of Nagar can only be explained on this assumption, namely the introduction of a micro-organism into the water supply, and the consequent spread of goitre in a typically epidemic form. Further the fact of the large percentage of goitrous children under one year in Chitral can be explained

in this way without having to conclude that these cases are congenital. It accounts also for such instances of the disease as cannot be traced to a water supply, and admits of the broader view that water, if it is the chief vehicle of infection, is not the only one. It explains readily the instance before us of the increase of the disease between Basin and Kashrote. It explains also the differences in the charts for the villages of Gilgit and Chitral, which to my mind seem to indicate the natural, if slow, end of an epidemic of this disease.

Exophthalmic Goitre.

I have observed no case of this disease in Chitral or Gilgit.

Treatment.

Thyroid extract was used in selected cases and caused very marked and very rapid improvement. The cases require to be symmetrical enlargements of recent development, and the subjects require to be young. The administration of thyroid extract is useless, as far as my experience goes, when the patient is beyond the prime of life, or the swelling of considerable standing, or caused by cystic or tumour growths.

As regards the effect of local applications, the following figures are those of the Mastuj Dispensary, in charge of Khan Sahib Pir Bakhsh. The total cases treated in the years 1900, 1901, and 1902 were 566. He sends me the following results:

Age.	Per cent. cured or improved markedly.
12 years	80 per cent.
12 to 30 „	50 „
30 to 50 „	20 „

The applications used were the red iodine of mercury ointment and liquor epispasticus. Painting the skin over the gland with strong iodine solution is not so satisfactory, but is attended with favourable results. In using external

remedies, to obtain good results it is necessary that the skin be blistered by them.

[I desire to express my indebtedness to my friend Mr. James Berry for the help and advice I derived from him in carrying out these observations and experiments.]

DISCUSSION.

Mr. JAMES BERRY thought that Captain McCarrison was to be congratulated very warmly upon the admirable piece of work that he had been carrying out. He thought it the most valuable contribution to the literature on the causation of goitre that had appeared for many years. Considering the very large extent to which this fell disease, with its accompaniments of physical and mental degeneration (cretinism and deaf mutism), was met with in various parts of the world, it was a matter of much importance to discover the true cause of it. Passing on to the consideration of the paper itself, it was noticeable that the districts in which Captain McCarrison had worked were similar to those in other parts of the world where goitre was most common. If a general review be made of the distribution of goitre over the world's surface, two facts stood prominently forward: first, the association of the disease with mountainous regions; secondly, its relation to limestone and other calcareous rocks. The Himalayas, Alps, Pyrenées, Andes, Cordilleras, and many other mountain chains were all noted haunts of goitre. On a smaller scale in our own country the occurrence of goitre was especially noticeable in many hilly districts. In the valleys on either side of the great Pennine range of hills, in the Cotswolds, and in the Mendips he had himself seen many cases of goitre. The speaker showed the Society a map of France published by the French Commission on Goitre. This showed clearly that the ten departments of France in which goitre was most prevalent were almost without exception those in which great mountain chains were found (Savoie, Haute Savoie, Hautes Alpes, Hautes Pyrenées, Vosges, Basses Alpes, Ariège, Aisne, Jura, and Alpes Maritimes). The close association of endemic goitre with calcareous rocks would not fail to strike any observer who had personally visited many districts in which goitre was common. In this respect the author's observations confirmed those of other investigators. McClelland's researches, carried out in another part of the Himalayas some seventy years ago, had illustrated this association in a very striking manner. Speaking of the inhabitants of the Valley of Shore (Kumaon) he had shown that 50 per cent. of those who lived upon and drank water from limestone rock were afflicted with the disease, while only 1¼ per cent. of those inhabiting the same neighbourhood, but living upon clay slate, were affected by it. In those parts of the same mountains where limestone did not exist he found the disease so rare that only one in five hundred of the population was subject to it. In most parts of the world it was noticeable that villages situated upon primitive rocks, such as granite, gneiss, schists, etc., were, as a rule, exempt from the disease. In dealing with the difficult

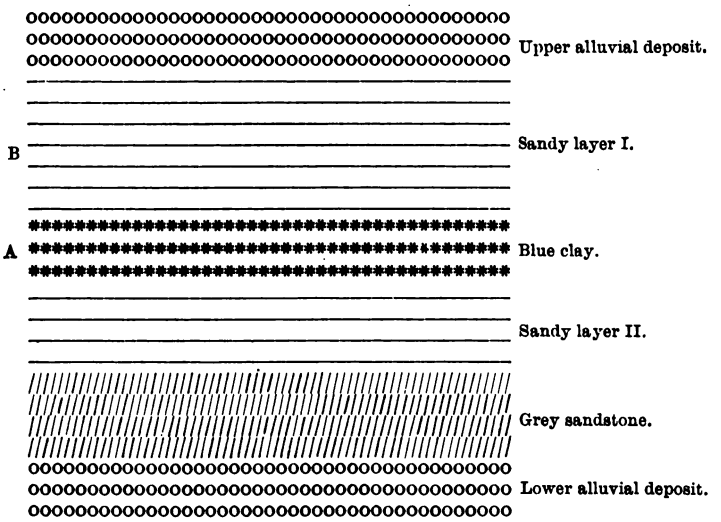
problem of the relation of geology to goitre in our own country, it was well to bear in mind the glacial drift which covered so large a portion of England. Conclusions drawn from consideration of ordinary geological maps upon which the drift was not marked might easily be fallacious. He mentioned a district in Cheshire in which he had found much goitre upon rocks not usually associated with the disease. Examination had shown, however, that the water supply of the district was derived from wells in the glacial drift, which itself was, in places, as much as 60 feet thick. He was glad to see that Captain McCarrison had accepted the view that the essential cause of endemic goitre was something contained in the drinking water, and that he had not thought it worth while to discuss any of the numerous other theories that were to be found in many text-books. He thought that the water theory of goitre was the only one that could be seriously maintained. He considered that the truth of the "water" theory of goitre had been proved up to the hilt. He cited various instances in which it was clear that the goitre-producing poison was to be found in the water, and referred also to the monumental works of St. Lager, Baillarger, and others, for abundance of evidence on this point. What it was exactly in the water that caused goitre was a vexed question, and one that had not as yet been satisfactorily answered. It was a noticeable fact that goitre was infinitely more common in country places, in villages, hamlets, and isolated houses than in large towns. He thought the explanation lay in the fact that large towns as a rule had public supplies of drinking water which, as a rule, was of good quality. A noticeable feature of goitrous villages in Savoy and on both the Swiss and Italian sides of the Alps that he had personally visited was that the inhabitants derived their water supply in so many cases from streams containing mineral matter in suspension. The grey nature of the waters at Gilgit alluded to by Captain McCarrison agreed exactly with that of so many goitrous waters that had come under his own observation in different parts of Europe. He cited the well-known goitre-producing water of the Buthier stream near Aosta, and showed a specimen of "grey" water taken by himself from this very stream. It was often said that goitre-producing water did not contain any undue amount of suspended matter. He was inclined, however, to the belief that most, if not all, goitrous waters were liable to contain much suspended matter, especially after rainfall, although such waters might be quite clear at other times. Captain McCarrison's remark about the supposed greater prevalence of goitre during the spring and early summer when the waters were grey—that was, contained more mineral matter in suspension—agreed in the main with the observations of Nivet in Auvergne. Referring to the old theory about goitre being due to snow water and to glacier water, he

thought that there was some truth in them. But care should be taken to distinguish between the water running on the surface of a glacier and that which came from under its snout. The former was a singularly pure water which could not possibly cause goitre. The latter was always a turbid, muddy stream containing a large amount of mineral matter in a very fine state of subdivision, just such a water that might be expected to produce goitre were anyone to drink it. Time did not permit of any review of the various theories which attributed goitre to various substances dissolved in the water. Lime and magnesia certainly could not be held responsible, and although much could be urged in favour of the iron theory, yet he was unable to accept it as a satisfactory solution of the problem of the causation of goitre. He agreed, therefore, with Captain McCarrison in believing that the goitre-producing poison existed in suspension in the water, and not in solution. Whether this poison in suspension was inorganic or organic was a point upon which he had not been able as yet to come to a definite conclusion. The author's observations with regard to Nagar and the supposed infectivity of goitre were most interesting. In the absence of further confirmation he preferred at present to keep an open mind on the subject. The observations seemed to him to be opposed to the facts observed in numerous other goitrous districts where evidences in favour of infectivity seemed to be quite wanting. Captain McCarrison had pointed to the village of Kashrote, where the water seemed most exposed to organic pollution, as one in which the disease was most prevalent. But this village was also that in which the greyness of the water, due presumably to mineral matter in suspension, was also most marked. Believing as he did that mineral matter in suspension was the cause of goitre, he was of opinion that the best way of preventing the occurrence of the disease was in the formation, whenever practicable, of subsidence tanks or reservoirs. He cited an instance where this had been done on a large scale by Nature herself, namely in the Lake of Geneva. The turbulent goitre-producing waters of the upper Rhone Valley discharged themselves into the upper end of the lake. The same water, having deposited practically all its suspended matter in the lake, issued at the lower end as a beautiful clear stream, which had been shown to have lost its goitre-producing properties. He was glad to be able to inform the Society that Captain McCarrison was continuing his investigations at Gilgit, and that he had recently written to him (the speaker) to say that he had obtained some fresh evidence which he thought tended to confirm the organic theory of the disease. He hoped that further information on the subject would be laid before the Society in the near future.

Dr. Louis E. Stevenson remarked on the difficulty of the

investigation of endemic goitre, evidenced by the large number of theories of its causation advanced from time to time, upwards of forty of which could be enumerated. He had no doubt whatever that the poison, whatever its nature, resided in the drinking water, the evidence for which was overwhelming. St. Lager related that the youths of a certain township in France, in order to escape military service, drank copiously for several months before the arrival of the recruiting authorities from a well whose waters were notoriously goitrigenous. Their thyroids rapidly enlarged, and by this means they escaped service. Other instances were mentioned by the speaker. One fact that was indisputable in the etiology of the disease was that the poison was absent from rain water. In Constantinople and Venice, where rain water was used, there was no goitre. The same fact obtained in Holland and the lower parts of Belgium. Cardinal Billiet had put on record a remarkable instance of goitre-incidence occurring in the village of Puiset, in Planaise. Here he found seventeen families more or less afflicted with goitre and cretinism from using the spring water of the country; one family was absolutely healthy, and used rain water only. Moreover, it was a well-known fact that a recent goitre would generally quickly subside if the patient drank rain water only. Many instances of this had occurred in the speaker's practice. The goitre poison accordingly was due to some deleterious substance formed in, or produced by, contact with the soil, and Dr. Stevenson wished that evening to speak briefly on two theories, both of which he considered important: (1) the bacillary, (2) the metallic salts theory. With regard to (1), which was originally advanced by the two Italian physicians Lustig and Carle, as the result of their work in the Vale of Aosta, these observers found a bacillus which they called the *Bacillus liquefaciens* in all the goitrigenous waters examined by them, but they did not prove that the elimination of the microbes took away from the waters their poisonous action, and all their experiments on animals by inoculation of or feeding with cultures of the bacilli were negative. The principal facts in favour of the bacillary theory were: (*a*) That filtration diminished and boiling actually destroyed the goitrigenous principle in water; (*b*) that the further a goitrigenous water flowed from its source the less dangerous did it become, eventually losing all poisonous action, exposure to oxygen and sunlight gradually killing the bacilli. This fact seemed to Dr. Stevenson to explain the greater frequency of goitre in mountainous regions. (*c*) That epidemics of goitre had occurred in the world's history. (*d*) That goitre occurred principally in rural districts, where little care was exercised in choosing a water supply; where, in many instances, surface water was used, or subsoil water which had merely percolated through a porous superficial stratum, and was recovered for domestic

use by the agency of the village pump. (Dr. Stevenson gave instances.) (*e*) The frequency of goitre on the limestones of the carboniferous series, because these rocks were freely jointed, and it might be that water from the surface percolated rapidly along these joints, carrying bacteria in its train. (*f*) The goitrigenous action of many river waters, a great part of whose volume was derived from surface drainage. Against the bacillary theory might be mentioned the fact that constitutional disturbance—*e. g.* fever, etc.—never seemed to have been recorded in epidemics of the disease, and also the negative results of inoculation, etc., with bacilli. In the speaker's opinion these bacilli existed in the water only in consequence of some chemical environment, and were probably a species of soil bacteria. With regard to (2) the metallic salts theory, with special reference to the action of iron-pyrites (FeS_2) and the results of its decomposition, one curious fact was that St. Lager found iron-pyrites in some of the Vale of Aosta waters examined by Lustig and Carle. Dr. Stevenson proposed to take a series of geological formation on which goitre was found, and see what evidence they afforded in favour of this theory. (*a*) *Ordovician shales:* Goitre was prevalent on this series in Cumberland, in the counties of Roxburgh, Selkirk, and Dumfries, also in Westmoreland. Examination of these shales showed abundance of iron-pyrites, occurring in its usual cubical form, and also in the rhombic form, as Marcasite. Instances were mentioned of goitre on these rocks from personal observation of the speaker. (*b*) *Marls:* Dr. Stevenson accounted for goitre on the Permian and Triassic series of rocks by the fact that in many instances he could mention the water came in contact with marls, many of which he had examined. He found them variegated, consisting of bands of various hues—yellow, blue, and black—besides the ordinary red variety. The yellow bands were due to limonite produced by the decomposition of iron-pyrites, while the blue and black bands owed their colour to the presence of iron-pyrites in dissemination. A very striking instance of a blue marl which produced goitre was given as occurring in the department of the Isère in the so-called region of the Molasse. The stratum marked A was one of these blue marls containing iron-pyrites in dissemination. In every village in this department where the drinking water came in contact with this marl goitre was endemic. In some localities where the superimposed sandy layer B was rendered hard and compact by calcareous cement, and where the water was held up at a higher level, there was no goitre. In England the blue marls of the Gault and Wealden series were goitrigenous—*e. g.* at Horsham, where goitre existed, and where these blue marls abounded. In France the marls corresponding to the above—the *marnes aptiennes* and the *marnes néocomiennes inférieures*—were found by St. Lager to be eminently goitrigenous, and both these



formations contained a superabundance of iron bisulphide. Other instances could be mentioned. (*c*) *Carboniferous limestones:* Lime itself was not a cause of goitre, as large tracts of country in many lands, situated on the jurassic limestones, for instance, were free from goitre. Dr. Stevenson had carefully examined the lower strata of the carboniferous series and found a large amount of iron-pyrites in the limestones, sandstones, and shales of this geological horizon. (*d*) *Chalk and chalk-marl:* Goitre on these formations was not frequent, but according to Mr. James Berry was found fairly uniformly. So far as the speaker was aware the only accidental mineral on these formations, with the exception of glauconite and disseminated lime phosphate, was iron-pyrites occurring as marcasite, which was a very readily decomposable form of iron-pyrites. Dr. Stevenson concluded by reading a paragraph from a book entitled 'Among the Himalayas,' by Surgeon-Major Waddell, I.M.S., in which the author stated his belief that the goitre he saw in a locality near the Jelep Pass was due to iron contained in the drinking water.

Captain J. H. Hugo, I.M.S., said that in Nepaul goitre was present in goats, horses, and pigs, and among the poor inhabitants, but not among the rich. The poor obtained their water from the rivers, but mostly from shallow wells, whilst the rich obtained their water from the hills, the water being stored in a reservoir outside the residential parts and brought in pipes to the city; the Nepal Resident's escort (who were composed of Hindus specially enlisted in India) drank the pipe water and did not suffer from goitre. No sediment was, as a rule, perceptible

in the surface water drunk by the poorer people. Many Tibetans came for treatment, and they considered themselves benefited by biniodide of mercury ointment. In Bakloh, a hill station where Gurkha troops were stationed, goitre was prevalent in the rainy season when surface turbid water was drunk, and disappeared afterwards. In Central India goitre was very rare. He had only seen two cases, in two women, both of whom came from the mountains. If goitre were due to a micro-organism, it would have been expected to follow the trade routes, which it did not. It was probably due to some suspended matter in the water. Mica suspended in the water was often met with in goitrous districts.

Mr. W. W. CLARIDGE said that goitre was practically unknown in West Africa except at one place called Mampon, in Ashanti, and at this point there was an outcrop of limestone. The water which supplied this district came out of the limestone. Ironstone was also present, but in much less amount than in other districts which were not goitrous. About 10 per cent. of the inhabitants of Mampon were affected with goitre. It seemed certain that the disease did not follow trade routes, for, although Mampon was on the direct trade route, goitre never occurred at other places on the route. He agreed with the former speakers that goitre never occurred when rain water was used.

A REVIEW OF 282 OPERATIONS FOR NON-MALIGNANT DISEASES OF THE STOMACH

BY

B. G. A. MOYNIHAN, M.S., F.R.C.S.,

LEEDS

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In the following paper I have analysed and summarised all the cases of non-malignant diseases of the stomach upon which I had operated up to the end of the year 1905.

The cases are arranged in four groups:

Class 1.—Perforating ulcer of the stomach and duodenum.

Class 2.—Cases operated upon urgently on account of hæmorrhage.

Class 3.—Chronic ulcer in its various forms; dilatation of the stomach.

Class 4.—Hour-glass stomach.

In all there have been 282 operations, with a total mortality of 18, equivalent to 6·3 per cent. The results are briefly:

Class 1,	24 cases,	9 deaths.	
„ 2,	27 „	4	„
„ 3,	209 „	2	„
„ 4,	22 „	3	„

Class 1.—Summary of Cases of Acute Perforati Ulcer.

Since April 30th, 1897, the date of my first operati I have had under my care 24 cases of perforating ul of the stomach or duodenum. In these 24 cases th were 15 recoveries (62·6 per cent.) and 9 deaths (3 per cent.). There were 8 cases in which a duodenal ul had perforated; 16 in which a gastric ulcer had p forated. In the first 10 cases there were 6 deaths; the last 14 cases there were 3 deaths. My first c recovered, and then in succession were 5 unsuccess cases.

The ages of the patients varied from 17 to 44. T cases of gastric ulcer were 16 in number; of these, were males, aged 23 and 24, 14 females of average 27 The cases of duodenal ulcer were 8 in number; of the 4 were males, aged 44, 25, 22, and 40; 4 females, ag 17, 17, 25, and 38.

An inquiry into the previous history of the cases gastric ulcer showed that in every case, with one exce tion—and in that no record of inquiry is made—t patient had suffered from symptoms referable to the ul for periods varying from a few weeks to several yea Of the 12 patients, 6 had been under treatment within year of the occurrence of the perforation for indigestic vomiting, or hæmatemesis and anæmia.

Similarly, in every case of perforated duodenal ul previous symptoms had been observed, and 4 of the patients had recently been under treatment. In none these cases had relief been afforded.

In the majority of the patients there had been increase in the severity of the symptoms during the f days preceding perforation. In 3 of the 24 cases, ho ever, a distinct and notable exacerbation is recorded.

The time which elapsed between the perforation of t

ulcer and operation varied from three hours and fifty minutes to four days.

In 5 cases the perforation was of the type described as "subacute." In one of these the operation was performed twenty-eight hours after the rupture; the patient died in the fourth week from a subphrenic abscess, with multiple points of suppuration within the abdomen. The second case was one of perforated duodenal ulcer, which was operated upon four days after perforation. The ulcer was closed, and a second posterior incision was made to afford drainage; the patient recovered. In the third case the ulcer was on the posterior surface and a collection had formed in the lesser sac. The general peritoneum was also involved. An anterior and a posterior incision were made in this case also. Recovery was most satisfactory.

The perforation was found on the anterior surface of the stomach in 14 cases, on the posterior surface in 2 cases. As a rule, the perforation was near the lesser curvature and towards the cardiac end. In one case two perforations were found, both on the anterior surface, about $1\frac{1}{2}$ inches apart. In one case the perforation occurred in the centre of an hour-glass stomach, and gastroplasty had to be performed. In the 8 duodenal cases the perforation was found in the first portion seven times, in the beginning of the second portion once. In 4 cases in the whole series gastro-enterostomy was performed immediately after the closure of the perforation; in 3 cases recovery followed. In 2 cases the subsequent performance of gastro-enterostomy has been necessary owing to the persistence of symptoms due to the ulcer, or to the scar left by it. There were, therefore, 15 cases of recovery from the perforation; in 3 of these gastro-enterostomy had been performed, and in 1 gastroplasty for an hour-glass stomach; of the remaining 12, 2 suffered to such a degree as to necessitate the performance of a second operation, gastro-enterostomy.

In the 24 cases there were, therefore, 7 in which an

immediate or a subsequent operation for the adjustment of the mechanical conditions of the stomach was necessary. Two of the patients suffered from perforation while they were waiting for operation—one in the hospital, one in a nursing home. Both had complained for years of indigestion and vomiting; both had dilated and hypertrophied stomachs for which a gastro-enterostomy was to be performed. In one a duodenal ulcer, in the other an ulcer at the pylorus, had perforated. In both the ulcer was closed and an immediate gastro-enterostomy performed. Both patients recovered and remained perfectly well. In one case the patient was operated upon for the perforation of a gastric ulcer and was apparently doing well. On the 13th day she was suddenly seized with acute pain, became collapsed, and died in an hour and a half. At the post-mortem a perforation of a duodenal ulcer was found.

The cause of death in 7 cases was shock, or a want of recovery from the condition of collapse, often profound, which existed before operation. In one case death resulted from empyema, and in one case from subphrenic abscess and suppuration at several points within the abdomen.

None of the patients who recovered suffered from any chest affection, from parotitis, thrombosis of veins, or from hæmatemesis during the time they were under treatment after the operation. In one of the fatal cases there was slight hæmatemesis. The question of drainage was determined entirely by the needs of each individual case. There was no rule in one's mind that had necessarily to be followed; what seemed appropriate to the case was adopted. As a rule, the earlier the case was seen, the less was the need for drainage. Lavage was adopted only when the case was of long duration. When the stomach was found distended with fluids, it was emptied by the stomach-tube during the operation. In all, drainage of the abdomen was adopted in 12 cases; in 2 of these posterior drainage as well as anterior was necessary, and in 2 others suprapubic drainage as well as drainage through the wound was established.

Class 2.—Summary of Cases in which Acute Hæmorrhage was the Immediate Cause of Operation.

In 27 cases the hæmorrhage was sufficiently severe to demand operation for its relief alone. In two of these no ulcer was found at the operation; in 14 gastric ulcers alone were found, four cases having multiple ulcers. The ulcers were situated near the pylorus in 10 cases and on the lesser curvature in 3.

In 7 cases duodenal ulcers alone were found, involving the first part in all but one.

In 4 cases duodenal and gastric ulcers were observed.

Hæmatemesis only (without melæna) occurred in 8 cases, 6 having gastric ulcer, 1 gastric and duodenal ulcers; in 1 no ulcer was found.

Melæna alone occurred in 4 cases, all of which had duodenal ulcers only.

Hæmatemesis and melæna together were noted in 15 cases, 8 having gastric ulcer, 3 duodenal ulcer, 3 gastric and duodenal ulcers; there was 1 in which no ulcer could be found.

	Hæmatemesis.	Melæna.	Both.
G.	6	—	8
D.	—	4	3
G. and D.	1	—	3

Mortality.—Four of these cases died—1 in four hours from the operation, at which no ulcer could be found; at the autopsy dilated gastric veins and cirrhosis of liver were demonstrated; 1 on the eleventh day from pneumonia; 1 on the eighteenth day from exhaustion; and 1 in three weeks from gradual exhaustion (in this case the blood contained only 47 per cent. hæmoglobin before operation).

In no case did hæmorrhage recur after operation. In 3 of the cases which recovered the estimation of hæmoglobin before operation was only 18 per cent.

Operative treatment.—In every case posterior gastro-jejunostomy was performed.

In 21 this was the only treatment adopted; 2 of these died.

Gastro-jejunostomy was combined with excision of the ulcer in 2 cases, 1 of which died.

Gastro-jejunostomy with infolding of the ulcer was done twice.

Gastro-jejunostomy with infolding of a pyloric ulcer in 1 case, which died.

Gastro-jejunostomy with infolding of the pylorus and of the ulcer was performed once; the patient recovered.

Class 3.

The following is an analysis of all cases of simple disease of the stomach (except those operated upon urgently for perforation and those operated upon for hour-glass stomach) upon which I have operated.

In this series there are 236 operations upon 230 patients.

In the 230 patients, evidence of an ulcer was found in 213.

Gastric ulcer alone was found in 150 cases
Duodenal „ „ 33 „
Both gastric and duodenal ulcer in 30 „

Of the remaining 17 cases, 5 suffered from pyloric obstruction due to chronic cholecystitis, no ulcer could be found in 11 (in 1 of these the symptoms were due to gastroptosis) and in 1 the condition found is not recorded.

As regards the symptoms in 230 cases, vomiting is noted as having occurred in the course of the patient's illness in 183 cases. Hæmatemesis had been noticed in 79 patients (including the case of cirrhosis and uraemia); in 21 of these the hæmatemesis was associated with melæna, while melæna only was noticed in 10 cases. Peristaltic waves were visible before operation in 52 cases. A palpable tumour was recognised before operation in 7 cases, it was due to inflammatory lump at the pylorus in 4 cases, to inflammatory lump at the pylorus and duodenum in 1 case, to inflammatory lump in the duodenum and chronic

pancreatitis in 1 case, and to universal gastric adhesions in 1 case.

Tetany of varying degree was noted in 10 cases; in all there was gastrectasis.

Coldness, lividity, and cyanosis occurred in 15 cases, and I feel sure in several others where I omitted to make a note of it.

As regards the relation between pain and gastric adhesions; in the histories of 189 patients pain is definitely noted; in 100 of these gastric or duodenal adhesions were found at operation. The pain is described as "severe" in 32 cases, 19 of which had adhesions. The occurrence of a former perforation is suggested, either by the previous history, or by the conditions found at operation, in 8 cases of this series. In 2 the perforation was "acute" in 6 probably "subacute."

Gastric Ulcer alone (70·4 *per cent. of the total number of Ulcers*).

Of the 150 cases where gastric ulcers alone were found, 101 (67·3 per cent.) were in females and 49 (32·7 per cent.) in males.

In 105 cases but a single ulcer could be found; in 67 of these it was at or near the pylorus, in 7 on the anterior wall, in 14 on the posterior wall, in 5 near the cardia, while the majority of the remainder were on the lesser curvature.

In 45 cases the ulcers were multiple, the greater number of these being at or near the pylorus, and on the posterior surface. In addition to these, 18 cases of single ulcer showed adhesions elsewhere. These adhesions undoubtedly marked the site of former ulcers, so that the proportion of single to multiple ulcers in the stomach only was 87 to 63.

The incidence of pain after food in 51 cases was:

Within 1 hour	51 per cent.
1 to 2 hours	27·5 „
2 to 3 hours	13·7 „
"Hunger pain"	7·8 „

Duodenal Ulcer alone (15·5 *per cent. of the total number of Ulcers*).

Of the 33 cases where duodenal ulcer alone was found, 24 (72·7 per cent.) were in males and 9 (27·3 per cent.) in females. In the 27 cases where the position of the ulcer was noted, it was situated in the first part in 23 (85·2 per cent.) ; in the second part in 2 (7·4 per cent.), while in 2 cases 2 ulcers were found, 1 in the first and one in the second part.

The incidence of pain after food in 21 cases was:

Within 1 hour . . .	14·3 per cent.
1 to 2 hours . . .	33·3 „
2 to 3 hours . . .	23·8 „
"Hunger pain" . .	23·8 „
At night	4·8 „

Duodenal and Gastric Ulcer (14·1 *per cent. of the total number of Ulcers*).

Duodenal combined with gastric ulcers were found at operation in 30 cases, 18 (60 per cent.) being males, and 12 (40 per cent.) being females.

In 21 cases only one ulcer was found in the stomach, generally situated near the pylorus ; in 7 cases more than one gastric ulcer was found.

The situation of the duodenal ulcer was noted in 22 cases, the first part of the duodenum was involved in 19 cases.

The incidence of pain after food in 15 cases was:

Within 1 hour . . .	40 per cent.
1 to 2 hours . . .	13·3 „
2 to 3 hours . . .	13·3 „
" Hunger pain . . .	26·7 „
At night	6·7 „

Comparison of Gastric with Duodenal Ulcer.

	Male.	Female.	
Gastric . . .	32·7	67·3	= 100
Duodenal . .	66·7	33·3	= 100

Hæmorrhage.—The relation between duodenal ulcer and hæmorrhage is brought out in the following table:

	Hæmatemesis.	Melæna.	Both.	No hæmorrhage.
Of all cases of peptic ulcer (213)	56	10	21	126
Of all cases of duodenal ulcer	7	8	12	36

Operative treatment.

Gastro-enterostomy	Gastro-jejunostomy	Posterior	Suture	216	Total 224
			Murphy's button	1	
		Anterior	Laplace forceps	3	
			Simple	1	
			Roux's	1	
	Gastro-duodenostomy Finney			2	
Pyloroplasty				3	
Enteroplasty				1	
Gastro-enteroplasty				1	
Entero-anastomosis	anastomosis in Y (Roux)			1	
	lateral anastomosis			4	
Excision of ulcer alone				1	
Exploratory				1	
			Total	236	

Three of the earliest gastro-jejunostomies were done with the aid of Laplace forceps; two of these were quite satisfactory, but the third relapsed after a month of relief, and when a second gastro-jejunostomy with Murphy's button was done the former opening was found almost completely closed.

Gastro-enteroplasty.—In two cases gastro-enterostomy had previously been performed by other surgeons, and after temporary relief the symptoms had returned. In one case the anastomosis had been made by Murphy's button, and I found the opening almost closed. In the other case the anastomosis, made by the aid of a bone bobbin, had contracted, and was found high up on the posterior surface, near the lesser curvature. In the former case the opening was considerably enlarged and the union of the stomach and the jejunum effected by suture; in the latter the opening was brought down to the greater curva-

ture by a plastic operation, and, owing to the existence of a long jejunal loop, a Roux's operation also was performed, the loop being divided, the distal end closed, and the proximal implanted into the side of the jejunum about three inches below the anastomosis.

Entero-anastomosis was necessary in four cases, owing to the constant vomiting of bile after the operation. Two of these cases occurred early in my experience, before I adopted the "short-loop" operation. The result in both was most satisfactory. In the third case anterior gastro-enterostomy had been performed by another surgeon. Persistent vomiting followed. I re-opened the abdomen and found the distal limb of the jejunum constricted by numerous adhesions. These were divided, and entero-anastomosis also performed. The result was good. In the fourth case a hernia of the small intestine through the opening in the mesocolon was found. Benefit was derived from reduction of the hernia, closure of the opening round the anastomosis, and entero-anastomosis.

Roux's operation was performed twice, once in the case mentioned above, and once in a patient upon whom I had previously operated for a perforating ulcer. Owing to the extremely dense and very numerous adhesions I could not obtain access to the posterior surface of the stomach, and I therefore performed Roux's operation to the anterior surface.

Enteroplasty was performed in one case. Gastro-enterostomy had been performed two years before by another surgeon, but after some months of relief vomiting returned and became serious at the last. On re-opening the abdomen I found the distal limb of the jejunum constricted by a very tight band, the division of which did not relieve the place of constriction in the bowel where a stricture had developed.

Two of the three cases of pyloroplasty required a subsequent gastro-jejunostomy, which effected a cure; one case relapsed five weeks, the other three years and six months, after the pyloroplasty.

Other secondary operations in this series are :

One gastro-jejunostomy by suture for return of symptoms two years after posterior gastro-jejunostomy by Murphy's button ; the former opening was found to be almost closed. One gastro-jejunostomy for return of symptoms after gastro-plasty for hour-glass stomach.

In six cases cholecystotomy and in one case cholecystectomy were performed at the same time as gastro-jejunostomy. In one case ovariotomy was simultaneously performed and in one case radical cure of a right inguinal hernia. In one case, gastric ulceration following the drinking of corrosive acid, the gastro-jejunostomy was supplemented by Senn's gastrostomy, and a catheter inserted through the latter opening was directed into the efferent jejunal limb, through which the patient was fed for two and a half weeks.

In one case perforation of a pyloric ulcer occurred three hours before the time arranged for operation. In a second case a perforation of a duodenal ulcer occurred about two hours before operation. At both operations the perforation was closed and gastro-enterostomy performed.

Hæmatemesis occurred shortly after gastro-jejunostomy in two early cases, but in neither was it lasting.

Obstruction due to hernia of the small gut through the opening in the mesocolon occurred thrice ; in two cases the hernia was reduced, once by myself, once by another surgeon ; the third patient died.

Stitch abscesses were noted three times, followed in one case by slight bulging at the site of the wound.

Parotitis delayed recovery in two cases, one gastro-jejunostomy and one gastro-duodenostomy.

Mortality.—In the 209 operations for chronic ulcer, apart from acute hæmorrhage, there were two deaths. In this series there have been 111 cases in succession without a death.

In this complete series all the cases were cured with the exception of 15 ; of these 10 may be classed as "relieved," and 5 as "no better."

Five cases which are no better:

(1) A case of contracted stomach with extensive perigastritis. The condition was possibly syphilitic. The last report is that "operation has not made much difference."

(2) A case of a girl in whom adhesions of the pyloric end of the stomach to the anterior abdominal wall were found. Pain and vomiting were continuous before the operation, ceased after operation while the patient was in the infirmary, but have returned as severely as ever. Dr. Stitt Thomson writes: "She is altogether in a very unsatisfactory condition." This, I think, is the most unsatisfactory case of all.[1]

(3 and 4) There are two patients whose symptoms were due to no ulcer discoverable at the operation. They are intensely neurotic, and I believe that that is the explanation, if it can be called one, of their condition. They are both in virtually the same condition as before the operation.

(5) A case of ulcer adherent to the under-surface of the liver. There was great improvement and a gain of two stones in weight, but lately pain and emaciation have been observed.

Ten cases which are improved:

In four cases the ulcer was on the lesser curvature close to the cardia, with adhesions to the under-surface of the left lobe of liver and diaphragm. These patients are all better since the operation; two of them have gained over one and a half stones, but all of them complain still of occasional pains, sometimes severe, radiating upwards into the chest. In one of these pyloric obstruction also was present due to a second ulcer. In one, the patient who gained over three stones after the operation, has lost almost two stones of this increase, and has to restrict her food almost entirely to semi-solids and fluids.

In 6 cases hyperchlorhydria was marked before the operation, and in these the lack of complete recovery may be due to a persistence of this condition. They all com-

[1] I have recently performed Roux's operation upon this patient, with absolute relief up to the present.

plain of "burning" pain in the epigastrium, fulness after meals, and flatulent distension of the epigastrium. All are relieved by a mixture containing bismuth, potassium bicarbonate, and morphine. All are improving slowly. In 5 of these cases there was no pyloric obstruction. In 3 of them no ulcer was found at the operation.

The total, therefore, in this series of cases is 209 cases, with 2 deaths; there are 5 patients who were not benefited by the operation in the least and 10 who are relieved to some extent only.

What are the lessons to be learnt from this series? Briefly, I think, the following:

(1) "Neurotic" cases are unsuited to operation. These patients have what may be called "sensitive stomachs"—that is to say, that food, instantly upon its entrance, causes pain. There is no interval of comfort after food, of a quarter to two or three hours' duration, as is almost invariable in gastric ulcer. Their complaints, moreover, are vague, uncertain, apt to vary. If, therefore, a neurosis of this sort be suspected, but because of doubt the abdomen be opened, the abdomen should be closed without any short-circuiting operation being performed.

(2) Patients who have pronounced hyperchlorhydria before operation should be treated by alkalies, etc., afterwards, and the supervision of the diet continued for a longer period than is necessary in ordinary cases.

(3) If the ulcer be at the pylorus, nothing better than the operation of gastro-enterostomy can be practised. In cases of definite pyloric obstruction gastro-enterostomy gives results which may be compared favourably with the results of any operation in surgery.

(4) Ulcers on the lesser curvature away from the pylorus, not causing obstruction, should, if possible, be excised. If adherent to the liver or the diaphragm, the adhesions should be broken down, the ulcer excised, and probably gastro-enterostomy also performed.

(5) Ulcers in the duodenum, at or near the pylorus, should be infolded and buried by suture, as is done when

perforation has occurred. This is especially necessary in duodenal ulcers, for perforation of these has been observed after gastro-enterostomy. The infolding of an ulcer is easier than excision and quite as effective.

(6) Adhesions affecting the body of the organ should be separated, especially when they affect the abdominal wall, the diaphragm, or the liver. Even if adhesions re-form they are not so likely to distort and drag upon the stomach as are those caused directly by ulceration.

(7) Chronic inveterate dyspepsia is due in the great majority of cases to conditions interfering with the proper mechanical action of the stomach. It is a condition which should be treated by operation.

Class 4.—Summary and Analysis of Cases of Hour-Glass Stomach.

The 22 cases are made up of 7 males and 15 females. In every case there had been previous symptoms pointing to chronic gastric ulcer. In 4 cases the history is strongly suggestive of a former "subacute" perforation, while in a third case the urgency of a perforation indicated operative measures.

The total mortality is 3—1 on the fourth day, from septicæmia, resulting from a strangulated rectal prolapse; 1 in the third week, from suppression of urine; 1 on the fifth day, from pneumonia.

The ulcer in the stomach was associated with duodenal ulcer in 2 cases (1 male and 1 female).

In 1 case a pancreatic cyst was also found at operation. Adhesions to the anterior abdominal wall were met with in 4 cases. Trilobed stomach was seen once.

The following operations were performed.—Gastro-enterostomy alone 7 times, 1 death, 6 cures. Gastro-gastrostomy and gastro-enterostomy 3 times, 2 cures, 1 great relief. Gastroplasty alone 7 times, 5 cured; in 2 secondary operations were necessary; gastro-enterostomy gave com-

plete relief. Dilatation of stricture, once; cure. Gastroplasty and gastro-enterostomy twice, one death. Gastro-gastrostomy alone, once; cure. Gastro-enterostomy and Loreta's operation once, the patient died.

Results.—Twenty-two cases, 3 deaths; 2 secondary operations (gastro-enterostomy) for return of symptoms; 1 secondary operation, entero-anastomosis for regurgitant vomiting after gastro-enterostomy.

One patient has since died of puerperal fever. The remaining patients are all living, all are completely cured, except one, who, though very greatly improved, still has occasional discomfort after heavy food. This patient had an hour-glass stomach and an hour-glass duodenum, there being four pouches and three constrictions.

For the preparation of the statistics in this paper I am indebted to Mr. H. Upcott, F.R.C.S.

DISCUSSION.

Mr. H. J. Paterson thought a most valuable point brought out in the paper was the steadily diminishing mortality after gastro-jejunostomy, being in his cases as low as a little over 1 per cent., or about the same as after appendicectomy in the quiescent stage. The after-history of gastric operations was often difficult to ascertain, and those given in the paper were very valuable. Of 116 consecutive cases of operation for perforation that he had collected, in 92 per cent. there was a definite history of ulceration, and in only a small proportion was there any history of hæmatemesis. The proportion of cases in which perforation occurred in the posterior wall was 12 per cent., showing that the ulcer was usually accessible. It was desirable to give a thorough trial of gastro-jejunostomy after suture of a perforated gastric ulcer to be done at the same time. This would probably diminish the mortality of the operation for perforation. This method had many advantages, among other things allowing calomel to be administered shortly after the operation, thus permitting of intestinal drainage. Hardly any of his cases in which Murphy's button had been used obtained complete relief, owing to the liability of the opening to close. Relapse was frequent after pyloroplasty. There was doubt as to the exact value of gastro-jejunostomy for hyperchlorhydria. In neurotic cases the operation was certainly inadvisable. As to hour-glass stomach, had Mr. Moynihan tried the operation of connecting each pouch separately with the jejunum, no operation being performed on the morbid tissue round the constriction?

Dr. Hale White said that as many of the cases which have been described by Mr. Moynihan came first to a physician he felt that physicians as well as surgeons owed a debt of gratitude to Mr. Moynihan for the work he had done on the subject. There was no doubt that many patients who were formerly left to linger as sufferers of chronic dyspepsia were now, thanks to the advances in surgery, made healthy, useful members of society. Perhaps the most difficult of the cases to which Mr. Moynihan had referred were those of gastric hæmorrhage, and in particular he (the speaker) would like to direct attention to two in which no cause was found at the operation to explain the hæmorrhage. He had collected twenty-five of these cases, all of which had severe vomiting of blood and in none of which could any cause for the bleeding be found, although in each of the twenty-five the interior of the stomach was carefully examined either at an operation or after death. There was no doubt that there was a distinct disease, the chief symptom of which was oozing of blood from the gastric mucous membrane, and that other symptoms were vomiting, pain after food, and pain and tenderness independently of food. This disease was mostly met with in young women between the ages of twenty and thirty, but

two of the twenty-five cases occurred in men. It undoubtedly tended to get well of itself, for it was rarely met with over the age of thirty-five or forty. Careful examination post mortem showed that none of the ordinary causes for hæmatemesis were present. There were no ulcers, no disease of the liver or heart. The cause was certainly not vicarious menstruation, for, as already mentioned, two occurred in men. Whether or not the disease bore any relationship to chlorosis was yet undecided. The blood could be seen at operations to be oozing from one or more points of the gastric mucous membrane. The best treatment was to keep the patient quiet and give her some ice to suck; the bleeding would then nearly always stop. Out of 32,000 medical cases at Guy's Hospital, many of which had been examples of hæmatemesis in young women, only four of these cases of oozing had been fatal; two of those were operated upon. There was no doubt that it was inadvisable to operate upon these cases, for all the figures showed a high mortality if the operation was done during hæmorrhage; it was a mortality of over 50 per cent., a serious matter when they considered that almost invariably the disease got well when left alone; and further, it was difficult to see what benefit could follow an operation when the blood was oozing from the stomach in several places. Nor was there any object in operating between the attacks. In the same way the speaker was strongly of opinion that even when the hæmorrhage was due to a gastric ulcer it was bad treatment to operate while the hæmorrhage was proceeding. The hæmorrhage was rarely the cause of death. Many patients had died shortly after they were operated upon if operation had been done during the bleeding, and probably any patient, however furiously he or she might be bleeding from the stomach, stood a far better chance of recovery if left alone than if operated upon during the hæmorrhage. If cases of genuine gastric ulcer vomited frequently the best treatment was to do a short-circuiting operation between the attacks of hæmorrhage.

Mr. Eve fully agreed with the remarks that had fallen from Dr. Hale White. He had himself reported cases of severe hæmatemesis in which no ulcer was found on opening and exploring the stomach. He considered that our present position in regard to the diagnosis of chronic ulcers was most unsatisfactory. There were no signs which could be in the least degree considered characteristic. He related two cases recently operated on by him in which no ulcer was found. Both patients presented all the so-called characteristic signs of chronic ulcer; namely, pain after food, vomiting, hæmatemesis, superficial hyperæsthesia, and deep tenderness. Both had been treated medically for considerable periods without relief. The uncertainty regarding diagnosis rendered it especially necessary that a most careful examination of the stomach and duodenum should be made after opening the abdomen, before clamps were applied and gastro-enterostomy performed. Palpation of the stomach wall sufficed

in some cases, but should not be too much relied on. In any case presenting the slightest doubt, he opened the stomach posteriorly and examined it with a head lamp and speculum by eversion of the mucous membrane, and if necessary he passed a forefinger through the pylorus into the duodenum. A clamp was subsequently applied near the edge of this incision into the stomach, and it was utilised for anastomosis with the jejunum. He agreed with most of the recommendations which formed the conclusion of Mr. Moynihan's able paper; but could not altogether follow him in regard to No. 4, which advocated the breaking down of adhesions to the liver or diaphragm and the excision of ulcers of the lesser curvature. He thought that such adhesions should be treated with the utmost caution. In one of his earlier cases an adhesion to the liver no larger than the tip of an index finger, when divided, proved to correspond with the base of an ulcer which penetrated deeply into the liver substance itself. In regard to excision of such ulcers, it must be remembered that they often involved a much more extensive area of the interior of the stomach than might be expected from the extent of the adhesion or surrounding induration. Mr. Eve asked Mr. Moynihan what he considered to be the typical symptoms of chronic ulcer? After opening the abdomen on what symptoms did he rely for recognising the presence of an ulcer? And roughly in how many cases in his series had he found it necessary to explore the interior of the stomach before performing gastro-enterostomy?

Dr. F. H. HAWKINS alluded to the rarity of death from even the severest hæmatemesis.

Mr. MOYNIHAN, in reply, said that the most difficult question in gastric surgery was that of operation for hæmatemesis. He had quite recently known of two deaths from hæmorrhage in duodenal ulcer without operation. Probably such cases did not obtain admission into hospital. The mortality from hæmorrhage in chronic gastric or duodenal ulcer was probably much greater than was usually computed. The constant recurrence of hæmorrhage made operation necessary. With symptoms of gastric or duodenal ulcer, and hæmorrhage at decreasing intervals and in increasing quantities, operation was called for. However definite the symptoms of gastric ulcer might be, cases occasionally showed no ulcer, but the chance from operation should be given. No single hæmorrhage, whatever its quantity, justified operative treatment. The after-history of these cases was of the utmost importance, to afford ground for a decision as to what operation was suitable in different cases. In all cases of perforation there should be gastro-enterostomy as well as suture, in view of the occurrence of multiple ulcers in the same patient. He cared less than ever for drainage in any abdominal operations. Plastic operations for hour-glass stomach were not, he thought, indicated. Operation should in no case be undertaken during the *hæmorrhage*.

NOTES ON ONE HUNDRED CASES OF INTRA-CRANIAL TUMOUR, WITH SPECIAL REFERENCE TO THE OCULAR SYMPTOMS

BY

A. W. ORMOND, F.R.C.S.,

OPHTHALMIC REGISTRAR TO GUY'S HOSPITAL AND ASSISTANT SURGEON, ROYAL EYE HOSPITAL, SOUTHWARK

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In the following paper I have collected from the 'Guy's Hospital Post-Mortem and Medical Reports' one hundred cases of intra-cranial tumour. These cases, with a few exceptions, have occurred since the year 1885, and have been taken consecutively. Dr. Hale White, in 1886, published a similar series of one hundred cases, and those, together with these, form a record of all the post-mortem cases of intra-cranial tumour which have occurred in Guy's Hospital since 1872.

In the last edition of Sir William Gower's book on 'Medical Ophthalmoscopy' there is a footnote which states that "the reader may be surprised to find so few references to researches on the pathology of optic neuritis since the appearance of the last edition. The reason for this is that the subject has not been carried further. The uncertainty that surrounds it has been lessened by only one discernment—that is, the important fact that neuritis subsides in most cases if intra-cranial pressure is diminished by early trephining."

This question has suffered recently from the neglect which many subjects undergo that cannot be considered finally settled; but I think a review of the theories which have been at various times advanced by different observers will be of some use and interest when taken in conjunction with the facts represented by these one hundred clinical cases.

The theories of the causation of optic neuritis by the presence of tumours within the skull may be classed in three main divisions:

(1) Theories attributing the optic neuritis to vasomotor effects.

(2) Theories which refer the neuritis to the results of increased intra-cranial pressure.

(3) Theories which assume the influence of inflammation as the primary cause.

The names of Schneller, Benedict, and Hughlings Jackson (1) are associated with the first theory, which, however, seems to entirely lack any anatomical support.

Does a vasomotor mechanism exist in connection with the cerebral vessels? That such a mechanism does exist is denied by many competent observers, and Hill asserts that in every experiment the cerebral circulation seems passively to follow the changes in the general arterial and venous pressures.

In 1860 von Graefe propounded the theory (1 A) that an increase of intra-cranial pressure, acting upon the cavernous sinuses, mechanically obstructed the return of blood through the retinal veins, and the unyielding nature of the structures forming the sclerotic ring produced a kind of strangulation at the optic nerve head. Stasis then ensued in the central vein of the retina, which led on to engorgement and œdema of the optic papilla.

In 1869 Seseman (2), and later Merkel, demonstrated that the communication between the superior orbital vein (into which the central retinal vein flows) and the angular vein was large, and so prevented any stasis which might be produced by compression of the cavernous sinus.

Stellwag von Carion (3) noticed that in some cases the sheath of the optic nerve was distended, and just behind the papilla an ampulliform swelling was to be found in cases of neuritis due to tumour and meningitis; when Schwalbe in 1869 (4) demonstrated that the subvaginal space around the optic nerve was continuous with the subdural space of the brain, attention was drawn to the idea that possibly the cerebro-spinal fluid and not the blood-stream was the channel by which the intra-cranial pressure was conducted to the optic nerve-sheath. These observations prepared the way for the Schmidt-Manz (5) theory, which is still regarded by many as being the best means of explaining the association of intra-cranial pressure with optic neuritis.

This theory is based on the following hypothesis: The existence of a cerebral tumour produces an increase of pressure in the cranium, which causes part of the cerebro-spinal fluid to pass into the subvaginal space of the optic nerve. From this passage of fluid under pressure there results in the first place an œdema of the sheaths; then the percolation of the pia mater by the liquid gives rise to an œdema of the optic nerve and papillæ, compression of the lamina cribrosa in front, and interference with the circulation.

Parinaud (6) in 1877 elaborated a theory which seems to me to be supported by much clinical and pathological evidence. It is based essentially on the coincidence of internal hydrocephalus and papillitis, which is demonstrated in a masterly way by the author.

The growth of a tumour gives rise to a hypersecretion of cerebro-spinal fluid; this is accumulated by pressure in the ventricles; it is internal hydrocephalus; from it results difficulty in the lymphatic circulation of all the brain. As the optic nerve is only an external portion of the brain, it undergoes the same difficulty of circulation, in consequence of which arises an œdema of the papilla—that is to say, from the point furthest removed from the brain. When for any cause whatever (by a mechanism which is not well

known) the cerebro-spinal fluid increases in such a manner as to modify the tension of the cavities which enclose it, it constitutes an obstruction to the lymphatics in the brain similar to the obstruction of a large vessel. The elements of the lymph carried by the blood circulation are retained in the tissues, where their accumulation produces a lymphatic œdema which does not essentially differ in its mechanism from that which is produced when the tension increases in the venous system.

Ulrich's (7) theory is similar to Parinaud's; he attributes the œdema to the optic nerve alone, the nerve-fibres compressing the central vessels in their axial course.

Johann Deyl's (8) theory is similarly based upon a mechanical hypothesis.

"The central retinal vein passes out from the optic nerve head through a narrow slit which can often be detected even by the naked eye as a gray line in the pial sheath (as a rule the vessels will be found close together here), the opening for the central vein being a little nearer to the eye than the point of entrance for the central artery of the retina. If the vein is compressed in the constricted orifice mentioned above (whose lip-like edge swells under the slightest œdema) the slight initial stasis that often occurs can be explained. The œdema of the optic nerve arises as a result of the increased tension and the consequent obstruction offered to the outflow of blood and lymph from the cranial cavity, the pressure in question being looked upon by the pathologist as a common and almost constant condition and recognised by the clinician in the living subject as well."

Sourdille's (9) theory is an extension of Parinaud's. The initial lesion, he thinks, is an œdema of the neuroglia of the ependyma, which, given the intimate connections which exist between the third ventricle and the chiasma, extends directly to the neuroglia of the chiasma and the optic nerve in a descending scale. The optic nerves, increased in volume, are strangled in their passage through the optic canal, and from this results a venous

stasis in all the orbital portion of the nerve, with consecutive dropsy of the sheaths. (The pressure of the cerebro-spinal fluid plays no part in this.) The artery and the central vein are compressed, a collateral circulation is established by the intermediary of the capillary plexus of the lamina cribrosa, by means of which the venous blood of the retina flows into the choroidal system and peripapillary sclera.

This dilatation of the plexus of the lamina cribrosa is the principal cause of the protuberance of the papilla.

Many observers and experimenters have found that choked disc may be caused in animals by the artificial production of increased intra-cranial pressure, and experiments by Schulten, Merz, Kampherstein, Heine (10, 11, 12), and others, have shown that a narrowing of the arteries and distension of the veins resulted when the pressure was raised. This led on to the appearance of the choked disc. Merz states pressure is necessary of from 15 to 20 millimetres of mercury, but of course this by no means proves that the same cause obtains the same results in human beings.

The mechanical theory falls in with surgical evidence also. Brudenell Carter (13), by puncturing the optic nerve sheath, succeeded in relieving the œdema of the nerve-head and lessening the neuritis, whilst the marked and rapid improvement in cases where trephining has been resorted to also supports this view. But, with regard to the latter, it must be remembered that improvement takes place whether the dura mater is opened or not; and we cannot argue that because the neuritis improves when the intra-cranial pressure is relieved therefore the pressure caused the neuritis, any more than we can say that by removing the peritoneal fluid in cases of tuberculous peritonitis the improvement resulting proves that the exudation is the cause of the malady. We may, however, accept the statement that increased intra-cranial pressure is capable of producing (theoretically and experimentally in animals) changes in the optic nerve which are ophthal-

moscopically similar to those seen in human beings suffering from choked discs. But whether optic neuritis is primarily due to œdema brought about by increased intra-cranial pressure or not, I feel sure, as a result of the clinical observation of a very large number of cases—that the existence of intra-cranial pressure considerably alters the ophthalmoscopic appearance of the neuritis. I believe that certain ophthalmoscopic appearances only exist where there is increased intra-cranial pressure, and in many instances one may accurately diagnose the absence or presence of increased intra-cranial pressure from the appearance of the neuritis, taken in conjunction with the other clinical symptoms. This is important, since a physician is often called upon to decide whether trephining of the skull would benefit the patient or not.

The number of observers who, actively or passively, support the theory that optic neuritis in intra-cranial tumour is due to, or at least influenced by, the increased pressure within the skull is a large one.

This pressure may affect the optic nerves either directly or indirectly—that is to say, either by the growth pressing directly on the optic nerves or their continuations or by a general increase of the pressure within the skull. General increase of intra-cranial pressure may be due to the size of the growth, to dilatation of the ventricles, or to an alteration in the brain-substance itself.

In many of the cases the tumour is so large that its existence within the cranial cavity at all indicates a very considerable modification of the usual cranial contents.

The cranial cavity is entirely filled with the brain, the blood, etc., and the presence of any foreign body, whatever the nature of it be, necessitates that the space occupied by it must be at the expense of one or other of the tissues usually occupying the cranium.

A slowly growing, infiltrating tumour doubtless makes room for itself by destroying the brain-substance and itself taking the place of the atrophied brain; in this way a large tumour may exist within the skull and give

no sign of any increased pressure, but in many instances this invasion of the skull by a foreign body is at the expense of the blood, and the larger the tumour the smaller is the total quantity of blood within the cranium. Theoretically, therefore, we should expect that the symptoms of increased intra-cranial pressure would be similar to those of cerebral anæmia, and that patients dying from either cause would show symptoms having points of resemblance. These symptoms are given as :

"Loss of consciousness.

"Epileptic spasm.

"Dilated pupils and nystagmus.

"Respiratory spasm.

"Slow heart.

"Rise of arterial pressure.

"Fall of arterial pressure, acceleration of the heart, cessation of respiration. The cortical and bulbar centres are first excited and then paralysed. The fatal symptoms arise when the bulbar circulation ceases.

"If an animal be in a state of collapse or deep anæsthesia, or if the anæmia be slow in onset, the excitatory symptoms fail to appear.

"In death from acute cerebral anæmia respiratory paralysis usually precedes vasomotor paralysis.

"Cheyne Stokes' respiration and Traube Hering curves are common in states of partial anæmia of the bulbar centres" (13A).

Clinically we find that a large number of cases in which death was caused by cerebral tumour show these signs, and Dr. Hale White, in his series of cases, has tabulated the method of death, and finds "that there was not a single case in which the heart ceased before the respiration stopped."

The brain is not capable of transmitting pressure equally in all directions, and the analogy of a piece of putty has been used to illustrate this fact; moreover, the existence of strong fibrous septa, such as the falx cerebri and cerebelli, and the tentorium, render such transmission

impossible. The same is also true of the ventricles: although they communicate with one another and may be filled with fluid, we find from post-mortem records certain evidence that one ventricle, or even only a part of a ventricle, may be dilated, and show signs of having been under the influence of increased pressure.

It seems probable that parts of the ventricles are not infrequently shut off and turned into closed cavities by one wall being jammed against the other, and in this way parts of these very irregularly shaped cavities are isolated.

Not sufficient notice is taken of the anatomical relation of the ventricles of the brain to the optic tracts and nerves. The pulvinar of the optic thalamus and the end of the optic tracts are within the ventricles, and the anterior and lower angle of the third ventricle is formed by the posterior two thirds of the optic commissure; there is, therefore, anatomically, a very close relationship between the ventricles and the optic nerves, and an increased pressure on the lateral ventricle or the third ventricle would be directly conveyed to the optic tracts.

Intra-cranial pressure may, however, be present when the tumour is small and the ventricles show no sign of distension, and the suggested causes of such a condition should be considered. The primary cause of increased intra-cranial pressure has been studied by Dr. Leonard Hill (14), and since the publication of his book by some other physiologists, among them W. B. Cannon (15), who has ventured to criticise Hill's conclusions. Hill's theory is, that since the brain is enclosed in a rigid case and the brain-substance itself is incompressible, this localised foreign body (in Hill's paper this is assumed to be a localised hæmorrhage) must occupy the space of a certain vascular area—that is, it must cause an obliteration of the capillaries and veins in the region it occupies. As a consequence the local cerebral tension will be equal to that of the arteries which normally feed the affected area. In the obliterated area there will be complete stasis of

blood. The transmission of the increased tension through the brain-substance to the veins and capillaries of the border areas will cause a higher blood-pressure and a lessened blood-flow in these vessels. In more distant areas the circulation is more normal, and the blood-flow may have even a compensatory increase of speed. The high blood-pressure in the border areas will lead to increased transudation of fluid, because plasma may pass more easily into the brain-substance than blood through the compressed capillaries. The transudation will take place at almost arterial tension, will increase the volume of the foreign body, and so lead to compression of other capillary areas, thus completing a vicious circle.

"The noteworthy feature of this theory," Cannon states in his criticism of it, "is the assumption that the transudation occurs because of the high blood-pressure in the capillaries of the border areas. It should be observed, however, that the high pressure in the vessels is due, not to a general increase in blood-pressure, but that external pressure in the brain-substance about the vessel which increases, until it partially overcomes the internal pressure in the capillaries themselves."

If, as Hill suggests, the plasma may pass more easily in the brain substance when tension is so high that the blood-vessels are being compressed, than the blood does through the compressed capillaries in which the flow can still occur, there would be the obviously impossible condition of fluids passing from a region of less to a region of greater pressure.

But even the assumption that plasma does pass from the vessels will not remove every difficulty. For if, as the theory states, the secondary increase in intra-cranial pressure is due to such transudation from the capillaries, this pressure must be dependent upon the pressure of the plasma. The pressure of the plasma is, in turn, dependent on blood-pressure, and is as much less than blood-pressure as the resistance which the tissues about the capillaries offers to the outflow from them.

Hill declares that to produce death intra-cranial pressure must equal the blood-pressure in the carotids. The difficulty arises in attempting to induce a method of compression manifestly less effective than arterial blood-pressure to produce such a result, for in the end by this reasoning the direct pressure of the blood through the free ways of the vessels must be greater than the lessened pressure of the transudate, and the flow will persist.

Cannon's theory is that increase in intra-cranial pressure is due to three factors—deprivation of normal nutrition in the brain-tissue, passage of water into these parts, with consequent swelling, and the rigid enclosure of the brain, causing the swelling in one region to affect markedly neighbouring regions.

Brain tissue deprived of blood undergoes chemical changes resulting in greater internal osmotic pressure and the passage of water into the tissue.

Brains placed in normal salt solution increase continuously in weight, even to 33 per cent. The swelling which the tissues undergo must cause them to compress neighbouring regions and thus further impair the circulation, with a result that new regions are involved in the process and a vicious circle established. The main force effective in causing swelling is probably osmotic pressure, which in brain-tissue may attain a degree so much greater than blood-pressure that the blood would really be prevented from entering the cranium.

It is difficult to understand—if Cannon's theory is correct, that intra-cranial pressure is due to increased osmotic pressure in brain-substance deprived of its proper nutrition—why every case of cerebral softening is not attended with signs of increased intra-cranial pressure.

Certainly large areas of softening are frequently found around small tumours, especially those which are encapsuled, but neither macroscopic nor microscopic examinations reveal changes spreading through the whole of the brain-substance.

Are we able by means of any of these theories to

account for the existence of neuritis in these one hundred cases?

In the majority of my cases there is direct evidence of increased pressure within the skull; in thirty-seven cases there is a definite statement that the ventricles were subjected to general or localised pressure; excluding those cases in which the condition of the optic disc is not mentioned, and also those cases in which optic neuritis is not present, we have left fifty cases in which no direct statement is made about pressure, although the symptoms of it, such as headaches, vomiting, fits, drowsiness, and death by coma are recorded, and in these cases optic neuritis was present.

In all the cases of cerebellar tumour in which the condition of the disc is mentioned optic neuritis is noted, and it seems to me that the existence of a tumour of even a very small size within the cerebellum would undoubtedly result in a local increase of pressure which would constrict the veins of Galen, and, as a consequence, the fluid within the ventricles would be increased in quantity.

It has often been pointed out that optic neuritis is more frequently observed in cerebellar than in cerebral tumours. The reason for this appears to be that—owing to the anatomical position of the cerebellum, which is rigidly enclosed by bone on the whole of its under surface and by the tentorium cerebelli on its upper surface—any increase of the contents of that small space would, of necessity, cause pressure upon the veins of Galen or upon the iter at some part of its course; this would inevitably lead to an increase of the fluid in the ventricles.

Such a condition of intra-ventricular pressure may very easily exist during life and not be obvious after death, because, the obstruction being mainly mechanical, the fluid from the ventricles might easily drain away after death into the general arachnoidal space, where it would be less noticeable.

If, then, we allow that pressure in the posterior fossa is likely to produce intra-ventricular pressure—and therefore

intra-cranial pressure—the remaining cerebral cases may be accounted for by the large size of the tumour. By a large tumour I mean one having a diameter of two inches or more.

The most difficult case to explain on this increased pressure hypothesis is No. 66, in which optic neuritis was existent, the tumour being in this case comparatively small, situated in the temporo-sphenoidal lobe, and did not reach the surface. As the patient suffered from fits, incontinence of urine and fæces, and died in coma, we may assume, however, that there was increased pressure.

The tumours that are situated at a distance, in the cortex of the cerebrum for instance, are also difficult of explanation, but it is frequently recorded in the post-mortem results that areas of softening and of œdema extended for some distance around and beyond the tumours, and according to the theories of Drs. Leonard Hill and Cannon, a wider sphere of influence must be allowed to every tumour than its actual size implies.

Increased intra-cranial pressure due to a small tumour in the cortex, invading the subarachnoidal space on the one hand or the ventricles on the other, might be explained, I think, by production of an increase of fluid consequent on the irritation caused by the growth. The association of fluid with cancers which involve serous cavities has been often noticed—the tunica vaginalis, the pleura, the peritoneum, or the subretinal spaces are instances of this. The condition, however, is not common; not a single instance of such a tumour occurs in these one hundred cases.

It is interesting to compare the results of increased pressure within the skull with those of increased pressure within that other rigid and inextensible cavity containing a portion of the brain, namely the eye. In increased intra-ocular pressure in children we find this wall yielding and producing the result known as buphthalmos, analogous to hydrocephalus, whereas in adults the unyieldingness of the sclerotic produces a similar train of symptoms to that

of increased intra-cranial pressure. The symptoms of glaucoma are undoubtedly due to increased pressure, but this condition is produced by many different causes.

The analogy between the symptoms produced by intra-ocular pressure and those of intra-cranial pressure is a close one.

We may compare the ocular cases, which vary from those in which the pressure effects are so slight as to be scarcely perceptible to those cases of fulminating glaucoma in which vision is entirely lost within a few hours, with those cerebral cases in which, on the one hand, a tumour may show signs of its existence merely by slight headache or congestion of the optic discs, lasting for months or even sometimes years, or, on the other hand, may evince fatal symptoms within twenty-four hours, as in Case 90.

Compare also the almost instantaneous relief afforded by trephining (*vide* Cases 60, 44, and 57) and the rapid disappearance of the glaucomatous symptoms when the eye is opened. There is a similar analogy in the frequent gradual return of the symptoms after operation, which is common to both types of disease.

A growth may exist within the eye for a long period without giving rise to any increased pressure; the same is undoubtedly true of a cerebral tumour, and the analogy still holds when we consider the primary causation of both diseases.

Gowers states that "the evidence in favour of increased intra-cranial pressure being the cause of neuritis is negatived by the fact that where the pressure is greatest no neuritis exists, as in hydrocephalus," but this is not good reasoning, for the principal condition is not adhered to, namely the rigidity of the enclosing surfaces. (Glaucoma does not exist as such in children.) We must, however, acknowledge that optic neuritis is often a very early symptom of intra-cranial trouble, and that these cases frequently exhibit no other clinical sign whatever of increased intra-cranial pressure. The existence of pressure considerably alters and modifies the course of the

neuritis, but I am sure that it is not its absolute primary cause.

When overcrowding occurs within the skull, the optic nerve undergoes those changes which we see in life, and which often lead on to complete atrophy, but if the increased pressure is by any means avoided, this condition of the optic discs may last for years, even as long as nine years (*vide* Case 100).

What, then, is the method by which this increased pressure influences the neuritis?

I have already shown that in the cases in which the ventricles are dilated the optic nerve and tracts are expressly involved, and that pressure is transmitted directly to the optic nerve fibres or their connections.

In the cases where the tumour is situated at the base of the brain immediate pressure on the nerve is probably the cause, but in the majority of these cases atrophy not preceded by any evident neuritis exists.

The general increased intra-cranial pressure produces an œdema of the optic tracts and nerves and probably of other cranial nerves as well, but the anatomical conditions of the optic nerves cause them to be strangled in their passage through the scleral canal.

Both increased intra-cranial pressure and optic neuritis are rarely absent from cases of cerebral tumour.

The presence of a foreign body of any description within the cranium interferes with the circulatory system. Increased intra-cranial pressure is usually general and not local, and therefore probably due to intra-ventricular pressure or to a large infiltrating tumour involving that part of the brain situated beneath the level of the corpus callosum. This general increased pressure accentuates a pre-existing optic nerve congestion, and when considerable results in complete strangulation of the nerve-head.

If we examine the cases presented here, we find that they may be divided into three classes:

(1) Those in which optic neuritis was present.

(2) Those in which it is definitely stated that optic neuritis was not present.

(3) Those in which no note is made of the condition of the optic discs.

In the first division we have seventy cases, in the second thirteen, and the remaining seventeen cases have no note of the ocular condition.

The proportion of cases in which optic neuritis is present is a very large one, much larger than in Dr. Hale White's collection. I venture to think that this result is probably due to the increasing use of the ophthalmoscope and the greater care taken in recent years in the completion of the medical reports. My own observations have led me to conclude that certain conditions of optic neuritis are very easily overlooked by physicians, which would, to an ophthalmic surgeon, be evidence of an inflammatory condition of the disc; there is a difference between a physician's neuritis and the neuritis of an ophthalmic surgeon, but it is mainly one of degree.

We must, however, accept the statements made and examine *seriatim* the thirteen cases in which optic neuritis is stated to have been absent. Of these, six are cases in which the tumour was situated at the base of the brain (14, 16, 40, 48, 51, 76). In No. 14 the base of the brain was invaded by a tumour growing from the basilar process, and it must be looked upon rather as an extra-cranial tumour; there was no evidence of any increased intra-cranial pressure.

In the other five cases there was direct pressure on the nerves, which produced atrophy, and in No. 51 the statement that no optic neuritis was visible, although carefully sought for by so acute an observer as Dr. Goodhart, must be read in the light of the condition seen post mortem—*i. e.* both optic nerves were involved in the growth.

This absence of neuritis in these six cases, where the tumour was directly pressing on the optic tracts or nerves, is certainly contrary to the theory that inflammation is the primary cause of optic neuritis; whereas the theory that

increased pressure leads to an œdema of the nerve-sheath receives some support from them, as the direct pressure would prevent any œdematous process spreading along the optic nerves or tracts.

In Case 32 we have an instance of a tumour being found post mortem, and not suspected during life.

Case 90 also gave no evidence of its existence before the day of death.

In Case 25 the first symptom noticed by the patient was defect of sight, but we are not given sufficient information to account for this, as a distinct statement is made that neither optic neuritis nor limitation of the fields of vision were present.

In Case 91 I have been unsuccessful in tracing the medical report, and the notes given are entirely from the post-mortem records.

The remaining cases, 4, 79, and 96, are really the only cases in which no extenuating circumstances can be found for their delinquency in not possessing optic neuritis.

So far, then, we may say that increased intra-cranial pressure is due to an œdema of the brain itself, and that Parinaud's theory would account for the existence of optic neuritis in many cases of cerebral tumour, if we suppose the œdema to travel down the optic tracts and nerves so as to produce the condition known as choked disc. We do not, however, find the neuritis present invariably following the recognised course of a papillitis, but it often simulates the neuritis seen in Bright's disease and other conditions. Often also the changes in the disc are present for years without affecting vision, and are not associated with any marked evidence of increased intra-cranial pressure. There is also abundant evidence to prove that histologically the changes in the optic nerves and tracts are of a true inflammatory nature.

An alternative theory to the mechanical one was first promulgated by Professor Leber (16) of Heidelberg, and was supported by the experimental and pathological work of Deutschmann (17) [illegible] ber

Deutschmann theory. According to this, papillitis is a peri-neuritis and a neuritis, extending from the chiasma to the ocular bulb. The leucocytic percolation which causes the œdema is due to the irritant action occasioned by the toxic products which are secreted by the tumour and come in contact with the nerve and its sheath by means of the cerebro-spinal fluid.

From the results obtained by Deutschmann, published in 1887 (first communicated by Leber to the Congress of London), he concludes that the papillary stasis is an inflammatory affection; it is not to be looked at as a stasis in the sense of the theory of Schmidt Manz, but is provoked by causes capable of engendering inflammation—that they may be of a chemical or parasitic nature.

It must be acknowledged that nearly all the observers who have relied upon the microscopical appearances of the nerves for the formation of their ideas as to the causation of optic neuritis in cerebral tumours agree that evidence of inflammation can be traced along the optic nerves. The inflammation extends from the meninges to the sheaths of the optic nerves, down which it spreads, invading the nerve-tissue by extension inwards along its fibrous framework (Edmunds and Lawford [18]).

"So I take it the changes found around tumours, etc., in the brain are of an inflammatory character, tending to spread in all directions or in certain directions, and in so doing frequently implicate the optic nerves, which really are modified portions of the brain outside the general cranial cavity" (Stephen Mackenzie [19]).

Krüchman (20) states that the material necessary for the production of a choked disc must be furnished by the cells of the human body itself, and refers its origin to hypertrophic material produced by the destruction of cells.

Fleming (21) concludes that a toxin of some kind is responsibe for the condition discovered in the neuroglial elements of the brain, and that optic nerves in cases of optic neuritis due to intra-cranial lesions show changes

which he thinks warrant the assertion that they are due to true inflammation and so are the cause of the inflammatory appearance of the nerve.

Saqui (22) has made observations about the changes which takes place around the tumours, and thinks that these changes produce the symptoms when the tumour itself causes little or no change.

Rosenberg (23), in a paper describing his work on some experimental research in the study of inflammation of the optic nerve and retina, remarks that the flow of the cerebro-spinal fluid is from the base of the cranium to the exit of the nerves. The optic nerve, viewed from an anatomical standpoint, is subjected to the most favourable conditions for being bathed by the cerebro-spinal fluid.

The toxins of the typhoid bacilli introduced into the subarachnoid space provoked an inflammatory process in the optic nerve, its membrane, and the retina, beyond interstitial modifications.

Elschnig also found that in no case in which papillitis was well marked was evidence of inflammation wanting. In thirteen of his twenty-one cases of tumour of the brain more or less intense inflammation of the meninges was found under such conditions that inflammation of the optic nerve sheaths was a natural sequence.

If we consider optic neuritis in general, and not only in association with cerebral tumours, we find it appears in connection with a very large number of very different diseases, but as our knowledge advances it becomes more and more conclusive that these diseases nearly all produce some degenerative changes in the general nervous system; for example, anæmia, Bright's disease, acute febrile troubles, diabetes, malaria, syphilis, lead-poisoning, etc., the optic neuritis in such cases being attributable to the influence of a toxin. Optic neuritis may certainly be produced by many different toxic bodies (27). No observer will deny that the ophthalmological appearance of neuritis in cerebral tumours may, and often does, present a distinctly different appearance to the neuritis

seen in Bright's disease, but, on the other hand, it has been equally acknowledged that in many cases the appearances are indistinguishable.

The primary cause of neuritis in cerebral tumours may, then, be either a chemical or bacterial irritant. There is no evidence of any bacterial invasion being constantly found in cerebral tumours, and the cases presented here suggest that the toxin depends for its existence upon some constantly present tissue, since the nature of the tumour varies so much. Probably, then, the nerve-tissue itself is the source of the irritant, and its production is due to the presence of the tumour.

The effect of this toxin is to produce those inflammatory œdematous changes constantly found by pathologists within the nerve-tissue. Neuritis is initially an œdema of the nerve-fibres and is, for several reasons which we will consider, essentially an early symptom.

Hoche (25) pointed out the similarity of the optic nerve fibres (as they pass through the scleral canal) to the fibres of the posterior nerve roots as they pierce the pia mater. Both sets of fibres lose their medullary and neurilemma sheaths, a point which has been recently dealt with by Orr and Rows (26), who prove that in tabes dorsalis the change in the posterior columns of the cord starts (owing to the absence of the myelin sheath) at the point where the axis cylinder is exposed to the influence of the toxic lymph current. They conclude: "We are, however, certain of the fact that whether the cerebro-spinal lymph is toxic from a peripheral source or from a general intoxication, the sensory fibres are prone to give way at the point where they lose their neurilemma sheaths." So also the fibres of the optic nerve lose their medullated nerve-sheaths at the lamina cribrosa.

Hoche denies the existence of any toxin in the cerebro-spinal fluid; but Mott and Halliburton (28) have shown that choline, a product of myeline degeneration of the nervous system, may be chemically and physiologically detected in the cerebro-spinal fluid and the blood in cases

where there is active degeneration of the nervous system. Donath of Buda-Pesth (29) has shown that choline is present in the cerebro-spinal fluid in a large number of diseases of the central nervous system, including cases of cerebral tumour. Neurine also and other toxic bodies have since the publication of the paper by Hoche been proved to exist in the cerebro-spinal fluid.

Optic neuritis may be associated with diseases of the nervous system other than cerebral tumours, such as tumours of the spinal cord, myelitis, tabes dorsalis, alcoholic peripheral neuritis, acute paraplegia, etc. (30, 31). Degeneration of the posterior columns of the spinal cord frequently occurs in cases of intra-cranial tumour (*i. e.* about 65 per cent.), and Batten and Collier (32) conclude that such degeneration is of root origin, and arises from the point where the root enters the spinal cord. The posterior roots are always less affected than the posterior columns and may show no degeneration. The same writers think that optic neuritis bears no relation to the occurrence of the posterior degeneration, and attribute the degeneration to traction on the posterior roots by distension of the arachnoid in consequence of the increased intra-cranial pressure. They, however, allow that the two conditions may have a common cause, and I have already shown that in tabes dorsalis the same part of the spinal cord is affected, and have given a reason why the toxin should display a selective action on certain portions of the nervous system.

Guillain (33) has shown that the lymph-spaces of the pia covering the posterior parts of the cord communicate with those of the posterior columns, and Homèn (34) shows that toxins are transmitted more readily by the posterior than by the anterior roots, so that the posterior columns are more exposed to irritants than the other parts of the cord.

From what we at present know we may say that neither the mechanical nor the inflammatory theory is sufficient to explain all the known clinical, pathological,

and experimental facts; on the other hand, certain well-established conclusions may be stated.

1st. That increased intra-cranial pressure produced experimentally can, if sufficiently great, cause changes in the optic disc which are similar to those frequently seen clinically in papillitis.

2nd. That microscopical examination of the optic nerves and tracts in cases of optic neuritis associated with cerebral disease, displays evidence of a genuine inflammation.

3rd. That a cerebral tumour within the brain-substance engenders some tissue changes around it.

4th. That, as is shown by the cases published in this paper, the kind of tumour which produces optic neuritis varies, being sometimes sarcomatous, carcinomatous, cystic, tuberculous, gummatous, etc.

5th. That optic neuritis may be associated with nearly all the infectious diseases, and that toxins circulating in the general blood-stream are particularly liable to affect the optic nerve, on account of its being surrounded by a lymph-sheath, perhaps also because the axis cylinders are exposed at the scleral canal, having lost their medullated nerve-sheaths.

We may conclude, then, that the presence of a tumour within the brain results in changes around it, whereby the brain-tissue itself undergoes a degeneration which produces certain toxic products. These products of nerve-tissue degeneration are passed into the cerebro-spinal fluid and, by the ordinary channels, reach the optic nerve-head. Here the exposure of the axis cylinders results in an irritation of the nerve-fibres, which causes an inflammatory œdema. This irritative stage may be of a varying duration, which depends on the power of the toxin and the resistance of the nerve, but if the irritation is severe it may pass into a definite inflammatory stage.

Further, if as in a case of cerebral tumour the lymph-channels behind the eye are under pressure, the inflammatory neuritis passes into the ordinary condition of choked disc.

In other words, optic neuritis may be produced primarily by toxines, due to the presence of a tumour within the brain, and accentuated by the existence of increased intra-cranial pressure.

The Pupils in Cerebral Tumour.

The condition of the pupils seems to depend in the majority of these 100 cases upon the condition of the optic nerve, and from being minutely contracted early in the illness, they frequently pass to a condition in which one or both are widely dilated and fixed. This is due to an interference with that most delicate of all reflexes, the light reflex.

In early conditions of neuritis the pupillary fibres of the third nerve are irritated and the pupils become contracted, thereby protecting the inflamed nerve from an excess of light; as atrophy develops they gradually enlarge until the atrophy is complete, then they are widely dilated and fixed.

If the atrophy is more marked on one side than the other, the pupil on that side is larger and reacts to light less vigorously.

Besides this condition, the pupils may be influenced by the direct involvement of the third or fifth nerve or some portion of the path by which the reflex arc travels.

In three cases the third nerve and in one case the fifth nerve were involved. In three other cases we are told the pupils reacted to accommodation and not to light (Argyll-Robertson phenomenon).

The association of the aneurysm with the internal carotid artery was shown in Case 42, by the involvement of the third nerve.

It appears to me that in uncomplicated cases the pupils are first of all contracted or normal in size, and dilate gradually as the vision fails, but the medical reports too often contain no reference to the condition of the pupils until these arrest attention by their dilatation and fixation.

The hemiopic pupil is not once mentioned, although it was undoubtedly present in several of the cases, so that any advantage to be derived from the pupils as localising agents has been lost.

Nystagmus.

This symptom is mentioned as being present in 14 cases: 9, 20, 23, 30, 44, 45, 48, 53, 55, 59, 62, 67, 77, 85. Of these, 9 cases are cerebellar, 2 temporo-sphenoidal, 1 affected the posterior part of the interior capsule and the corpora quadrigemina, the remaining two being cases of complete blindness following atrophy of the optic nerve. It is interesting to note the presence of nystagmus as a symptom in the temporo-sphenoidal cases; as in certain affections of the ear, the diagnosis between cerebellar and temporo-sphenoidal abscess is assisted by the presence or absence of nystagmus, but the symptom is by no means a characteristic one.

Knee-Jerks.

The condition of the knee-jerks is mentioned in forty-three cases; 29 of these are cerebral and 14 cerebellar.

In the cerebral cases the knee-jerks were normal in ten cases—11, 24, 25, 30, 33, 66, 72, 74, 84, 98; absent in five—37, 46, 51, 68, 96; increased in eight—10, 29, 31, 60, 63, 69, 71, 79; and diminished in one—76; in five cases they varied on the two sides—47, 48, 58, 79, 93.

It has been stated that the knee-jerks in cerebellar cases are often absent. Out of twenty-seven cases of cerebellar tumour contained in this paper their condition is mentioned in 18. In six (27, 43, 52, 57, 77, 85) they were increased on both sides; in five (35, 53, 55, 61, 75) they were absent; in five (26, 49, 62, 90, 94) they were normal; in one case (34) the knee-jerk on the side of the lesion was increased and on the opposite side diminished.

In the remaining nine cases the condition is not mentioned.

We must conclude, therefore, that the knee-jerks in cerebellar disease may be increased, absent, or normal, and that they vary at different periods of the illness, as in No. 35 they were present at the commencement and disappeared about five weeks before death.

Surgical Interference.

In sixteen of the cases the surgeon's aid was resorted to—23, 28, 29, 34, 44, 45, 55, 57, 60, 73, 74, 75, 81, 83, 84, 93.

In ten of these some improvement is recorded, it being usually a lessening of the headache, temporary improvement of the sight, and some increased brightness in the patient's mental condition. The operation was not, however, undertaken in every case in order to relieve the symptoms, but was sometimes advisable for the verification of a diagnosis; in several instances the patient's condition was so critical that trephining was only resorted to as a last resource. These records are by no means to be taken as enabling the reader to form an opinion as to the advisability or inadvisability of operation; they exemplify, however, some of the penalties consequent on surgical interference, hernia cerebri, meningitis, and paralyses, with a gradual return to the condition existent previous to the operation. Case 81 is an illustration of the best that can be expected from surgery, and where the headache is intense that symptom may be alleviated by trephining; also, when the neuritis has not passed beyond an initial stage and the optic nerve fibres are not irrevocably damaged by pressure, the vision may be preserved; but this subject has been treated by Dr. Paton in a paper read before the Ophthalmological Society this year, and his statistics show much more encouraging results.

With regard to the quest [illegible] tumour, I do not think any of [illegible] n this

direction, for in all either the tumour was too large, or it was of an infiltrating nature, or structures too important to be touched were involved, or it gave no localising symptom.

Appended is an epitome of those cases which were operated on and the results.

CASE 23.—Was trephined over the temporo-sphenoidal lobe, and also over the cerebellum. Marked evidence of intra-cranial pressure found at the operation. Hernia cerebri resulted.

CASE 28.—Was trephined and a part of the tumour removed from the right frontal lobe. Patient had less pain and was brighter and more intelligent after the operation. He died from erysipelas one week later.

CASE 29.—Was trephined over frontal lobe on the left side. Some bone was removed, and the dura mater opened. There was considerable intra-cranial pressure, and the brain bulged into the wound. Patient was brighter and more alert after the operation but still had headache. He lived one month.

CASE 34.—Was trephined on two occasions, and the first time the dura mater was opened; the second time the lateral ventricles were drained. He died from suppurative meningitis.

CASE 44.—Aspiration was performed at angle of anterior fontanelle, and two or three ounces of fluid removed. The child's condition immediately improved; he opened his eyes, moved his arms; the pulse and respiration improved, and the pupils reacted to light.

CASE 45.—Was trephined, a large hernia cerebri resulted. The patient died two days later.

55.—Was trephined; bone was removed and the ter opened. Hernia cerebelli resulted. The head-

aches were better after the operation, but the sight remained the same. The patient died ten days later.

Case 57.—Was trephined over the parietal eminence (the patient sat up and drank some water within a few hours of the operation). A large hernia cerebri resulted.

Case 60.—Was trephined and abscess opened and drained. This patient subsequently recovered sufficiently to leave the hospital.

Case 73.—Was trephined over the posterior parietal region, but died six hours later from shock.

Case 74.—Was trephined. Evidence was found of marked intra-cranial pressure. Vision improved, and the headaches were less after operation but only for a short time. The wound became septic, and the patient died six weeks later.

Case 75.—Was trephined and some bone removed. There was marked evidence of intra-cranial pressure. Hernia cerebri resulted.

Case 81.—This patient was trephined on four occasions, with marked improvement in the headaches and also in the vision; the case has been fully reported by Dr. Hale White in Vol. LV of the 'Guy's Hospital Reports.'

Case 83.—Was trephined, and some fluid was removed from the cyst by aspiration. Patient died of suppurative meningitis.

Case 84.—Was trephined, and the symptoms were relieved for a time. He lived three months after the operation.

Case 98.—Was trephined over the right parieto-occipital region and some bone was removed. The ptosis and squint disappeared, and the headache improved. Patient lived for about a month after operation.

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TABLE OF CASES.

On condition of (

No.	Index.	Position.	Nature.
1	1874, F., aged 23, P.-M. 376½, Dr. Pye-Smith	A cyst 1½ in. in diameter containing ʒij of clear albuminous fluid in the centre of the cerebellum, extending through its thickness from the superior to the inferior surface. The ventricles contained an excess of fluid. Ependyma thickened	Solitary me simple cy
2	1874, M., aged 16, P.-M. 137	Tumour the size of two Barcelona nuts which enlarged the left half of the pons, and displaced the 5th and 7th nerves. There were two similar masses in the left side of the cerebellum, reaching to the surface	Tubercle
3	1874, F., aged 20, P.-M. 113	A tumour 2½ ins. in diameter was found in the cerebrum on the right side, occupying the occipital lobe, and pressed on the right half of the cerebrum. The ventricles were dilated	Round- and spin celled sarcom
4	1878, E. H—, F., aged 36, P.-M. 190	Thin cyst which bulged into the left ventricle and pushed inwards the left basal ganglia, optic thalamus, and the posterior part of the corpus striatum. It did not approach the frontal convolutions, but these were compressed	Glioma
5	1878, F., aged 34, P.-M.	A tumour in the left frontal lobe of the brain which destroyed the cribriform plate and the sella turcica. The whole anterior half of the left hemisphere was much softened, the optic commissure flattened and wasted	—
6	1878, M—, aged 40, P.-M. 45	There was a growth occupying the lateral and posterior columns of the medulla, pushing the olivary body aside. In the pons it lay on the right side, outside the normal structure. The 5th, 7th, 8th, 9th, 10th, 11th, and 12th nerves were involved in the growth	Glioma

n Intra-cranial Tumour.

r symptoms.	Other symptoms.	Period.	Notes.
discs were ob- ıring fits, when ɜcs were as red ɜst of the cho- outlines of the ıg invisible. The	Vomiting, giddiness, weakness of the arms and legs, headache, pain at the back of the neck, fits, complete deafness	18 months	—
'e large and tortuous" (Mr. Higgens). Towards the end of the illness the led almost entirely. Photophobia. The pupils were dilated but reacted. us. Diplopia. Left 6th nerve was paralysed			
ritis early in the ater the sight Right external was impaired, ıs, diplopia	Paralysis of the right side of the face, power of mastication imperfect, staggering gait, hearing imperfect, sickness, diminished sensation in the left side of the face, the tongue protruded towards the right, occipital and frontal headache	6 weeks	—
nt was blind in ɜs; the right ɜt and the left a r. Extreme neu- ı bright spots at No note of the 'ision. External us. The right ıs dilated and mall	Fits, paralysis of the right side, headache, earache, vomiting. The patient died in coma	3 months	—
ıeuritis or atro- ıe pupils were ɔd. The eyes ro- the right side; ɛy were drawn and to the left	Drowsy, right hemiplegia, mental confusion, difficulty in swallowing, speech affected. The patient died in coma	5 months	—
uritis of both tosis of the left ɔnvergent stra- Right pupil ɔntracted than	Drowsiness, intense headache. The patient died in coma	8 months	—
uritis present. t failed. Pupils to light and ac- ıtion	Neuralgia of the 5th nerve, paralysis of the soft palate, fits, right hemiplegia, which subsequently disappeared, partial facial paralysis side, noises d deafness, allowing	2 months	—

No.	Index.	Position.	Nature.
7	1885, Harry S—, aged 5¼, P.-M. 117, Reports 25, Mr. Durham	Mass in posterior fossa 1 in. in diameter, to which the under surface of the right lobe of the cerebellum was adherent. Softening of surrounding brain-tissue. The tumour was encapsuled, and pushed into the posterior part of the under surface of the cerebellum. Pons was adherent to the growth	Sarcoma, rour celled
8	1885, Margaret D—, aged 60, P.-M. 218, Reports 91, Dr. Pye-Smith	Right side of the brain distinctly bulging in the region of the posterior part of the 2nd and 3rd frontal convolutions. Size of the tumour 2¼ by 1¼ in. A horizontal section of the centrum ovale showed the tumour invading the internal capsule, lenticular nucleus, and part of the optic thalamus of the right side	Glioma, ?
9	1885, Caroline R—, aged 34, P.-M. 228, Reports 74, Dr. Pavy	A firm, flattened tumour, about 1¼ in. by ¾ in., lying in a bed it had pressed out for itself in the right side of the pons, the bulb, and the anterior half of the lower surface of the cerebellum. The pons below the tumour was completely flattened. The 5th nerve was pressed on, the 4th nerve was not implicated, and the 6th only just. All the rest were hardly distinguishable	Small round-c sarcoma
10	1885, Joseph B—, aged 50, P.-M. 317, Reports 99, Dr. Taylor	A large gliomatous tumour was found, occupying nearly the whole of the right frontal lobe, and destroying the anterior lip of the internal capsule. Both olfactory nerves and the surface of the brain-substance in their proximity were œdematous, especially on the right side. The tumour extended to within ¾ of an inch of the grey matter in front and to within 1¼ in. of the surface. Backwards it extended as far as the internal capsule, involving the lenticular nucleus and the two capsules for their anterior two thirds	Glioma

ılar symptoms.	Other symptoms.	Period.	Notes.
cornea sloughed. ction of the right Strabismus. No the optic discs	Facial paralysis on the right side. 5th, 7th, and 8th nerves were involved in the growth	Indefinite	Case of sarcoma of the naso-pharynx and tympanum fungating into the cranium, and involving part of the cerebellum. The main symptoms were, at first, difficulty of respiration, and, later on, difficulty in swallowing, both due to direct interference by the growth. There were no symptoms directly due to the pressure exerted on the cerebellum.
reacted to light ommodation. No mus. The optic ere not examined	Admitted for hemiplegia. Severe headaches, loss of power on the left side, which became a total hemiplegia, speech indistinct at times, some impairment of sensation in limbs, slight trace of albumen, difficulty in swallowing, Cheyne-Stokes' breathing	4 months	This patient showed no particular mental abnormality. Her trouble was mainly due to pain in the head, difficulty in deglutition and respiration. She died quietly
of the 6th nerve right side. Nyus on looking lly. No note of tic discs	Five years before her last illness the patient had complete deafness, which persisted, and 7th nerve paralysis on the right side. The right side of the tongue wasted. The palate was partially paralysed. The left arm and leg hemiplegic, and later the right arm and leg were affected. The right sterno-mastoid wasted. The vocal cords were paralysed. Tâche cérébrale	5-6 years	The patient died from lung trouble.
neuritis was well d on the right It was present in ft eye, but very — Dr. Brailey. [redacted] conjugate the	Fits, left facial paralysis, exaggerated reflexes. Loss of power in the left arm. The tongue deviated to the left side. Rigidity of the left leg and both arms. The patient was mentally confused. He passed and fæces under tory of C_2H_6O. coma	4 months ?	He passed into stupor for two months, which gradually increased.

No.	Index.	Position.	Nature.
11	1886, John W—, aged 36, P.-M. 49, Reports 80, Dr. Pye-Smith	Glioma of the right cerebrum. Right parietal lobe involved at the centrum ovale, just above the corpus callosum. The ventricles were not affected. The tumour was 2¼ in. in diameter and surrounded by yellow œdema. It was situated in the white matter of the parietal lobe; the anterior extremity of it corresponded with the fissure of Rolando, whence it spread backwards to within about 2 in. of the tip of the occipital lobe. Above it reached the surface in the superior parietal convolution, and below it corresponded to the upper surface of the corpus callosum	Glioma
12	1886, George R—, aged 17, P.-M. 264, Reports—C., Dr. Carrington	Three masses the size of a hazel-nut in the cerebellum. Two were placed symmetrically one on each side of the hemispheres, about the middle of the extreme outer part of the under surface; the other was in front of the vermiform process, just at its anterior extremity. Another mass in the medulla, on the right side, the size of a pea, occupied the median portion of the corpus olivare	Tubercle
13	1886, E. G—, aged 1, P.-M. 78, Reports 14, Mr. Howse	Multiple growths of the skull, etc., which invaded the brain. The occipital, frontal, and parietal lobes were involved. There was a large mass resting on the orbital plate of the frontal bone on the left side. The 1st and 2nd frontal convolutions were affected	Very vascular [illegible] celled sarcoma [illegible] ginating in [illegible] skull-bones
14	1886, J. W—, aged 35, P.-M. 245, Reports 15, Mr. Durham	A large, soft growth, which started in the left half of the basilar process and extended extensively downwards to the trachea, and produced the respiratory trouble from which the patient died. It extended also into the left cavernous sinus, destroying the nerves in that sinus, and apparently the carotid artery. The 6th, 7th, and 8th nerves were involved by the growth behind the sinus	The growth [illegible] composed [illegible] great number small round cells with strands spindle-cells forming a kind stroma. It was true sarcoma

ymptoms.	Other symptoms.	Period.	Notes.
itis in both well marked. ies were seen lisc	Left hemiplegia came on suddenly. Fits. Falling to the left side. Facial paresis on the left side. Knee-jerks were present. Headache on the top of the head. The tongue was drawn to the left side when protruded. Delirium and death in coma	6 weeks	—
s made of the e pupils were and dilated; ed to light. ernal strabis- left eye	Emaciation. The patient died of general tuberculosis. There was no medical report	14 days	—
or paralysis. of the optic	There were no brain symptoms. Wasting and drowsiness	2-3 months	The patient was thought to be tuberculous. There were growths in the lungs, abdomen, liver, etc.
were unequal. pil was double f the right; ght reacted to ation but not The eyes were by Dr. Brailey. eye complete a with irido- partial para- he muscles of pplied by the —that is,ptosis, f superior and ecti, and per- the inferior E. V. = $\frac{6}{6}$, = $\frac{6}{6}$, optic disc Large physio- ps present.	Pain in the neck. No headache. Swallowed with difficulty. The left side of the face was paralysed	8 months	The symptoms were mainly attributable to the extension of the growth down the neck.

No.	Index.	Position.	Nature
15	1886, Robt. M—, aged 42, P.-M. 123, Reports 87, Dr. Moxon	Tumour of the pons on the left side, involving the middle peduncle of cerebellum and the 5th and 7th nerve nuclei.	Glioma
16	1886, G. C. C—, aged 15, P.-M. 340, Reports 160, Dr. Moxon	A tumour involving the dura mater and bones of the base of the skull to the right of the basilar process and the sella turcica. It involved the basilar process, sphenoidal and ethmoidal cells, and the anterior part of the right petrous bone. It surrounded and pressed on the right cavernous sinus; extending across the skull, it involved the left anterior part of the left petrous bone. The under surface of the right temporo-sphenoidal lobe was also pressed on	Sarcoma
17	1887, Eliza B.—, aged 28, P.-M. 42, Reports 340, Clinical 340, Dr. Taylor	A tumour growing from the meninges in the right temporo-sphenoidal region, pressing into the brain-substance, but not infiltrating it. It was surrounded by a large area of softening, which invaded the lenticular nucleus. Size of the tumour ½ by 2 by 1¼ in.	Fibro and round-celled sarcoma
18	1887, Reuben D—, aged 39, P.M. 111, Reports, Clinical, 106, Dr. Hale White	The left hemisphere flattened and bulging. Left centrum ovale majus occupied by a growth measuring antero-posteriorly for about 3 in., and laterally for about 2 in., by the side of the corpus striatum. It approached to the surface superiorly and externally to within ⅜ in. The superior, anterior, and external part was converted into a cyst loaded with albumen. Recent hæmorrhage into the post part of the growth	Glioma

ular symptoms.	Other symptoms.	Period.	Notes.
optic neuritis n to atrophy. The 's sight failed '; the pupils were uently dilated and e. The right pupil 'ger than the left. of the right side. sis of the external on the right and f the 3rd nerve.	There was weakness of the right half of the mouth. The patient was drowsy and absent-minded. Vomiting. No pain or headache. Difficulty in swallowing. Constipation. The patient died quietly	2 months	—
ight eye looked down and in. Conjunc- sensitive. The left eye refused to go above rizontal plane. Later there was a double 'ent squint. The eyes oscillated indepen-			
Corneal ulcer The right ex- rectus weak. Dip- The pupils reacted t and accommoda- here was no defect on. Fields full. $\frac{9}{9}$ in each eye. both the external were weak, the ıore than the left. n the patient had)f vision, and both were atrophied. of the right side. sis of the right rve	Shooting pains in the head. Anæsthesia of the right half of the face. Drowsiness	10 months	—
neuritis of both Transient attacks lness, which lasted ıutes. The pupils :ontracted; they to light and ac- lation	The patient had had severe occipital headache for two years. Delirium, fits, coma, severe vomiting. The patient had granular kidneys and albuminuria	2 years	It was treated and diagnosed as a kidney case in the ward.
neuritis, more l in the left eye ome doubt of its ce ?). Dilated left Sight and ocular ents were good. tagmus, amauro- ıemiopia	Right hemiplegia, anæsthesia of the right arm and leg below the knee. Fit which lasted two hours, temporary loss of speech. The patient was dull and drowsy, slight aphasia. Paralysis of the 7th nerve on the right side. Anæsthesia of the right side of the face; e deviated to ide	3 weeks	The history of this case was doubtful, as it was obtained from the patient alone, who was not sufficiently alert to remember accurately.

No.	Index.	Position.	Nature.
19	1887, Grace J. S—, aged 4, P.-M. 237, Reports 105, Clinical, Dr. Hale White	Ventricles much distended. In each optic thalamus was a tuberculous mass larger than a marble. These two masses were joined together by a tubercular mass passing through the fornix and under surface of the corpus callosum; the whole was dumb-bell shaped. It pressed on the veins of Galen	Tubercle
20	1887, Charles L—, aged 10, P.-M. 329, Reports, Dr. Hale White	Caudate nucleus was much enlarged by the growth, which bulged in the left ventricle on the left side. The lenticular nucleus and all the nuclei on the left side were enlarged by the growth, which extended out to the claustrum, but did not reach the cortex. The internal capsule was softer and more destroyed in the posterior limb than the anterior, although this had not escaped. The upper part of the optic thalamus was affected. The cornuæ of the lateral ventricle were much dilated on both sides. The growth extended backwards beneath the anterior corpora quadrigemina, and extended to the posterior border of the posterior corpora quadrigemina, and just beyond into lateral part of the pons	Glioma
21	1888, Edw. M—, aged 4, P.M. 374, Reports, Mr. Howse	Tuberculous tumours were found in the brain, a large number of yellow nodules of various sizes on the left side of the cerebrum, especially numerous in the quadrate lobe. One was found in the right optic thalamus. Near both anterior and posterior cornuæ were large soft and diffluent masses of softening. Another mass was found above the corpus callosum. The internal capsule had escaped. The fluid in the ventricles was turbid. There was no general meningitis	Tubercle
22	1888, Michæl C—, aged 43, P.-M. 399, Reports 61, Clinical, Dr. Pavy	(1) Tumour in the grey matter at the posterior part of the left frontal convolution. Size $\frac{1}{3}$ in. (2) A large tumour in the under surface of the right temporo-sphenoidal lobe, but no other gumma or softening seen. Some thickening of meninges in the outer peduncular space	Gumma

ular symptoms.	Other symptoms.	Period.	Notes.
e made of the con- of the optic discs. t. Ptosis of the side.	The patient was sick, drowsy, and cried during sleep. Left 7th nerve paralysed. Temp. 102°. Rigidity of the right leg. Ataxy	10 days	The child was always feeble, and had never learnt to talk. When admitted she was irritable and drowsy. Patient was trephined, and aspiration of the ventricles performed. Some right hemiplegia after the operation. Patient only lived a few days.
igmus, squint, ptosis, double neuritis	Tremors, complete paralysis of the right arm, and paresis of the right leg. Aphasia, dysphagia, paresis of the right 7th nerve, sickness, incontinence. Death by syncope	17 months	—
te made of the op- ics. The left pupil ilated and fixed. eft 6th nerve was ed	General convulsions. Cheyne Stokes' respiration. The patient died in coma	4 months	The patient had had the right hip excised for tuberculous disease.
of the right side. le optic neuritis marked. Pupils ed to light and ac- odation and were small. Paresis of 3th nerve on the side	Left hemiplegia. Paralysis of the 7th nerve. Headache in temporal region. Syphilis in 1872. No sickness	Indefinite	—

No.	Index.	Position.	Nature.
23	1888, Havel C—, aged 8, P.-M. 240, Reports 60, Dr. Goodhart	A tuberculous mass the size of a hazel-nut was on the right side of the brain, lying on the under surface of the pons, close to its posterior border and pressing on the auditory and facial nerves at their origin from the medulla oblongata. A similar mass lay beneath the amygdala of the cerebellum on the left side	Tubercle
24	1889, Fanny B—, aged 66, P.-M. 101, Reports 111, Dr. Pavy	Tumour in the right occipital lobe half an inch in diameter and about the size of a pigeon's egg. It infiltrated the surrounding tissue and extended forwards to the level of the genu of the internal capsule. Behind, it pressed on the descending part of the lateral ventricle, which was dilated with glairy fluid	Glioma
25	1889, William R—, aged 56, P.-M. 448, Reports 112, Dr. Pavy	The lateral ventricles were dilated, especially the left. In a horizontal section of the brain the tumour first became visible at the level of the superior temporo-sphenoidal convolution on the right side. It was external to the lateral ventricle, extending behind level with the posterior cornu and forwards as far as the middle of the cavity. Below it projected into the under surface of the temporo-sphenoidal lobe	Sarcoma, with many round and fewer spindle cells and a good deal of necrosis
26	1889, Ellen P—, aged 14, P.-M. 412, Reports 113, Dr. Pavy	Cerebellar tumour the size of a walnut occupying the left lateral hemisphere at its upper and front part, and invading the corpora quadrigemina at its post part. The veins of Galen were evidently obstructed. The lateral ventricles were much dilated, and about one pint of cerebro-spinal fluid escaped on removing the brain	Glioma
27	1889, Henry K—, aged 33, P.-M. —, Reports 111, Dr. Goodhart	Cerebellar tumours on the left side. The ventricles were greatly distended with fluid. The foramen of Munro would admit the little finger. Soft growth almost entirely replacing the left lobe of the cerebellum. Autopsy not made in Guy's Hospital	Glioma (?)

ar symptoms.	Other symptoms.	Period.	Notes.
"Optic disc in of moderate on." Later: l optic neuritis eyes. Left in- rabismus. Nys-	Discharge from the right ear. He was trephined for abscess over the tem- poro-sphenoidal lobe and also over the cerebel- lum, but without result. Marked evidence of intra-cranial pressure at the operation. Wasting. Headache. Dull and apathetic condition. Hernia cerebri. Cheyne-Stokes' respiration. The patient died quietly	"For a few weeks"	—
ls were equal in 'he left reacted dly to light, and t in the left eye ctive. No note phthalmoscopic ice	Fits. Thrombosis of the veins of the leg. Loss of power in the left side, arm, leg, and face, and also sensation on the left side. Knee-jerks, etc., present. Coma	13 months	—
itis or atrophy. symptom noted ctive sight. Note Medical Regis- here was no optic The patient with either eye. im for hemianop- could obtain no of its presence." pupil was larger right, and they sluggishly	Fits. Headache. Left hemiplegia, affecting the arms and face only. Jerks present	5 months	—
of both eyes, on to atrophy. ht side was con- nd blurred round s and somewhat being greyer in nd not so white left. Left optic ite, with con- arteries	Headache. Extreme anæ- mia. Vomiting. Giddi- ness. Knee-jerks and wrist-jerks all present	7 months	There had been appar- ently recent hæmor- rhage into the tumour.
euritis with re- æmorrhages in s. The pupils re- light and ac- ation; the left little larger and uggish than the Swelling of the ics. The fields of ere taken with a er and were full. tient was blind e died	Headaches. Vomiting. Plantar reflex. Wrist- and knee-jerks brisk. Abdominal reflex on the left side feeble. No ankle clonus	14 months	—

No.	Index.	Position.	Nature.
28	1890, Henry A—, aged 31, P.-M. 434, Reports 117, Dr. Goodhart	Tumour in the frontal region on the right side. The mass left after the operation was attached to the longitudinal sinus at the upper portion of the ascending frontal convolution. The deficiency in convolution extended posteriorly to the fissure of Rolando, below to 1¼ ins. of the ascending frontal convolution, and was 2¼ ins. in antro-posterior diameter. No note was made as to whether the ventricles were distended or not.	Spindle-cell sarcoma
29	1890, Samuel Y—, aged 44, P.-M. 470, Reports 118, Dr. Pye-Smith	The left temporo-sphenoidal angular and supermarginal regions were much enlarged and softened. An irregular, nodular, tough, caseous mass ran transversely and abutted on the lenticular nucleus, near part of the optic thalamus. It was found reaching the surface at the posterior part of the 3rd temporo-sphenoidal convolution. The growth was nowhere near the internal capsule or the crus, and the right hemiplegia was probably due to œdema or pressure on one of these. There was some fluid in the subarachnoid space	Glioma
30	1890, George F—, aged 40, P.-M. 94, Reports 119, Dr. Shaw	A cyst the size of a billiard ball in the right temporo-sphenoidal lobe; it lay within the anterior half, and was covered by a lamina of white and grey matter about half an inch in thickness. The ventricles were slightly dilated	Simple
31	1891, John P—, aged 40, P.-M. 183, Reports 74, Clinical, Dr. Shaw	In the right cerebral hemisphere towards the frontal lobe were two cysts with smooth walls; they did not communicate with each other. The brain around was gliomatous. The cysts measured 1¼ in. by 1 in., and ¾ by ⅝ in.; they were filled with pale straw-coloured fluid	Glioma
32	1891, Emily Caroline M—, aged 6 months, P.-M. 120, Reports 165, Dr. Perry	A tumour close to the tip of the right temporo-sphenoidal lobe; it was the size of a walnut	Round-celled sarcoma

lar symptoms.	Other symptoms.	Period.	Notes.
euritis of both th exudation and streaks. Marked ; of the right isc. Pupils un-	Loss of power in the left arm and leg. Facial paralysis on the left side. Left spastic hemiplegia. Intense headache	2 years	The patient was trephined and part of a tumour removed from the right frontal lobe. He died from erysipelas one week after the operation. The patient had less pain and was brighter and more intelligent for the few days he lived after the operation
optic neuritis. ›ils were unequal, ıt being smaller e left and not re- ›o light. Left in- ;rabismus noticed e operation, limi- ›f movements to ıt side. With the er some defection ields was noticed, ing to partial ɜmianopia	Symptoms mainly suggested G.P.I., with ideas of wealth, etc. Temporary loss of memory. Knee-jerks increased. Fits. Slight paralysis of the 7th nerve	6 months	The patient was trephined over the frontal bone on the left side. The bone was removed and the dura mater opened. Brain bulged, tension great. Nothing found at the operation. The patient was brighter and more alert after the operation, but still had headache. The patient lived one month after the operation.
optic neuritis, æmorrhages and patches. When ient was first ex- the pupils were ly contracted; hey became di- the right pupil ger than the left. ıystagmus	No paralysis or anæsthesia. Slight vomiting. Headache. Partial loss of taste. Knee-jerks present. Hallucination of smell. The patient died in coma	12 months	—
›ils were unequal ıted, and did not › light. No note ›ptic discs	No paralysis detected. Pulse 52. Knee-jerks exaggerated. Coma	?	The patient was brought to the hospital in a comatose condition and died shortly afterwards.
neuritis noticed, pils reacted to	Some rigidity and then weakness of the left arm and leg. Fits. Vomiting	14 days	The patient died of suppurative meningitis following otitis media, and Dr. Perry found the tumour during the course of the post mortem; its existence had not been suspected during life. "The tumour had nothing whatever, I think, to do with the meningitis."

No.	Index.	Position.	Nature.
33	1891, John P—, aged 19, P.-M.384, Reports 106, Dr. Hale White	The left side of the cerebrum from the frontal lobe to the occipital lobe appeared softened and infiltrated by a soft growth. It was impossible to localise the tumour. Only the basal half of the hemisphere appeared affected. The external capsule and basal ganglia were affected	Glioma?
34	1892, Herbert H—, aged 5, P.-M. 400, Reports, Mr. Lucas	The lateral ventricles were dilated. The cerebellum was distended by a large cyst, which did not communicate with the 4th ventricle. The iter and 4th ventricle were not distended. The foramen of Majendie was patent. The cyst invaded the left half more than the right; it pressed on the veins of Galen, and so led to hydrocephalus	Cyst
35	1892, Thomas G—, aged 4, P.-M. 27 *a*, Reports 79, Dr. Taylor	Tumour in the right lobe of the cerebellum, visible mainly on the inferior surface. Size 3 by 2¾ by 1½ in. There was much fluid found in the ventricles. The tumour extended across the middle line for ½ inch and pressed on the pons and medulla. The foramen of Majendie closed by pressure. The veins of Galen pressed upon	Tuberculous caseating ma
36	1892, James C—, aged 26, P.-M. 67, Reports 78, Dr. Taylor	On the under surface of the left lobe of the cerebellum there were masses of growth, forming together an irregular mass 1½ by ½ in. The ventricles were much dilated by the pressure on the foramen of Majendie and the veins of Galen	Gumma
37	1892, George P—, aged 56, P.-M. 463, Reports 89, Dr. Goodhart	Cerebral tumours. Between the frontal lobes, just in front of the corpus callosum, and constituting an abnormal commissure between the cerebral hemispheres, was a firm mass of growth. On sect it was found to be almost entirely on the left side, and first volved the anterior wall of lateral ventricle on this side. second tumour lay beneath the level of the corpus callos corresponding to the white tissue beneath the supra-marg and the 1st and 2nd temporal gyri, invading only the o edge of the lenticular nucleus. This mass was 1½ in. tr versely and rather less in the other diameters	Glioma

lar symptoms.	Other symptoms.	Period.	Notes.
s, advanced in the and early in t eye. Internal The patient had ive involvement ular muscles on side; later both rnal recti were d. Partial right psia. The pupils ated and fixed	Right hemiplegia, headaches, fits, knee-jerks present, paralysis of the facial muscles, coma	5 months	—
h nerves were d. Optic neuritis eyes, followed phy. Internal us of the left No nystagmus. lilated	Headache, vomiting, fits, left leg and arm rigid, paresis of the left side. The head was enlarged; it was trephined over the fissure of Rolando but the dura mater was not opened. Later, the right leg was noticed to be drawn up, facial twitchings. Trephined again and the lateral ventricles drained. Knee-jerk on right side diminished, on left side increased	5 months	After the commencement of the illness the patient was quiet and stupid; memory weak; shaky and tottery in walking; incontinence of urine and fæces. Died from suppurative meningitis.
optic neuritis. pils were widely at the end of the Paralysis of the rnal rectus. Con- strabismus. paralysis of lev. erioris and supe- us on each side	Unsteady gait and increasing ataxia, vomiting, emotional fits, incontinence of urine and fæces, knee-jerks absent for five weeks before death	12 months	The optic nerves on section showed a large amount of cell-infiltration, with engorgement of perivascular spaces.
uritis was not on the first exa- ; it was noticed months before d was then very rked, with exu-	Numb feeling in the upper lid, sickness, headache in the frontal and occipital region, knee-jerks present but not marked	6 months	The patient died suddenly from cardiac syncope. The most marked symptom was headache.
optic neuritis, rked in the left right eye, with tches. The pu- re dilated and	Pins and needles in the fingers, paresis on the left side, incontinence of urine and fæces. Constant headache, drowsiness, fits, knee-jerks absent, plantar reflexes present, no vomiting	3 months	The very general nature of the symptoms precluded the idea of surgical interference.

No.	Index.	Position.	Nature
38	1893, Alfred E—, aged 16 months, P.-M. 484, Reports 29, Dr. Hale White	Two large nodules of firm caseous material, ½ in. across, were found on the anterior and left part of the cerebellum, and a third, still larger, occupied the greater part of the pons. This left a mere trace of nervous tissue, less than $\frac{1}{16}$th in. thick, on the posterior surface, and rather more on the anterior. The mass was more than an inch long, but did not extend as far as the medulla. No meningitis and no tubercles were seen on the surface of the brain	Tubercu
39	1893, Eliza L—, aged 51, P.-M. 81, Reports 12, Mr. Golding-Bird	Tumour in the right occipital lobe; it was oval in shape, and measured 1 by 1¼ in. It had a distinct fibrous capsule which could be peeled out. The white matter alone formed the hollow in which the tumour lay, and it probably grew from the meninges	Glioma, havin with many t
40	1893, Robert V—, aged 20, P.-M. 377, Reports 350 Clinical, Dr. Pitt	The base of the skull was infiltrated by a mass a little more than 1 in. from side to side, which began at the middle of the anterior fossa and spread more to the right than to the left side; it extended back to the margin of the foramen magnum. The growth was continuous with a naso-pharyngeal sarcoma. The right optic nerve, the olfactory nerve, and the 3rd nerve were all much involved in the growth, and were apparently considerably pressed on	Round- and spi celled sarcon
41	1893, William B—, aged 52, P.-M. 384, Reports 69, Dr. Taylor	A cyst the size of a tennis ball occupied the right temporo-sphenoidal lobe, with evidence that the pressure extended to lenticular nucleus and the internal capsule	Cyst with sarc tous wall ; sm round cells
42	1894, M. C—, F., aged 34, P.-M. 36, Reports, Dr. Hale White	Aneurysm, ⅞ by ½ in. in diameter, growing from the left external carotid just before its bifurcation. It pressed on the 3rd nerve and lay at the side of the posterior communicating artery, without implicating it. Sinuses healthy	Aneurysm

symptoms.	Other symptoms.	Period.	Notes.
notes of this	Emaciation, general tuberculosis	3 months	—
the eye con- he report	Headaches, weakness	—	The patient had a scirrhous tumour removed from the right breast 1 week before death. The pulse failed after the operation, but cerebral condition was not suspected until after death had occurred.
the right optic little evidence ling neuritis. were slightly and tortuous. rhage or exu- al blindness of t eye. Mr. ported that the was white and atrophic. Pto- ight side. The acted to light ccommodation al ?)	Bleeding from the right nostril, later occlusion of both nostrils. Loss of flesh, weakness, etc., headache, giddiness, drowsiness. The patient slept in the day as well as at night	21 months	—
otic neuritis in s, evidence of and hæmor- he retina. The re contracted l, and did not ght	Left hemiplegia. Fits, restlessness, excitability, headaches, incontinence of urine and fæces, coma, death	5 months	—
disc hyper- a little indis- iplopia, ptosis eft side, left strabismus. paralysis of the nve. No reac- to light	Fits, headache, sickness, retraction of the head. The patient died from rupture of the aneurysm	3 weeks	There were no symptoms at all before the three weeks that preceded death. Case reported in 'Clin. Soc. Trans.,' vol. xxviii, 1895.

No.	Index.	Position.	Nature
43	1894, Louisa D—, aged 30, P.-M. 386, Reports 280, Dr. Goodhart	Nodules of growth found scattered about in the dura mater. A mass of growth the size of a thrush's egg loosely attached to the inner side of the dura mater, lining the anterior part of the outer surface of the middle fossa, and pressing laterally on the anterior part of the outer surface of the cerebellum. There was much cerebro-spinal fluid; the pineal gland was large. There was another irregular nodulated mass of hard, yellowish-white growth about the size of a large walnut in the anterior and under surface of the right lobe of the cerebellum, which had laterally caused pressure on the medulla. The tumour appeared to have arisen from the pia mater and not from the brain itself	Large round sarcoma
44	1894, Henry A—, aged 9 months, P.-M. 109, Reports 143 Clinical, Dr. Goodhart	Several tuberculous masses as large as peas in the cerebellum. The lateral ventricles were large, and contained some fluid. There was tuberculous meningitis	Tubercle
45	1894, John M—, aged 11, P.-M. 284, Reports 112, Dr. Pye-Smith	A tumour measuring 3 by 2 by 1½ in. on the left side of the cerebrum, above the caudate and lenticular nuclei in the frontal lobe; the tumour occupied the left ascending frontal and superior frontal convolutions, and on the inner surface occupied the marginal and callosal convolutions. There was no meningitis or phthisis	Tubercle
46	1894, Florence H—, aged 5, P.-M. 410, Reports 348, Dr. Hale White	A few small nodules of growth were found on the under surface of both temporo-sphenoidal lobes. In the right lower border of the cerebellum were found growths, one as large as a pea and another as large as a cherry, which partially excluded the iter. The spina was invaded at the junction of the middle and lower thirds. The ventricle enlarged and distended with fluid	Round and celled sarc

,r symptoms.	Other symptoms.	Period.	Notes.
The right 6th s affected. In- ›ptic neuritis. ›ils reacted well and accommo- ınd were equal. s. Paralysis of t external rec- vergent squint, velling of the The fields of ›re full	Headache, vomiting, fits, loss of flesh, speech slow, hearing defective on the right side, memory for words defective. Incoordination and loss of power in the right arm. The patient dragged her feet in walking. Movements of the neck slow and difficult, no 7th nerve trouble. Superficial and deep reflexes exaggerated. Defective taste on the right side of the tongue, difficulty in passing water, lost power in the right leg, coma	8 months	—
›he pupils were ıey did not react and accommo- no conjunctive ' A poor view of s was obtained ıe after admis- d they seemed ıt the edges and els were some- tuous, but there ıufficient ground ıiagnosis of neu- ystagmus later	Pain, fits, hydrocephalus, bulging fontanelle, Cheyne-Stokes' breathing, coma, rigidity of limbs. Aspiration performed at the right angle of the anterior fontanelle and 2-3 oz. of fluid were removed; the child's condition immediately improved. "He opened his eyes and moved his arms; the pulse and respiration improved and the pupils reacted to light"	14 days	The child died from general tuberculosis.
uritis followed hy. Slight nys- ıt the end of the slight internal Corneal ulcer of ›ye	Sickness, headache, right hemiplegia, numbness on the right side, loss of speech, loss of control over sphincters, head enlarged. The patient was trephined and a large hernia cerebri resulted. The patient died two days later	19 months	—
uritis was well paralysis of the rnal rectus; the ere dilated; in- ıuint	Headache, fits, vomiting, loss of sensation in the right leg, plantar and knee reflexes absent, chronic hydrocephalus. The child died after a succession of fits	2½ months	—

No.	Index.	Position.	Nature.
47	1894, Mabel B—, aged 9, P.-M. 473, Reports 324, Dr. Hale White	A hard growth encircling the iter, midway between the anterior and posterior border of the pons. The lateral ventricles were much distended	—
48	1894, Jane R—, aged 9, P.-M. 36, Reports 26 Clinical, Dr. Pye-Smith	A tumour the size of a pigeon's egg, visible in the interpeduncular space; it involved the left optic nerve, which was thickened. The right optic nerve was also pressed on. It bulged above into the floor of the 3rd ventricle in front of the corpora quadrigemina. Both lateral ventricles were distended	Glioma
49	1894, Jesse G—, aged 24, P.-M. 282, Reports 149, Dr. Goodhart	Several small yellow tubercles were scattered through the cerebrum on both sides of the brain. There was a mass the size of a pea on the left side just posterior to the Island of Reil, and a smaller one in the corresponding position on the right side. Slight excess of fluid in the ventricles, the anterior and posterior cornuæ being dilated. There were also three large caseous masses in the cerebellum, and a mass the size of a pea in the pons	Tubercle
50	1895, Mary S—, aged 33, P.-M. 96, Reports	The anterior quarter of the left frontal lobe was occupied by a cyst, the size of a golf ball, containing a clear watery fluid with no deposit. The wall of the cyst appeared to be healthy brain-substance, being of the normal colour and consistency. The upper and outer part of the cyst reached the surface and was bounded only by pia mater over an area about the size of a sixpence	Cyst
51	1895, Joseph [illegible] aged 40, P.-M. 329, Reports [illegible] Dr. Goodhart	A tumour at the base of the brain in interpeduncular space [illegible] corpora [illegible] and pituitary [illegible] On the [illegible] appearance [illegible] cherry, [illegible] dental [illegible] 21 by [illegible] corpora [illegible] the [illegible]	?

ar symptoms.	Other symptoms.	Period.	Notes.
uritis present in eye; atrophy of t eye. The right sloughed at the he illness	Vomiting, ataxy, headache, left hemiplegia, fits with rigidity, left 7th nerve paralysed, convergent deviation to the right during the fits. Knee-jerks absent on the left side and diminished on the right. Hydrocephalus	16 months	The patient's father died at the age of 40 from cerebral tumour.
(?) going on to . The patient ite blind. The vere dilated and react to light. ception of light. nystagmus. The s came on very d it is not clear dition of the atrophy or not	Fits, extreme vomiting, opisthotonousheadaches, weakness of the legs, knee-jerks present on the left side only and diminished	4 months	—
optic neuritis, adation and hæge. No hemian- With the peri- he fields of vision ll. The pupils ated and reacted Photophobia	Vomiting, giddiness, loss of power in the legs and hands, noises in the ear, headaches, taste affected ("everything tastes nasty, even water"), knee-jerks present	5 months	The patient died of general tuberculosis.
ion made of ocu- ptoms in report	Fits. No albuminuria. The patient was 5 months pregnant; she developed fits, which were preceded by a "cry." Labour was induced by puncture of the membranes, but the patient died shortly after the birth of a child	—	The patient has a brother sufferingfrom epilepsy
dhart, on two examinations, nothing amiss discs. The l at first, re di- Th	Weakness in the legs and pains in the back and forehead. Headaches and sickness. Knee-jerks and ankle-clonus absent	5 months	The patient was very quiet, slow to apprehend, and had a vacant look in the eyes.

No.	Index.	Position.	Nature.
52	1895, Charles G—, aged 5, P.-M. 395, Reports 509 Clinical, Dr. Taylor	A tumour the size of a walnut occupied the median line of the under surface of the cerebellum, which was in contact with the medulla. The lateral ventricles at the right posterior cornua were 1 in. across	Round-celle sarcoma
53	1895, Ed. C—, aged 17, P.-M. 433, Reports 2, Dr. Taylor	The right lobe of the cerebellum contained a cyst 4½ in. across. In the posterior cyst-wall was a small rounded tumour the size of a walnut. The cyst pressed on the anterior part of the 4th ventricle. The lateral ventricles were much dilated	—
54	1895, Samuel F—, aged 52, P.-M. 49, Reports 35, Dr. Goodhart	A large tumour, mainly in the corpus callosum, which grew from the choroid plexus and extended more to the right than the left side of the brain and higher on the right. The growth ran down the floor of the lateral ventricle on the right side, invading the hippocampus major	—
55	1895, Will. J—, aged 9, P.-M. 134, Reports 114, Dr. Hale White	Tumour seen on the under and median surface of the cerebellum, slightly more on the left side than the right. It was bounded on the anterior side by the pons. It pressed on the posterior part of the 4th ventricle, and the lateral ventricles were distended	Glioma
56	1895, Susan L—, aged 59, P.-M. 326, Reports 638 Clinical, Dr. Pitt	A cerebral tumour in the non-motor part of the brain. The left temporo-sphenoidal lobe was occupied by a large growth, 3¼ by 2 by 1½ in., which extended forwards to the island of Reil. The left occipital region was invaded, also the wall of the descending cornua of the lateral ventricle. Some turbid fluid in the ventricles	Glioma
57	1895, Daisy M—, aged 11, P.-M. 482, Reports 508 Clinical, Dr. Taylor	A large number of tuberculous tumours were attached to the under surface of the dura mater, and projected into the cerebellar fossa and the posterior end of the falx. Small tuberculous masses were found invading the brain everywhere, but more especially the cerebellum. No meningitis or recent tubercle in the brain. Some distension of the lateral ventricles at the post mortem, extreme at the time of the operation	Tuberculous

cular symptoms.	Other symptoms.	Period.	Notes.
ıarked optic neuri- both eyes. The reacted to light ccommodation, and qual	Vomiting. Intense pain in the head and ataxia. Drowsiness. Pain about the left supra-orbital and frontal regions. Knee-jerks brisk	1 month	—
neuritis followed rophy. Dilatation ils and nystagmus	Fits, headache, vomiting not severe, no knee-jerks. The patient's intellect was impaired and his head became enlarged while in the ward	2–3 years	—
neuritis of both the right pupil than the left. Hæ- age on the right Divergent squint, ight eye turning	Vomiting, fits, headache, disordered sense of smell	—	—
optic disc atro- Left optic disc ic. Later both atrophied. Pupils dilated. Nystag-	Headache, vomiting, inability to walk, no fits, drowsiness, no knee-jerks obtained	4 months	The patient was trephined and died 10 days later. The bone was removed and the dura mater opened; hernia cerebri resulted. The patient's sight remained the same after the operation, but the headache was better.
d neuro-retinitis, xudation and hæ- ages (seen in the). Incipient catar- a both eyes, and so s not seen in life	Vomiting, fits, loss of intelligence and memory, melancholia. Died in coma	5 months	—
neuritis of both going on to atrophy. of the left upper	Giddiness, vomiting, severe headache, loss of flesh, knee-jerks were exaggerated, weakness of the right arm and leg	5 months	The patient was trephined over the parietal eminence without much result; but the headache was better. Large hernia cerebri, little or no pyrexia, severe attacks of delirium. The patient sat up and drank some water within a few hours of the operation.

No.	Index.	Position.	Nature.
58	1896, Bessie G—, aged 15, P.-M. 392, Reports 334, Dr. Washbourn	A tumour weighing 8¼ oz. just to the right of the median line and to the right side of the falx cerebri. It arose from the pia arachnoid, and covered the quadrate and cuneus lobes. The posterior part projected between the posterior extremities of the hemisphere; anteriorly it extended to the corpus callosum	Small round-c sarcoma
59	1896, Isabel P—, aged 29, P.-M. 450, Reports 535 Clinical, Dr. Taylor	A tumour situated at the tip of the right temporo-sphenoidal lobe, spreading to the frontal lobe and the greater portion of the temporo-sphenoidal lobe. It was a large lobulated tumour, the greatest diameter being 5½ in.	Myxo-sarcor
60	1897, Ethel H—, aged 8, P.-M. Reports 4, Dr. Taylor	An abscess on the left side of the frontal lobe	*Staphylococcus genes citre*
61	1897, W. H. P—, aged 19, P.-M. 49, Reports 28, Dr. Pye-Smith	A small tumour rather to the left of the mid-line, in the left lobe of the cerebellum. It was the size of a walnut, and it hung over the roof of the 4th ventricle, and obstructed the foramen of Majendie. There was an excess of cerebro-spinal fluid present	Glioma
62	1897, Eliza W—, aged 8, P.-M. 104, Reports 25, Dr. Taylor	A large mass in the outer and under surface of the cerebellum. A mass the size of a cherry in the right temporo-sphenoidal lobe. A caseous mass the size of a walnut in the left side of the pons	Tubercles
63	1897, James D—, aged 45, P.-M. 37, Reports 42, Dr. Pye-Smith	A large globular mass of growth on the left side of the anterior frontal lobe of the brain. It was not visible on the surface, but was in contact with the inner surface of the right frontal lobe. Also a breaking-down growth substance in the lateral ventricle	Sarc

ılar symptoms.	Other symptoms.	Period.	Notes.
neuritis of both ith hæmorrhages xudation. The ; was blind on ad- ı. The pupils of ɜs were dilated	Frontal headache, hearing affected, knee-jerks exaggerated on the right side, weak on the left, vomiting	7 months	—
arked optic neu- both eyes. The were dilated and l to light. Slight mus on lateral ent	Frontal headache, going to the right side and then to the back of the neck, no vomiting or paralysis, changed mental condition, giddiness and staggering gait. The patient died in coma	3 months	—
neuritis of both ith hæmorrhages xudation. The were equal and	Coma, vomiting, fits, wasting, frontal headache, slow pulse, knee-jerks were exaggerated, *tâche cérébrale*	—	The patient was trephined and the abscess opened and drained, 3 to 4 oz. pus. The pulse rose at the operation from 60 to 150, and the breathing improved markedly in a few minutes. The patient subsequently left the hospital.
is of both eyes. tient was blind	Headache, vomiting, giddiness, with a tendency to fall to the left side, loss of power in the limbs, knee-jerks absent	12–14 months	—
neuritis of both The left pupil was than the right. uted strabismus h nerve). Nystag- Ulcer of the left Conjunctivitis	Left facial paralysis, fits, affecting the left side of the face and the left arm and leg, ataxia, difficulty in swallowing, nasal voice, staggering gait, tremors, the tongue deviated to the right on being protruded, knee-jerks normal	—	—
neuritis present. unequal	Pain in the head, loss of memory, frontal and occipital headache, vomiting and drowsiness in the latter half of the illness, staggering gait, increased reflexes, incontinence of urine, etc., coma	3 months	—

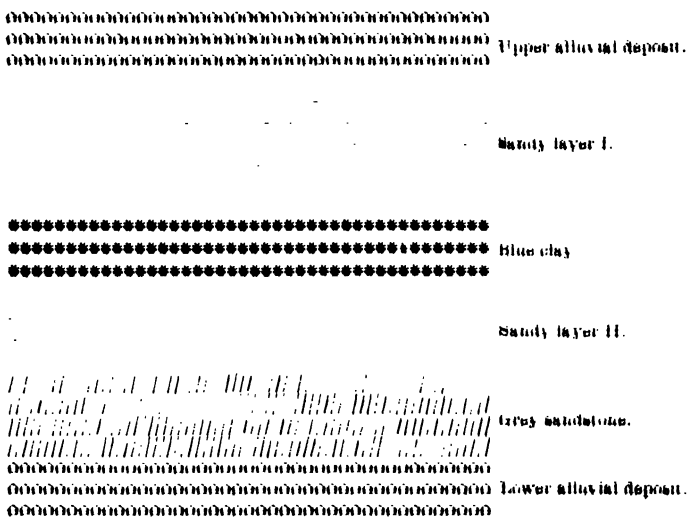
No.	Index.	Position.	Nature.
64	1897, Lucy K—, aged 56, P.-M. 177, Reports 164, Dr. Hale White	There was glioma, the size of a hazel-nut, in the hinder part of the left ventricular nucleus, and behind it was an area of softening. Tumour at the hinder end of the left lenticular nucleus	Glioma
65	1897, Esther P—, aged 34, P.-M. 318, Reports , Mr. Higgens	An oval tumour 2½ by 3 in. beneath the under surface of the frontal lobes; it was attached by a slight pedicle in front of the Sylvian fissure, and was adherent to crista galli and the cribriform plate	?
66	1897, Henry J. S—, aged 40, P.-M. 357, Reports 315, Dr. Pye-Smith	A tumour 1 by 1½ in. situated under the 1st temporo-sphenoidal and ascending parietal convolutions on the right side of the cerebral hemispheres. Only the white matter was affected	Glioma
67	1898, Eliza W—, aged 54, P.-M. 262, Reports 219, Dr. Goodhart	Numerous nodules of growth on the left side of the cerebrum. In the cerebellum a nodule 2½ in. in diameter, which affected both sides, but the left more than the right	—
68	1898, Julius B—, aged 38, P.-M. 389, Reports 349, Dr. Goodhart	A tumour which affected the anterior horn of the lateral ventricle on the right side; it extended across to the ventricle on the left side, but did not open that. It pressed on the olfactory lobe and the right optic nerve. Dilatation of the ventricles	Sarcoma
69	1898, Jas. S—, aged 56, P.-M. 48, Reports 70, Dr. Pye-Smith	A tumour, 2⅞ × 2¾ × 1¼ in., on the right side of the cerebral hemispheres. It occupied the occipital lobe and the posterior part of the parietal and temporal lobes. It appeared on the surface and the dura mater was adherent to it	Endotheliom

ar symptoms.	Other symptoms.	Period.	Notes.
ent died shortly lmission to the , and no note in the reports as cular condition	Loss of power in the right leg and arm, aphasia, loss of memory, incontinence of urine, no vomiting. The patient died in collapse, no coma	23 weeks	Phthisis in both apices.
euritis of both The patient was	Slight vomiting, fits	—	—
uritis in the right e left eye was not ed. The pupils to light and ac- lation	Left hemiplegia, fits, incontinence of urine and fæces, left 7th nerve affected, knee-jerks present; the patient's mind was confused, he died in coma	2-3 months	—
euritis of both he pupils reacted and accommoda- Nystagmus	The primary site of growth was in the lower jaw, from which a tumour was removed five years previously, and some recurrent growths. Headache in the occipital regions. Giddiness, vomiting	3 months	—
euritis of both with exudation. ils were unequal, it larger than the	Knee-jerks absent. Vomiting, tremors, ataxia, frontal headache. No anæsthesia. The patient could not walk or stand alone. He died in coma	6 weeks	—
e sight. The were equal and to light and ac- lation. The visual ere limited when by a perimeter. ystagmus. The appeared opaque. tient was hyper- hic	The patient was under Dr. Hale White in July, 1897, for myxœdema. He was unable to walk, suffered from headache, loss of memory, and depression. There were intervals of recovery. Bladder and rectum trouble. Weakness of the legs and hands. Increased knee-jerks. Deafness in the left ear. Smell and taste normal	2½ years	—

No.	Index.	Position.	Nature.
70	1898, Anne R—, aged (?), P.-M. 92, Reports 14, Dr. Pitt	A tumour the size of a finger which projected into the iter; it adhered slightly to the roof of the 4th ventricle, and extended as a thin layer of vascular growth over the upper surface of the right superior peduncle. The tumour measured $\frac{7}{8}$ of an inch antero-posteriorly, and extended one inch to the right of the middle line and half an inch to the left. There was some excess of cerebro-spinal fluid, with distension of lateral ventricles	Sarcoma
71	1898, Arthur K—, aged 30, P.-M. 93, Reports 4, Dr. Taylor.	A mass, 3 × $1\frac{3}{4}$ × $\frac{3}{4}$ in., was found in the anterior part of the caudate and lenticular nuclei, involving the cortex on each side in the median line. The growth extended down to the inferior surface of the brain, becoming apparent immediately anterior to the optic commissure. It pressed on the 3rd nerve. The anterior cornua of the lateral ventricles were slightly distended, but not the posterior cornua	Glioma
72	1898, Martha B—, aged 16, P.-M. 374, Reports 388 Clinical, Dr. Pye-Smith (Miriam)	Degenerated cystic tumours of the right internal capsule. Breaking-down glioma at the posterior part of the internal capsule, with a cavity therein 1 × $\frac{3}{4}$ × $\frac{1}{4}$ in. The lenticular nucleus and optic thalamus were slightly involved	Glioma
73	1898, William R—, aged 18, P.-M. 409, Reports 276, Dr. Taylor	A pontine tumour. The posterior part of the pons dorsal surface was infiltrated with growth. The growth occupied the anterior half of the 4th ventricle	Glioma
74	1899, George L—, aged 37, P.-M. 456, Reports 412, Dr. Hale White	A tumour the size of a tangerine orange which pressed on but did not invade the base of the frontal lobe. It was chiefly on the left side, and apparently grew from the dura mater in front of the sella turcica. The ventricles were much distended. P. M.—Septic destruction of the right parietal lobe	Spindle-cel sarcoma

ılar symptoms.	Other symptoms.	Period.	Notes.
arked optic neu- both eyes, going trophy	Vomiting, giddiness, pains in the head, weakness of the legs, incontinence of urine. The patient was restless, talkative, and had delusions. She refused her food	—	—
neuritis of both leading on to y. Slight ptosis left side. The pupil was larger ıe left. Both were	Headache, mental derangement, weaknes sand wasting, vomiting, incontinence of urine, slight rigidity of the limbs, and inability to walk. Exaggerated knee-jerks. The patient was drowsy and feeble-minded	16 months	The patient died from broncho-pneumonia
neuritis of both ıternal strabismus right. The pupils lilated and equal. ;ate deviation to ;ht	Headaches, fits, weakness, left hemiplegia, left 7th nerve paralysis was transient, speech affected, knee-jerks present, vomiting. Temperature 104°. Paralysis of the soft palate. Rigidity of the arms and legs. incontinence of urine. The patient died from cardiac failure	20 days	Some of the symptoms in this case were transient
optic neuritis of yes. The left field ın was contracted. ıtient was blind. sis of the left exrectus. Diplopia. dilated (atropine?)	Vomiting, persistent headache. The patient was trephined over the posterior parietal region, and died six hours after the operation from shock	2 months	Some of the cerebrospinal fluid from this case was chemically examined, sp. gr. 1008. Alkaline reaction. Trace of proteid present. Reducing substance pyrocatechin (?) or dextrose (?).
ness started with e attacks of blind- ınd the intervals ın these attacks llybecame shorter ımplete blindness ened. Optic neu- both eyes, going trophy	No marked mental symptoms. Slight headache. The left 7th nerve was paralysed after the operation. Left arm and leg weak. The patient was trephined. Marked intra-cranial pressure. The wound became septic and the patient died six weeks later. Knee-jerks present	5-6 months	The vision improved after the operation, and the headaches were less, but only for a short time.

use by the agency of the village pump. (Dr. Stevenson gave instances.) (*e*) The frequency of goitre on the limestones of the carboniferous series, because these rocks were freely jointed, and it might be that water from the surface percolated rapidly along these joints, carrying bacteria in its train. (*f*) The goitrigenous action of many river waters, a great part of whose volume was derived from surface drainage. Against the bacillary theory might be mentioned the fact that constitutional disturbance—*e. g.* fever, etc.—never seemed to have been recorded in epidemics of the disease, and also the negative results of inoculation, etc., with bacilli. In the speaker's opinion these bacilli existed in the water only in consequence of some chemical environment, and were probably a species of soil bacteria. With regard to (2) the metallic salts theory, with special reference to the action of iron-pyrites (FeS_2) and the results of its decomposition, one curious fact was that St. Lager found iron-pyrites in some of the Vale of Aosta waters examined by Lustig and Carle. Dr. Stevenson proposed to take a series of geological formation on which goitre was found, and see what evidence they afforded in favour of this theory. (*a*) *Ordovician shales:* Goitre was prevalent on this series in Cumberland, in the counties of Roxburgh, Selkirk, and Dumfries, also in Westmoreland. Examination of these shales showed abundance of iron-pyrites, occurring in its usual cubical form, and also in the rhombic form, as Marcasite. Instances were mentioned of goitre on these rocks from personal observation of the speaker. (*b*) *Marls:* Dr. Stevenson accounted for goitre on the Permian and Triassic series of rocks by the fact that in many instances he could mention the water came in contact with marls, many of which he had examined. He found them variegated, consisting of bands of various hues—yellow, blue, and black—besides the ordinary red variety. The yellow bands were due to limonite produced by the decomposition of iron-pyrites, while the blue and black bands owed their colour to the presence of iron-pyrites in dissemination. A very striking instance of a blue marl which produced goitre was given as occurring in the department of the Isère in the so-called region of the Molasse. The stratum marked A was one of these blue marls containing iron-pyrites in dissemination. In every village in this department where the drinking water came in contact with this marl goitre was endemic. In some localities where the superimposed sandy layer B was rendered hard and compact by calcareous cement, and where the water was held up at a higher level, there was no goitre. In England the blue marls of the Gault and Wealden series were goitrigenous—*e. g.* at Horsham, where goitre existed, and where these blue marls abounded. In France the marls corresponding to the above—the *marnes aptiennes* and the *marnes néocomiennes inférieures*—were found by St. Lager to be eminently goitrigenous, and both these



formations contained a superabundance of iron bisulphide. Other instances could be mentioned. (*c*) *Carboniferous limestones:* Lime itself was not a cause of goitre, as large tracts of country in many lands, situated on the jurassic limestones, for instance, were free from goitre. Dr. Stevenson had carefully examined the lower strata of the carboniferous series and found a large amount of iron-pyrites in the limestones, sandstones, and shales of this geological horizon. (*d*) *Chalk and chalk-marl:* Goitre on these formations was not frequent, but according to Mr. James Berry was found fairly uniformly. So far as the speaker was aware the only accidental mineral on these formations, with the exception of glauconite and disseminated lime phosphate, was iron-pyrites occurring as marcasite, which was a very readily decomposable form of iron-pyrites. Dr Stevenson concluded by reading a paragraph from a book entitled 'Among the Himalayas,' by Surgeon-Major Waddell, I.M.S., in which the author stated his belief that the goitre he saw in a locality near the Jelep Pass was due to iron contained in the drinking water.

Captain J. H. Hocg, I.M.S., said that in Nepaul goitre was present in goats, horses, and pigs, and among the poor inhabitants, but not among the rich. The poor obtained their water from the rivers, but mostly from shallow wells, whilst the rich obtained their water from the hills, the water being stored in a reservoir outside the residential parts and brought in pipes to the city; the Nepal Resident's escort (who were composed of Hindus specially enlisted in India) drank the pipe water and did not suffer from goitre. No sediment was, as a rule, perceptible

No.	Index.	Position.	Nature.
80	1900, Edith S—, aged 21, P.-M. 282, Reports 299 Clinical, Dr. Fawcett	A tumour the size of a walnut on the right side of the cerebrum springing from the caudate nucleus to the outer and lower side of the anterior horn of the lateral ventricle anterior to the foramen of Monro. The growth was on both walls of the lateral ventricle, the floor being free. There was some mechanical obstruction of the foramen of Monro and marked distension of the lateral ventricles	Glioma
81	1900, M. A. R— F., aged 26, P.-M. 331, Reports 267, Dr. Hale White	The lateral ventricles were much distended, especially their posterior cornua. A tumour of the caudate nucleus, which measured 20 by 25 mm., was on the left side and bulged across to the right, affecting only the inner two thirds of the caudate nucleus	Spindle-cell sarcoma
82	1900, J. T. S—, M., aged 33, P.-M. 323, Reports 270, Dr. Hale White	A tumour at the anterior part of the left cerebral hemisphere. It started in and involved the left caudate nucleus, and spread across the median line to the right side for about 15 mm. distance. There was some softening beyond the growth	Gumma
83	1900, Percy C—, aged 15, P.-M. 92, Reports, Mr. Golding-Bird	Cyst in the Rolandic area	Cyst
84	1901, A. D—, aged 41, P.-M. 40, Reports 24, Dr. Hale White	A cerebral tumour pressing on the cavernous sinus connected with the pituitary body, stretching forwards and to the right in the middle fossa on the right side, and running into the sphenoidal fissure. Intra-cranial pressure was much increased. The tumour was spreading towards the left side of the skull, as evidenced by the post-mortem and clinical symptoms	Small round-c sarcoma
85	1902, Emma C—, aged 39, P.-M. 324, Reports 56, Dr. Hale White	The right hemisphere of the cerebellum contained a malignant growth, and around it was much softening extending to the surface in the posterior fossa. It involved the greater part of the right side of the cerebellum	Secondary dep Carcinoma

Ocular symptoms.	Other symptoms.	Period.	Notes.
Optic neuritis of both eyes, with hæmorrhages and exudation	No localising symptoms, vomiting, vertigo, and headache. Slight rigidity of the legs. Retraction of the head and abdomen. Incontinence of fæces	3-4 months	—
Optic neuritis of both eyes. Going on to atrophy	Headache. No localising symptoms	8 years	*Vide* 'Guy's Hospital Reports,' vol. lv. The patient was trephined on four separate occasions. With marked improvement in vision and general condition
Double optic neuritis; choroiditis present in each eye. The pupils reacted to light and accommodation. Diplopia early in the illness. Fields normal	Fits, paralysis of both hands and the lower part of the face, slight aphasia	2 years	—
Ptosis of the left eye	Numerous and frequent fits, loss of power in the left arm and leg, slight paralysis of the 7th nerve. The patient died from suppurative meningitis	6 months	The patient was trephined and fluid removed by aspiration. No report of this case.
Right ophthalmoplegia, ptosis of the right eye, optic neuritis of both eyes with exudation and hæmorrhages, followed by atrophy; field diminished in the left eye (convergent strabismus). The 6th nerve of the left side was affected 1 month before death. The right 3rd, 4th, and 6th nerves, and the second division of the 5th affected in the above order	Left hemiplegia (late), fit, 7th nerve paralysis, hyperæsthesia along the course of the 5th nerve, vertigo, retching, headaches, knee-jerks normal	5-6 months	The patient was trephined and the operation relieved the symptoms temporarily. He lived three months after the operation.
Optic neuritis of both eyes; nystagmus of both eyes	Vomiting, headache, giddiness, loss of power in the right arm and leg, increased knee-jerks, ankle clonus. The patient was irritable and had delusions. No urinary trouble	6 months	The patient had her breast amputated at St. George's Hospital in 1899.

No.	Index.	Position.	Nature.
86	1902, William W—, aged 52, P.-M. 318, Reports 132, Dr. Pitt	A large tumour, the size of a cricket ball, with cysts inside occupied the upper part of the right hemisphere, extended to the ascending frontal convolutions, and reached the parietal lobe. There was an area of softening 4 in. in diameter, which involved all the motor area. The ventricles were greatly distended	Glio-sarcoma
87	1903, John H—, aged 27, P.-M. 43, Reports 55, Dr. Beddard	A tumour, the size of a blackbird's egg, in the posterior extremity of the temporal lobe on the right side. It reached to the meninges, with a large area of softening. No excess of fluid in the ventricles	Gumma
88	1903, David S—, aged 48, P.-M. 99, Reports 101, Dr. Pitt	Tumour in the right occipital region	Mixed-celled sarcoma
89	1903, Edw. S—, aged 18, P.-M. 314, Reports 392 Clinical, Dr. Shaw	The left frontal bone and the anterior half of the left parietal bone, squamous part of the petrous bone, and the orbital parts of the left side of the sphenoid were all replaced by a dense white mass of sarcomatous growth, which was not breaking down, but invaded the left orbit and not the brain in this region. A secondary mass as large as a blackbird's egg was in the lower part of the *right* frontal region imbedded in the brain-substance, free from the other mass and not connected with the meninges	Sarcoma
90	1903, Charles E—, aged 15½, P.-M. 263, Reports 463 Clinical, Dr. Bryant	Growth found in the left lateral lobe of the cerebellum into which hæmorrhage had taken place. Size 5·5 cm. × 6 cm. The lateral ventricles were dilated and filled with hæmorrhage	Glioma
91	1903, Thomas W—, aged 38, P.-M. 330, Reports —, Dr. Shaw.	A tumour the size of a horse-chestnut was found in the right frontal lobe, close to and in front of the Sylvian fissure, and between the claustrum and internal capsule. Above it was a patch of softening. A second focus of growth was found in the region of the 7th nerve nucleus, on the right side of the pons	Glioma
92	1904, John F—, aged 53, P.-M. 209, Reports 127, Dr. Hale White	A cyst the size of a tangerine orange was found in the left temporo-sphenoidal lobe, and parts covered by 2nd and 3rd temporo-sphenoidal convolutions	Gliomatous cyst

ıcular symptoms.	Other symptoms.	Period.	Notes.
neuritis well ed, with hæmor- ıs and exudation	Headache, fits, paralysis of the 7th nerve, left hemiplegia, sensory aphasia, auditory and visual. The patient died in coma	6 months	—
under observation 01 the discs were al, but the patient he night following e-admission to the tal before his eyes examined. Ptosis	Fit, headache, paraplegia, loss of sensation in the feet, difficulty with passing his water. No note was made of the olfactory sense	2 years	This case was thought to be one of syphilitic myelitis
pupils reacted to ımodation but not ght. Double optic tis, with hæmor- ı in the retina	Left hemiplegia, fits, headache, incontinence of bladder and rectum, coma	15 months	—
ɔsis of the left orbit. neuritis of both Paresis of the left ıal rectus = 3rd	Headache, giddiness, loss of power in the right leg, paralysis of the left vocal cord	—	The growth extended down the neck. The patient died from gangrene of the lung, and secondary deposits were found in the kidney, liver, and mediastinum.
pupils were equal reacted to light. ptic neuritis. The were examined	Headaches, vomiting, and malaise. Slight trace of albumen in urine. Knee-jerks present. No history of any symptoms before day of death	1 day	The patient was brought into the hospital unconscious and died shortly afterwards
ɔtic neuritis	Fits, ill-marked hemiplegia. Two fits—one 4 years previously with partial paralysis of the 7th nerve, followed by one 2 years later with complete 7th nerve paralysis, which persisted	4-5 years	—
upils were unequal, ft smaller than the . Optic neuritis hæmorrhages. The s reacted to light ccommodation	Motor aphasia, motor agraphia, frontal headaches, fits, slight 7th nerve paralysis. The olfactory sense was affected	4 months	—

No.	Index.	Position.	Nature.
93	1904, Mary W—, aged 62, P.-M. 116, Reports 36, Dr. Pitt	A tumour the size of a small tangerine orange in the right hemisphere of the cerebrum. The right side of the cerebral hemisphere was much bulged. Some atheroma of the cerebral vessels	Glioma
94	1904, George D—, aged 2, P.-M. 128, Reports 104, Dr. Pitt	Tumours found in the cerebellum and also in the cerebrum, especially in the occipital lobe. Excess of fluid in the ventricles, temporal and frontal lobes were also affected. No meningitis	Tubercle
95	1904, Catherine S—, aged 8, P.-M. 332, Reports 232, Dr. Pitt	Large fungating mass occupying the left orbit, and extending from a growth in the left frontal lobe. The left frontal lobe was almost completely involved, but the internal capsule and basal ganglia were not affected. The tumour in the brain reached as far as the caudate nucleus, at its anterior end.	Sarcoma
96	1904, Henry H—, aged 45, P.-M. 457, Reports 364, Dr. Perry	Cerebral tumour. A lobulated growth was found in the under surface of the left sphenoidal lobe, which grew from the dura mater covering the front of the petrous portion of the temporal bone. Size 2½ in. × 1 in. The tumour did not invade the brain substance much softening above it, reaching as far as the optic thalamus and lenticular nucleus. On right side, in front of lenticular nucleus, was a softening growth size of two-shilling-piece	—
97	1904, W. Jno. F—, aged 2 years 2 months, Reports 633 Clinical	A caseous tubercular mass in the left side of the cerebrum, which involved the corpus callosum. There was a patch of softening in the optic thalamus. There were signs of tubercular meningitis on the right side of the cerebellum.	Tubercle
98	1905, Kate H—, aged 43	Tumour on the right side in the parieto-occipital region	Glioma

)cular symptoms.	Other symptoms.	Period.	Notes.
: neuritis of both more marked in the than the right. lysis of the external ıs on each side. The ınt could not move eyes up or down.) ptosis of each lid, : marked on the left	Hemiplegia of the left side. Incontinence of urine and fæces. Fits, drowsiness, exaggerated knee-jerk of the left knee. Coma	6 months	—
: neuritis of both ptosis of the left strabismus due to lysis of both internal . The pupils were ed, the left larger the right, they did react to light, later ıome ptosis of the t lid	Temperature, drowsiness, irritability, knee-jerks, and ankle clonus present, retraction of the head	5 months	The patient had tubercles in the intestines and lungs also.
-marked optic neuri-)f both eyes, later left eye was entirely royed by being ıed forward beyond lids by the growth, t pupil fixed	Wasting, the whole of the left side of the face was swollen and œdematous, vomiting, headache	15 months	—
ptic neuritis. The ls were equal and ted to light, etc., but gishly	Headache, coma. No knee-jerks. Alteration of mental attributes. The patient was violent, talked to himself, and was generally strange	2 months	—
)te of the optic discs. quint	Fits, raised temperature, Cheyne-Stokes' respiration. Rigidity of the limbs on the left side. Retraction of the head	1 week	—
ɔ neuritis well ked. Ptosis. Paresis he left external rec- Ptosis of both upper The pupils were ted but equal, and ted to light and accommodation	Headache, pain in the neck, knee-jerks present, no vomiting. Coma. Death	—	The patient was trephined over the right parieto-occipital region. Some bone was removed. The patient was considerably improved by the operation, squint, ptosis, and headache disappearing. Post mortem refused at death, which took place on August 12th.

No.	Index.	Position.	Nature.
99	1905, W. V—, aged 42. Dr. Pitt	A large soft tumour invading the right side of the base of the brain; it came to the middle line on the inner side of the temporo-sphenoidal lobe. The tumour extended forwards into the frontal lobe, and backwards into the parietal lobe. The growth infiltrated the brain-substance, so that it was impossible microscopically to define its limits	Glioma
100	1905, Edward F—, aged 52. Sir A. Fripp	Abscess in the occipital lobe on the left side situated in the angle between the falx cerebri and the tentorium cerebelli. Some purulent meningitis on the left side	Abscess

DISCUSSION.

Dr. H. H. Tooth said that the cause of optic neuritis was a subject of much difficulty, and he had never yet been able to come to any conclusion in his own mind in relation to it. A small tumour, as of the cerebellum, might be associated with intense optic neuritis, or a very large tumour, say in the frontal lobe, might not be associated with any. As to the question of toxins, the author of the paper had referred to Mott and Halliburton's work on cholin; but this was done in general paralysis of the insane, and if the toxic view were the right one, it would have been expected that optic neuritis would be common in that disease, which it was not, although optic atrophy was not infrequent.

Dr. A. J. Whiting wished to refer to the frequency of optic neuritis in cases of cerebral tumour. If he had not mis-

Ocular symptoms.	Other symptoms.	Period.	Notes.
ptic neuritis of the right ye; optic neuritis and xtensive retinal and re-retinal hæmorrhage f the left eye; left-ided hemianopia; some iplopia, with vertical isplacement of the nages; erythropsia of he left eye. The left upil was larger than the ight. No paralysis of ny cranial nerve. No ystagmus	History of "odd sensations" for 3 years. Voices sounded distant. Hallucinations of smell. Fits. Right-sided convulsions. Pain over the eyes and behind the ears. Slow pulse. The patient was very slow in answering questions. Weakness of the left arm, leg, and face. Knee-jerks exaggerated, spasticity when moving slowly. Bladder and rectum not under control. Memory for recent events was bad. Died in coma, August, 1905	3 years	—
ptic neuritis, not much welling. The discs were lurred and red, and the essels much enlarged. he left pupil was di-ated	Swelling in the occipital region, frontal headache, signs of intra-cranial pressure. The patient wandered in his mind, and his temperature went up and down. Paresis and anæsthesia of the right arm. Cheyne Stokes' breathing	—	The patient was under the care of Mr. Hartridge at the Westminster Ophthalmic Hospital in 1896, when a condition of optic neuritis was discovered. An abscess was found in the base of the right lung at the P.-M.

understood Mr. Ormond, he had found only three unequivocal instances of its absence among his hundred cases of tumour of the brain. This he considered was much too low a figure to represent the fact. According to Oppenheim it was absent in from 10 to 20 per cent. of all cases, and according to Gowers and Allen Starr in 20 per cent. In two out of three cases he had more recently seen, within the last few months, with signs of greatly increased intra-cranial pressure in both, there was never any trace of optic neuritis in either; one was that of a woman suffering from so-called idiopathic epilepsy, who developed a slow left hemiplegia taking months to reach its full extent, with some weakness of the opposite side and sphincter paralysis; there was a very large glioma of the right frontal lobe, extending far backwards and markedly excavating the left hemisphere. The other case was that of a middle-aged woman with a deliberate hemiplegia of the thrombotic type, who shortly before death developed double sixth nerve paralysis, but never any optic neuritis. A rather large glioma was found in the parietal lobe.

He agreed with the author that increased intra-cranial pressure could not alone account for the optic neuritis, as both the cases he had quoted illustrated, but he was not yet prepared to follow him in regard to the toxic theory he had advanced. On the other hand, he thought that the effect of trephining on the swelling of the optic discs showed it was an important factor. Mr. Ormond had said, as against the pressure theory, that the optic neuritis subsided whether the patient was trephined or not, which was true, yet he thought did not adequately represent the position. If the skull were not opened, as a rule the neuritis subsided after a long time, with more or less consecutive atrophy and more or less complete blindness. When the skull was opened diminution of the swelling could be recognised almost from day to day, and if taken early enough, the papillitis might disappear without leaving any but the slightest ophthalmoscopic evidence of its occurrence, and with complete preservation of sight.

Dr. F. E. BATTEN alluded to the statement made in the paper that the degeneration of the posterior roots which was present in cases of cerebral tumour was due to a toxic process, and asked, if such were the case, how Mr. Ormond explained the fact that it was the cervical roots, whose course was most transverse, which were commonly involved, when, as in other conditions which were obviously due to toxic processes, it was usually the lumbar and sacral roots which were affected.

Dr. HERBERT FRENCH, in reference to the toxic factor, said that doubt had been thrown on the point of fact whether cholin had any bearing on the production of general paralysis. It was even doubtful whether excess of cholin had ever been demonstrated in the blood in these cases. The test that had been relied upon had been that of obtaining cholin platino-chloride crystals, and Mr. R. W. Allen and himself had shown that the platinum chloride test, as it had hitherto been applied to blood, was unreliable owing to the fact that the potassium which was always present gave the typical crystals in all cases, whether cholin were also present or not.

Mr. ORMOND, in reply, said that his suggestion was that a toxic factor was concerned. He had tried to produce optic neuritis in rabbits by injecting cholin without any result. As to the frequency of cases without optic neuritis—3 in 100—the figure was arrived at by explaining away certain cases; there were only three unexplained. He believed such cases to be much less frequent than people thought.

MITRAL STENOSIS AND PREGNANCY

BY

HERBERT FRENCH, M.D., M.R.C.P.,
ASSISTANT PHYSICIAN, GUY'S HOSPITAL;

AND

H. T. HICKS, F.R.C.S.,
OBSTETRIC REGISTRAR, GUY'S HOSPITAL

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INTRODUCTION.

THERE is a large amount of literature upon this subject. Many of the papers contain accounts of small numbers of cases only. References are given at the end of this.

Berthiot's (3) book, published in 1876, and MacDonald's (11), published in 1878, have long been the standard works upon the subject. More recent publications which go fully into the question are those of Handfield-Jones (8) and Allyn (1), in 1896; Jess (9), who has collected all the published material upon the subject up to 1898; and Nicholson (13) and Mackenzie (12) in 1904.

There are certain points in regard to valvular heart disease and pregnancy upon which there is general agreement. These we do not propose to discuss further, because they appear to be well established. They are the following:

(1) Of all the varieties of chronic valvular heart disease, mitral stenosis is the most commonly accompanied by heart failure during pregnancy.

(2) Aortic lesions without mitral are rare in women; few cases of pregnancy in women who have aortic without mitral disease come under observation.

(3) When symptoms of heart failure have preceded pregnancy they are made worse by pregnancy.

(4) Repeated pregnancies at short intervals cause greater risk of heart failure than do few pregnancies at longer intervals.

There are, on the other hand, some points upon which there is not the same agreement. Among these, one of the most important, perhaps, is the question of whether a young woman with mitral stenosis should marry. It is this question in particular that we devote our attention to in the present paper.

The Views of Others.

The serious view that has been taken of the prognosis in cases of mitral stenosis who become pregnant is shown by the following quotations:

Jellett, in his 'Manual of Midwifery,' 1905, p. 591, says: "Finally, the question must be answered, Should a woman with valvular disease marry? The answer to the friends or relatives of the patient must be 'No.' Our advice will probably not be taken, but, all the same, it should be given, and none the less definitely on that account. There is no use in 'hedging' by saying that if failure of compensation has ever occurred, or if the damage to the valve is considerable, or if some particular valve is affected, she should not marry. In view of the sequence of events which we know to be usual in any case of valvular lesion, and remembering that a woman has duties as a wife and as a mother which require her health and strength for their due performance, there should be no hesitation in the mind of the physician as to what answer he would give to such an inquiry. It is astonishing how frequently the question is raised in text-books and how evasively it is answered. That 'the perils of marriage should be clearly

stated to both the contracting parties,' as advised by a very recent American treatise on 'The Heart,' is not the way out of the difficulty. The physician has many puzzling questions to answer, but this is not one of them, and, as his opinion has been asked, it should be given in a definite and unequivocal manner."

P. Brouardel (21), quoting Porak (22) ('Thèse d'Agrégation,' 1880, p. 109, "De l'influence réciproque de la grossesse et des maladies du cœur"), confirms the axiom, "Pour une cardiopathe, jeune fille, pas de mariage ; mariée, pas de grossesse."

These opinions are based upon the following statistics

MacDonald's figures:

	No. of cases.	No. of deaths.	Maternal mortality
Mitral stenosis	14	9	64·4 per cent.
Mitral regurgitation	8	3	37 „
Aortic regurgitation	5	2	40 „

Porak's figures:

	Premature births.	Maternal mortality.
Aortic lesions	25 per cent.	23 per cent.
Mitral regurgitation	50 „	13 „
Mitral stenosis	30 „	61 „
Mitral stenosis and regurgitation	42 „	45 „
Complex lesions	43 „	50 „

We would point out, however, that these statistics are based upon what are virtually selected cases. They only cover those in whom the cardiac symptoms had led the patients to seek medical advice. They do not include the cases in whom pregnancy produced little or no heart failure.

This is a very important omission. We have not been able to find an analysis of any large number of cases of women suffering from mitral stenosis in which this source of fallacy has been taken into account.

We have, therefore, analysed the obstetric histories of 300 consecutive cases of mitral stenosis in women over twenty, who have been in Guy's Hospital.

We realise that it is extremely difficult to be certain of the date at which a grown-up woman with valvular heart disease first acquired it. In many cases of mitral stenosis there is no history of acute rheumatism or chorea. The mitral stenosis may be proved by autopsy to be old. It is believed that such cases have had endocarditis in childhood, when the joint pains have been so slight that they have escaped the attention of the parents.[1]

Even when there has been an attack of rheumatic fever in early youth there is often no means of determining with certainty that the valvular disease has dated from it. In our analysis we have excluded all cases where granular kidney was possible, and also those cases where the patient stated that rheumatic fever first occurred after twenty years of age. We have taken those in which the clinical diagnosis has been old-standing mitral stenosis, with or without other lesions, and in which there has been either rheumatic fever or chorea in childhood or youth, or no history of acute rheumatism at all. We have accepted the same evidence in all the cases, whether in married women not pregnant, in married women pregnant, or in single women over twenty, so that the analyses of each class are comparable. Our cases are given in tables at the end of the paper.

Many Mitral Stenosis Cases bear Children well.

The likelihood is, that any woman who has mitral stenosis will, sooner or later, suffer from the results of failing compensation. There are all degrees of mitral

[1] Taylor, in 'The Practice of Medicine,' 1904, p. 157, says: ". . . the cardiac lesions may occur without any obvious affection of the joints at all. This greater liability on the part of the heart is especially frequent in children. . . ."

stenosis, and of the power of different hearts to maintain their compensation. Some hearts will fail early, whatever the woman does. Other hearts seem able to carry on their work almost as well as if no valvular disease were present. Even when heart failure comes on during pregnancy or the puerperium it is difficult to be sure that the heart would not have failed in any case, even had there been no pregnancy.

We have analysed our 300 cases as justly as we are able, attributing heart failure to child-bearing in as many as we felt we honestly could. We have come to the conclusion that the greater number of pregnancies in women with mitral stenosis, whose compensation has not previously failed, run their course as naturally as do the pregnancies of healthy people.

Thus, of the 300 consecutive cases, 205 were married. Of these, 135, or 66 per cent., did not attribute their ultimate heart failure to pregnancy, nor could we satisfy ourselves that there was any direct relation between the pregnancy and the heart failure. In one of these cases there had been as many as 17 children born alive, and the average number of children was 4·5 per mother. If 135 mothers with mitral stenosis can bear 608 children without losing cardiac compensation, it would seem unjust to prevent a young woman with compensated valvular heart-disease from getting married.

We found a direct relation between child-bearing and heart failure in 57 women, or 28 per cent. In many of these, however, there had been previous children born without trouble. In one case, indeed (No. 168), the labours with twelve children had been uneventful, heart failure occurring for the first time with the thirteenth. Upon twelve separate occasions this case might have come into our group of cases without heart symptoms; but the thirteenth transfers her to our group of cases where heart failure is related to pregnancy. It seems worth while to represent the relationship between pregnancy and heart failure in mitral stenosis in another way, as follows:

	Associated with heart failure.	Not associated with heart failure.
1st pregnancy	15	177
2nd „	16	139
3rd „	10	116
4th „	14	95
5th „	13	74
6th „	14	61
7th „	5	50
8th „	8	38
9th „	1	30
10th „	2	26
11th „	2	18
12th „	2	13
13th „	2	10
14th „	0	7
15th „	0	2
16th „	0	2
17th „	0	1

The Time at which, when related to Pregnancy, Heart Failure sets in.

We appreciate fully the fact that an existing tendency to failure of compensation is aggravated by child-bearing. Some of these patients, when they do go wrong, break down badly. Others, however, respond no less readily to treatment than do non-pregnant cases. It is difficult to determine the prognosis in any given case.

Amongst the 57 patients (see Table, Nos. 149–192) in whom we relate the cardiac failure to child-bearing we were uncertain in 7 whether the symptoms came on before, during, or after the birth of the child. In the remaining 50, 25 dated their heart trouble to the time when they were carrying, 25 went to term without difficulty and the cardiac symptoms set in during the puerperium.

The Prognosis when Heart failure is Related to Pregnancy, Labour, or the Puerperium.

The prognosis in regard to heart cases is always difficult to estimate from hospital records. Many patients recover sufficiently to go away to their homes, but there is no evidence to show how long their cardiac compensation is maintained. Some such cases doubtless die comparatively soon. Others remain chronic invalids for years. A few recover sufficiently to do their work for a longer or shorter time. It is a matter of every-day experience to find heart cases, men and women alike, coming into hospital for a few weeks, recovering cardiac compensation to some extent, going away to their homes, only to return again and again to the hospital. Those who die at home are not heard of again. Those who recover completely for the time being are also lost sight of. They change their address and cannot be traced. There is the greatest difficulty, therefore, in determining whether women with mitral stenosis, whose cardiac compensation has broken down in relation to child-bearing, have a worse prospect of life than have other cases whose heart failure has been due to other causes.

The proportion who die in the hospital is really no criterion, because we do not know what proportion of the others die soon after discharge; but since this source of error is common to all hospital statistics, we give the proportions for what they are worth:

(*a*) Of 135 mitral stenosis women who had borne children, but whose heart failure did not date from child-bearing, 44, or 33 per cent., died in hospital.

(*b*) Of 57 mitral stenosis women who had borne children, and whose heart failure did date from child-bearing, 20, or 35 per cent., died in hospital.

(*c*) Of 13 mitral stenosis women, married but never pregnant, 6, or 46 per cent., died in hospital.

(*d*) Of 95 mitral stenosis women, unmarried, 17, or 18 per cent., died in hospital.

At first sight this would seem to indicate that the prognosis was worst in the sterile women, best in the unmarried, intermediate in those who had had families. A glance at the relative ages in the different groups shows that this deduction is unwarranted; for the average age of all the cases in the four groups were:

	Average age.[1]	Maximum age.	Minimum age.
(*a*)	41 years	71	22
(*b*)	32 „	48	20
(*c*)	34 „	55	25
(*d*)	30 „	60	20

The average age of the single women was less than that of the married; the mortality amongst them should naturally be less. Could we trace the unmarried cases forward into the ten years to come, we should find that many would ultimately die in hospital, and some of these would probably have entered into the married state before they died. Many of our married cases had come in and out of hospital half a dozen times or more before they ultimately died.

We think the hospital mortality statistics afford no sound basis for any deduction; but if we drew any deduction at all it would be that, allowing for differences of age, the mortality of matrons is not materially different from that of spinsters, each having mitral stenosis.

The Prognosis when Heart Failure sets in during Pregnancy.

The paragraph above indicates how difficult it is to say whether or not a given woman, a hospital patient suffering from mitral stenosis, with symptoms of heart failure, will ultimately die in hospital or not. It is less difficult to

[1] The average age at death of married women with mitral stenosis is obviously less than that of healthy women. If the fact that the wife is likely to predecease the husband is regarded as a bar to marriage in all cases, then we agree that women with mitral stenosis should not marry. Our point is that we think the grave influence of pregnancy upon mitral stenosis has been over-estimated.

say whether or not a given woman, being pregnant, and admitted to hospital with cardiac symptoms from mitral stenosis, will leave the hospital alive, and whether or not she will approximately reach term and bear a living child.

Amongst our 300 consecutive cases, 22 were admitted whilst actually pregnant. For the details of these we refer to the table at the end of the paper, Cases Nos. 4, 5, 8, 149, 151, 152, 153, 155, 161, 163, 165, 166, 168, 169, 171, 174, 177, 178, 180, 182, 183, 184. In addition to these, we have found fourteen other pregnant mitral stenosis patients, who came into the hospital either before or after the period of our 300 consecutive cases. The following are notes of these additional patients:

(i) Aged 43. She was admitted for retroverted gravid uterus, and had no cardiac symptoms; there was well-marked mitral stenosis. The uterus was replaced, the patient being in the ward only five days. She had been married fifteen years, had had seven living children and one miscarriage. The last labour was seventeen months before, at full term. She was now pregnant four months.

(ii) Aged 36. She was admitted when seven months pregnant for orthopnœa, precordial pain, hæmoptysis, and bronchitis, without œdema. She gave no history of acute rheumatism, but was found to have old mitral stenosis. With rest in bed and digitalis she improved rapidly. She went to term. The labour was natural. The mother and child both did well. She had had ten living previously, and with each pregnancy had had some dyspnœa in the later months, but recovered completely soon after labour.

(iii) Aged 22. She was admitted when eight months pregnant for her eleventh attack of acute rheumatism. She had mitral stenosis and regurgitation, and aortic stenosis and regurgitation, but neither now nor previously had she suffered from her heart. She went to term; labour was natural; mother and child did well. She had

had one child previously, stillborn at full term, without difficulty. She had been in Guy's Hospital eleven times before, once for hæmatemesis and (?) gastric ulcer, ten times for acute rheumatism. The heart lesion was old.

(iv) Aged 40. She had been married only six months, and was five months pregnant on admission. She came in for dyspnœa. She rested in bed for a fortnight, and went out on the twenty-fourth day, free from dyspnœa, still pregnant. The heart lesion was old mitral stenosis.

(v) Aged 25. She came in for dyspnœa when four months pregnant, and was found to have a large irregular heart and mitral stenosis and regurgitation. She was only in the ward six days, when she went home of her own accord, still pregnant. She had had rheumatic fever four times.

(vi) Aged 19. She came in when pregnant nearly to term for a sudden hemiplegia. This was found to be due to cerebral embolism from mitral stenosis. There were no cardiac symptoms. She went to term. Labour was natural. Mother and child did well, but the hemiplegia recovered but partially. There was weakness of the affected side a year later, but no heart failure. There was no history of rheumatic fever.

(vii) Aged 33. She came in for acute bronchitis and orthopnœa, without œdema, when six months pregnant. She was found to have mitral stenosis, but gave no history of acute rheumatism. She was immediately relieved by rest in bed, and went out in fifteen days, still pregnant. She had had some trouble with her first pregnancy, but had recovered completely, and had borne seven living children.

(viii) Aged 20. She had had acute rheumatism many times, first when eleven. She had aortic stenosis and regurgitation, and mitral stenosis and regurgitation. She had had one living child two years before without difficulty,

and had now missed two menstrual periods. Up till just before admission she had worked hard at a jam factory, carrying trays of jars of jam up and down stairs. She was seized with acute rheumatism again, and came to hospital with a certain amount of dyspnœa also. She rested in bed, recovered rapidly, and went out on the twentieth day, able to walk actively without dyspnœa. It was jam-jar carrying rather than pregnancy that had caused the cardiac symptoms.

(ix) Aged 29. She gave no history of acute rheumatism, but had old mitral stenosis. She had had four children previously without difficulty. Eighteen days before admission orthopnœa and cough came on simultaneously with an abortion. She was attended by the Charity and transferred to the wards. She rested, and had digitalis; on the twenty-sixth day she went out, free from dyspnœa.

(x) Aged 25. She had had acute rheumatism at sixteen and at twenty-one. She came in for dyspnœa in the later months of pregnancy, and was found to have mitral disease. The notes are incomplete; it is not known if she was married nor if she had had a previous pregnancy. With rest and digitalis she became free from dyspnœa, and went out on the twenty-fourth day, still pregnant.

(xi) Aged 27. She had had no acute rheumatism, but had old mitral stenosis. She had been married four years. Her first pregnancy ended at the seventh month in delivery of a still-born child. The second pregnancy went to term naturally, and there was no heart failure, but when two and a half months pregnant she had a "fit," which left her with hemiplegia. This passed off completely after labour. Dyspnœa first began fourteen months ago, and on admission she was eight and a half months pregnant, orthopnœic, and cyanosed. With rest in bed and digitalis she reached full term, and was delivered of a living female child weighing 6 lb. 8 oz. Both mother and child did well, and went out early in the puerperium. The

dyspnœa was still present on exertion, but not with ordinary walking.

This patient foolishly became pregnant again a year and a half later. She was admitted at the fourth month for hæmatemesis, and rapidly recovered from this, but all through the pregnancy there was severe dyspnœa and swelling of the feet. Cyanosis became extreme, and just before term labour was induced. Delivery was spontaneous twenty-four hours later, and was accompanied by post-partum hæmorrhage. The child was 17 inches long, weighed 6 lb. 8 oz., and lived. The mother had severe dyspnœa and bronchitis during the early part of the puerperium, but under treatment the œdema disappeared and the cough decreased. She walked from the hospital, but readily became dyspnœic on exertion.

(xii) Aged 22. She gave no history of acute rheumatism, but was found to have mitral stenosis. She did not come in for heart failure in the ordinary sense, but for acute pericarditis. She refused to stay in the hospital. On the third day she insisted on going home, notwithstanding that she had acute pericarditis and was very seriously ill. She was pregnant five months at this time, and had borne one child eighteen months previously without developing cardiac symptoms.

(xiii) Aged 26. She gave no history of acute rheumatism, but died, and was found to have chronic valvular heart disease, both aortic and mitral, and a fatty heart. She had been married a year, and was pregnant nearly to term. She had developed acute dyspnœa three weeks before. Labour was induced and a living male child born. The patient became much worse the day after the confinement, and the heart did not respond to any treatment. The mother died on the ninth day after labour, the child lived.

(xiv) Aged 24. She gave no history of acute rheumatism, but had mitral stenosis. She had had rely

thirteen months before. The infants were born living, but both died. There had been no cardiac symptoms with that pregnancy. When five months pregnant for the second time she became very dyspnœic and cyanosed. When admitted, it was thought she must die; she recovered rapidly with rest in bed and digitalis, and was able to go home, still pregnant. She was re-admitted at the seventh month, extremely dyspnœic, with œdematous legs and a rapid, irregular pulse. She was venesected and given digitalis, and rested in bed. The pregnancy continued naturally; the cardiac symptoms all abated; she was delivered at full term of a living child weighing 5 lb. 6 oz. Both mother and child did well, and the mother was free from dyspnœa on ordinary exertion when she left the hospital.

We have, therefore, 36 cases in which mitral stenosis patients have come into Guy's Hospital when pregnant. These are all we have been able to find in a period of over twenty-five years. Leaving out cases under twenty years of age, the number of women with mitral stenosis who were admitted during the same period was something like 750. If cardiac symptoms from mitral stenosis were the rule during pregnancy, surely more cases would have sought admission when actually pregnant.

Of the 36 patients, not one died during pregnancy, if we exclude Cases No. 149 and xii, who refused to stay in, and whose fate is not known. Not one died during labour. Nine had no heart failure, but came in for other things (Nos. 4, 5, 8, 165, 168, i, iii, vi, xii). Twenty-four went out with restored cardiac compensation (Nos. 4, 5, 8, 151, 152, 153, 155, 161, 163, 165, 166, 168, 169, 171, i, ii, iii, iv, vi, vii, viii, ix, x, xiv). Only five died within three months of labour (Nos. 174, 177, 180, 183, xiii), and of these one (No. 180) died, not of mitral stenosis, but of chorea gravis and infective endocarditis.

In regard to the children, the fate of ten is unknown, because the mothers recovered and went out to be delivered elsewhere. Of the remaining 27, 23, including

twins in one case, were born living, at term, or within a month of term (Nos. 4, 5, 8, 151, 155, 161, 163, 165, 166 (twins), 169, 174, 177, 178, 182, 183, ii, iii, vi, xi (?), xiii, xiv). In two cases (Nos. 153, 171) the child was born at or near term, but dead. There were two abortions (Nos. 180, ix), and the former of these two was due to chorea gravis.

These figures are very different from those of MacDonald (11), as will be seen by comparing them side by side:

	No. of cases.	Maternal mortality within three months.	Abortions.	Lesion.
MacDonald: (Published cases)	14	64·4 per cent.	14·3 per cent.	Chronic mitral stenosis only.
Ourselves: (Consecutive hospital cases)	36	13·9 „	5·5 „	Chronic mitral stenosis, with or without other lesions.

We very much wish we had a larger number of cases in which the course of pregnancy in mitral stenosis had actually been observed in hospital. We feel that the great difference between MacDonald's statistics and our own is in part due to the small number of cases we each have. Nevertheless we feel convinced that MacDonald's figures overstate the seriousness of the prognosis. His own words are: "We have thus nine cases out of fourteen, or 64·4 per cent., fatal, which indicates a tendency to death which is surely sufficiently grave. It will be observed that the deaths occurred either suddenly during the labour or within a few days or weeks afterwards." We agree that the cardiac failure, once begun, may become very grave during the puerperium, but we have no single instance in which death occurred during labour.

The patients behave very much like other cases of heart disease. Even when the heart condition seems hopeless they may recover and bear other children. An instance in point is No. 169, whose history was shortly as follows:

She became dyspnœic during her first pregnancy, and

had had cardiac trouble many times since. On two separate occasions her symptoms were so grave that labour was induced at the eighth month ; on one of these there was post-partum hæmorrhage, which nearly proved fatal. After her fourth child she was discharged from the hospital, with the note in her report that she was "a wreck" ; at that time it was thought impossible that she could live, but she recovered at home, and bore two more children. The last, and sixth, was born at term, without induction of labour ; it was a transverse presentation, and version had to be performed ; the mother and child both did well.

The Treatment of Mitral Stenosis Cases when Pregnant.

The cases of mitral stenosis who have come into Guy's, Hospital pregnant have, almost without exception, been treated as though they had not been pregnant. Rest in bed, with digitalis, given with the same precautions as in other cases, have almost invariably brought relief, and enabled the patient to go on to natural labour at or near term. Induction of labour has hardly ever been resorted to, as reference to the cases at the end of this paper shows. Labours have in almost all cases been easy and natural, and free from post-partum hæmorrhage.

It is true that the same might not hold good for ladies in higher ranks of life. The physical work of Borough women is hard, that of most well-to-do women is less so. The relief to the Borough woman's heart is proportionately greater than is that to the rich lady's when she goes to bed. Nevertheless, we hold the view that the treatment of a pregnant woman with mitral stenosis should not be different from that of a non-pregnant woman with the same heart lesion. If the patient can be up and about, without cardiac symptoms, it is better for her to live as usual, and by moderate exercise maintain the reserve power of her heart, rather than lie up and diminish this

reserve power by prolonged rest. If cardiac symptoms supervene, the treatment should then be rest on a couch for mild cases, rest in bed for severer cases, rest in bed and digitalis for severer still. The pregnancy should, if possible, be allowed to run its course. Induction of labour in cardiac cases brings no immediate abatement of symptoms, as it does in many cases of eclampsia, for example. The puerperium is not less dangerous than is pregnancy itself to a case of mitral stenosis. The cardiac condition should be restored to as fair a state of compensation as possible before the time of labour arrives, and then forceps may be used to assist Nature. In a word, treat the patients exactly as though they were non-pregnant; treat them for mitral stenosis, do not treat them for pregnancy.

Sterility in Mitral Stenosis.

The opinion has been expressed that many women with mitral stenosis are sterile. Allyn (1), for example, says that "mitral disease, particularly stenosis, is much graver, as a rule, than aortic, but there is an attempt at a natural prevention of this, owing to the high proportion of sterile women among the subjects of mitral stenosis."

We do not agree with this. Out of the 205 married women in our table, only thirteen had not been pregnant. One of these had but recently got married, so that the proportion of presumably sterile women was only 5·8 per cent. The remainder had borne, upon the average, between four and five children apiece.

The Liability to Abortion in Mitral Stenosis.

Allyn (1), quoting Porak (22), states that cardiac disease in the mother has a very grave influence upon the fœtus, abortion being very common.

Unfortunately, this point was not particularly attended to in many of our cases. In our epitomes we have only put down whether abortions had occurred or not when we

had definite statements from the patient to that effect. We have left the doubtful cases blank.

In 90 of the women who had been pregnant we ascertained the history in regard to abortions, and found 40 of them had never had any abortion at all. The remainder had had 91 abortions between them. The general average was thus 1 per mother. The majority did not tend to abort, but in a few there were repeated abortions—in Case No. 56 as many as six.

It will be noticed that some of the abortions occurred when there was no heart failure at all. In these the association was possibly adventitious. In others the heart failure dated from an abortion, and it seems likely that in some of these the heart trouble was directly responsible for the miscarriage.

Upon the whole, however, we do not think that the tendency to abortion is obviously greater amongst mitral stenosis cases than it is amongst other Borough women.

Cases in whom we know the Mitral Stenosis certainly Antedated the Pregnancies.

As we have pointed out in the early part of this paper, it is impossible to state with absolute certainty that the mitral stenosis was present before marriage in a large number of cases. We have said that this is a flaw in our arguments, and might render the deductions we have drawn from our 300 cases invalid. There are, however, a small number who had been in the hospital, or under observation, years previously, and in whom we know that mitral stenosis was present before marriage. We will now consider these, seventeen in number, by themselves, and see whether what we have said about the generality of the cases holds good of these also.

Case No. 6.—Valvular disease was known to exist at ten. There had been one child, and there had never been cardiac symptoms. The patient was admitted for a

fourth attack of acute rheumatism, with good cardiac compensation.

Case No. 12.—There had been acute pericarditis before marriage. There had been one living child and one miscarriage. The patient was admitted for recent cardiac symptoms, not related to child-bearing.

Case No. 59.—The physical signs of mitral disease had been present for thirty years. The patient had borne ten children without difficulty. Heart failure did not set in till she was fifty-six.

Case No. 75.—The mitral bruits were present at twelve. The patient had had five children. She came in for acute rheumatism, and had never had cardiac failure.

Case No. 89.—Heart disease was known at fourteen. There had been one child, without difficulty. The patient came in for lobar pneumonia, and recovered without a symptom of heart failure.

Case No. 90.—The bruits were known before marriage. There had been three children, born without difficulty.

Case No. 91.—The bruits were known before marriage. The patient bore five children, and her heart failure did not come on in relation to any of these.

Case No. 92.—Heart disease was known at thirteen. There had been three children, pregnancies and labours being uneventful.

Case No. 93.—Heart disease was known at thirteen. There had been four children and two miscarriages, without trouble.

Case No. 94.—Heart disease was known at sixteen. The four children had been born without cardiac symptoms.

Case No. 95.—Heart disease had been known for ten years. There had been eight children, and no heart failure with any of them.

CASE No. 96.—Heart disease was known in girlhood. There had been one child, born without trouble.

CASE No. 97.—The bruits were known to be present at nineteen. There had been one child, born without trouble.

CASE No. 138.—Heart disease was known at sixteen. There had been six children. Cough and dyspnœa had occurred during each pregnancy, but there had been good recovery of compensation each time.

CASE No. 148.—Heart disease was known at sixteen. The first five children had caused no cardiac symptoms. Failure of compensation set in with the sixth.

CASE No. 153.—This patient had been in and out of hospital seven times for heart failure before marriage. She married notwithstanding. The cardiac symptoms were severe during pregnancy. A dead child was born at the eighth month. The mother recovered rapidly enough to leave the hospital on the fourteenth day after labour.

CASE No. 161.—This patient was in hospital when eighteen for heart disease. She married after this, and bore four children without heart trouble. When pregnant with her fifth child, cardiac symptoms appeared. The patient lay up in hospital for four days only, and then went home and went naturally to term.

There were, it will be seen, many children borne by women who were known to have heart disease before marriage. In 13, or 76·5 per cent., the ultimate heart failure was not directly related to child-bearing. In 4, or 23·5 per cent., pregnancy and heart failure coincided, but even in some of these previous children had been born without causing heart trouble. None of the patients died during pregnancy or labour. All recovered and left the hospital.

If we compare these figures with those for the generality of women with mitral stenosis, we find—

	Heart failure not directly related to pregnancy.	Heart failure directly related to a pregnancy not necessarily the first.
When the mitral stenosis was old, but of unknown date (175 cases, taken consecutively)	69·7 per cent.	30·3 per cent.
When the mitral stenosis was known with certainty to date from before marriage (17 cases, taken consecutively)	76·5 „	23·5 „

The results are closely similar. We are fully conscious that the number of cases in which we know the mitral stenosis certainly preceded marriage is small. In the remainder the evidence that the mitral stenosis was present before marriage is presumptive only. We do not know how to collect a large number of cases where this presumption is avoidable. We have taken only those cases where the bruits suggested an old-standing valvular lesion, and have only accepted cases where there had either been acute rheumatism or chorea in youth or else no rheumatism at all. The fact that the results are so similar in the total number of cases to what they are in those where heart disease was known to antedate the pregnancies affords, we think, additional ground for the justness of the conclusions we have drawn.

Association of other Heart Lesions with the Mitral Stenosis.

Most observers are of the opinion that the prognosis is less good when aortic or other disease is present as well as mitral stenosis. We have taken our cases consecutively as they entered the hospital, and have made no distinction between cases where mitral stenosis alone was diagnosed and those where other lesions of the heart were present also. Amongst the associated lesions will be found mitral regurgitation, aortic regurgitation, aortic stenosis, aortic stenosis and regurgitation, pulmonary stenosis, tricuspid stenosis, pericarditis, and adherent pericardium. Notes

of these are given in the epitome of cases in the table at the end of this paper. They should make the prognosis in the affected cases proportionately worse. We do not intend to enter upon this question here. We have discussed the cases as though they were suffering from mitral stenosis only.

The Incidence of Fungating Endocarditis.

In all the patients who died the diagnosis was verified by autopsy. We have been struck by the large proportion of mitral stenosis cases who die of a terminal fungating endocarditis. Thus—

Of 43 fatal cases where failure was not dated to pregnancy, 10, or 23 per cent., died of fungating endocarditis.

Of 22 fatal cases where failure was dated to pregnancy, 9, or 41 per cent., died of fungating endocarditis.

Of 6 fatal cases who were married, but had not been pregnant, 0 per cent. died of fungating endocarditis.

Of 18 fatal cases who were single, 7, or 39 per cent., died of fungating endocarditis.

Of the total 89 fatal cases, 26, or 29 per cent., died of fungating endocarditis.

At first we thought there might be a special tendency for pregnancy or the puerperium to lead to fungating endocarditis, but we do not think this can really be so, seeing how high the proportion of cases of terminal fungating endocarditis is in single women with old mitral stenosis.

Summary.

We believe that heart failure is to be expected sooner or later in almost all cases of valvular heart disease.

We do not deny that pregnancy may cause serious, and even fatal, cardiac failure in cases of mitral stenosis.

We think, however, that the dangers of pregnancy in these cases have been overstated.

We attribute the overstatement to the fact that previous

statistics have been based mainly upon cases of mitral stenosis which came under observation because heart failure had developed during, or soon after, pregnancy. We feel that statistics so obtained leave out of count all those cases of mitral stenosis who go through pregnancy without developing cardiac symptoms.

We have tried to obviate this source of error by analysing the obstetric histories of 300 women over twenty who had mitral stenosis with or without other lesions. We have not selected our cases, but have taken them consecutively as they came into Guy's Hospital.

We conclude:

(1) That comparatively few are sterile.

(2) That they are not especially liable to abort.

(3) That the majority bear children well.

(4) That when heart failure develops in relation to pregnancy it is very often not with the first pregnancy, but after several.

(5) That the treatment should be the same as for a non-pregnant case of mitral stenosis.

(6) That it is not just to absolutely negative marriage in all women with mitral stenosis. The dogmatic "no" of Jellett and of Porak (p. 560) is, we think, unjustifiable. It is right that the physician should make clear to the contracting couple, or to their near relatives, the risk run. He should use his discretion, and distinguish between one case and another. The risk should not be minimised, but it should not be exaggerated. Whether the woman marry or not, it is likely that she will not reach old age. She should not have successive children rapidly. But if she has survived the age of twenty, with good cardiac compensation, the likelihood that pregnancy will accelerate the time of heart failure does not seem to be so great as has in text-books been declared.

We thank the Treasurer of Guy's Hospital and the Physicians to Guy's Hospital for their kind permission to use the statistics embodied in this paper.

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ANALYSIS OF 300 CONSECUTIVE CASES OF MITRAL STENOSIS, WITH SPECIAL REFERENCE TO PREGNANCY AND LABOUR. NO CASE IS INCLUDED UNDER THE AGE OF 20; AND IN ALL RHEUMATISM OR CHOREA HAD OCCURRED BEFORE 20, OR NOT AT ALL.

A. *Those who had been Pregnant, and did not date Cardiac Symptoms to Pregnancy or Labour.*

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.*
1	22	None	1	0	Mitral stenosis, acute bronchitis, erythema nodosum	Œdema and dyspnœa	7 weeks	Married 18 months. One child, full term, 8½ months ago without trouble	R.
2	24	19	1	0	Mitral stenosis and regurgitation, infective endocarditis, various emboli	Pyrexia and rigors	No heart failure	The pyrexia and sepsis date from 1 month after labour; the pregnancy and labour had been free from cardiac symptoms. The infection may have been directly due to the puerperium, but there was no cardiac failure	D.
3	25	None	1	0	Lobar pneumonia (double), mitral stenosis	Pneumonic	No heart failure	The child was born at full term 12 days before admission. There were no cardiac symptoms at all	R.
4	27	„	3	0	Chorea, mitral stenosis	Chorea	Ditto	Two full-term children without trouble. At present 7 months pregnant; subsequently went to term without cardiac symptoms	R.
5	27	13	1	0	„ „	„	Ditto	Patient unmarried, and 4½ months pregnant on admission. Recovered from chorea; went to term naturally	R.
6	27	6	1	0	Acute rheumatism (4th), mitral stenosis	Rheumatism	Ditto	Known to have had heart disease at 10; no cardiac symptoms since	R.
7	33	10	4+ 1 D†	1	Acute rheumatism (2nd), mitral stenosis and regurgitation	„	Ditto	Last confinement was 4 years ago; miscarriage 10 weeks ago. No heart failure at labours	R.

* R. = recovered and went home. D. = died in hospital. † D. = stillborn.

Case Number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
8	36	None	8	0	Acute rheumatism (1st), old mitral stenosis	Rheumatism	No heart failure	Had had 7 children, last 2 years ago. Now admitted at term; labour natural; no cardiac failure	R.
9	25	18	3	0	Cerebral embolism, mitral stenosis and regurgitation	Hemiplegia	Ditto	First child born at 18, second at 19, third at 28 no cardiac failure with any of them. Transient hemiplegia 4 months ago; complete, 7 months ago	R.
10	24	15	1	—*	Mitral stenosis and regurgitation, bronchitis, enlarged liver	Precordial pain and dyspnœa	1 month	The child was born without trouble 2 years ago	R.
11	28	None	3	2	Mitral stenosis, tricuspid regurgitation, œdema	Cyanosis and dyspnœa	3 weeks	There had been no cardiac symptoms with any of the pregnancies	R.
12	30	20	1	1	Mitral stenosis and regurgitation	Dyspnœa	Acute	There had been pericarditis before marriage; the pregnancies had been uneventful	R.
13	31	16	2	—	Mitral stenosis and regurgitation, pleurisy with effusion	„	1 year	Pregnancies uneventful	R.
14	32	14	2	—	Mitral stenosis and regurgitation	„	Recent	„ „	R.
15	32	None	1	—	Mitral stenosis, tricuspid regurgitation	Ascites	3 months	Child was born 7 years before	R.
16	33	Childhood	5	—	Mitral stenosis and regurgitation, tricuspid regurgitation, pleurisy	Dyspnœa and rheumatism	Recent	Last child was born 2 years before, without trouble	R.
17	34	None	1	0	Mitral stenosis and regurgitation, tricuspid regurgitation	Œdema	„	Child was born 5 years before	R.

* The mark — signifies that it is not known whether there has been any miscarriages or not.

18	36	None	1	—	Mitral stenosis and regurgitation	Œdema and dyspnœa	5 years off and on, acute 3 weeks	Child was born 11 years ago, without cardiac trouble	R.
19	36	„	2	—	Mitral stenosis, aortic regurgitation	Precordial pain, anginal	Acute 14 days	Pain of an anginal character had been present off and on for several years; the pregnancies had been uneventful, without heart failure or increase of pain	R.
20	36	19	6	—	Mitral stenosis, aortic stenosis and regurgitation	Dyspnœa and œdema	18 months off and on; acute 3 months	There had been no dyspnœa except on exertion until quite lately; the pregnancies had occurred without heart failure	R.
21	36	Childhood.	6	—	Mitral stenosis and regurgitation	Dyspnœa and cough	Acute recently	She had not noticed any cardiac symptoms until 3 years before; the pregnancies had been uneventful	R.
22	37	16	2 + $1\frac{7}{12}$*	2	Mitral stenosis and regurgitation	Dyspnœa	Recent	The patient stated that she had not felt thoroughly well for many years; had had no trouble with any pregnancy or labour, and had only recently felt worse than usual	R.
23	38	8	3 + 1 d.	—	Mitral stenosis and regurgitation, tricuspid regurgitation	Œdema and dyspnœa	1 year	Pregnancies uneventful	D.
24	38	Childhood	8	2	Mitral stenosis	Dyspnœa and precordial pain	On and off for 12 years; acute 1 month	Had been married 18 years. Though there had been shortness of breath on exertion for 12 years, the pregnancies had not caused any serious trouble	R.
25	38	16	2	0	„	Œdema of legs	14 days	Last child was born 14 years ago	R.
26	38	None	8	—	Mitral stenosis, tricuspid regurgitation, big liver	Hæmoptysis and hepatic pain	2 weeks	There had been twins twice. With each of these there had been hæmoptysis, but beyond that no heart trouble till 2 weeks ago	R.
27	39	None	6	—	Mitral stenosis and regurgitation, big liver, ascites	Œdema and ascites	2 months	Pregnancies uneventful	R.
28	39	Childhood	2	1	Mitral stenosis and regurgitation, tricuspid regurgitation, ascites	Dropsy	2 months	„	R.

* $\frac{7}{12}$ = 7 months child.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
29	39	None	8	4	Mitral stenosis and regurgitation, pericarditis	Precordial pain	Acute	Pericarditis was the main cause for admission. No previous heart failure	R.
30	39	„	3	—	Mitral stenosis	Dyspnœa	On and off for 4 years	Last child 12 years ago	R.
31	40	„	13	—	Mitral stenosis, big liver	Dyspnœa and œdema	On and off for 7 years; acute for 5 months	Pregnancies uneventful	R.
32	40	14	1	0	Mitral stenosis, aortic regurgitation, tricuspid regurgitation	Palpitations and œdema	12 years on and off	Child 23 years ago	R.
33	40	None	0	2	Mitral stenosis and bronchitis	Dyspnœa	2 years on and off	Miscarriages were 20 years ago with first husband. Married a second time, no children	R.
34	42	„	2	—	Mitral stenosis, tricuspid regurgitation, bronchitis	„	Ditto	There was hemiplegia 11 years ago; the pregnancies were uneventful, and there was no cardiac failure till 2 years ago	R.
35	42	Girlhood	4	—	Mitral stenosis and regurgitation, ascites	Œdema and ascites	2½ years on and off	Last child 6 years ago	R.
36	43	None	1 + 3 d.	1	Mitral stenosis and regurgitation	Dyspnœa and precordial pain	2 years	Last child 7 years ago	R.
37	43	20	8	—	Mitral stenosis, tricuspid regurgitation	Dyspnœa and cough	8 years off and on	Last pregnancy long preceded heart symptoms	R.
38	43	3	3	3	Mitral stenosis and regurgitation	Ditto	14 days	Pregnancies uneventful; miscarriages without heart failure	R.
39	43	17	1	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Œdema and cough, ascites	2 years, ascites 6 weeks	The pregnancy was 25 years ago	R.

40	44	10	2	0	Mitral stenosis	Dyspnœa and precordial pain	Slight	The patient was married at 17 and quickly had 2 children	R.
41	44	9	1 + 1 d.	1	Mitral stenosis, angina pectoris	Angina hæmoptysis	6 years	Pregnancies uneventful	R.
42	45	None	1 d.		Aortic stenosis and regurgitation, mitral regurgitation, pericarditis	Precordial pain and dyspnœa	2 months	Child was stillborn 20 years ago	R.
43	46	14	7	0	Mitral stenosis and regurgitation, aortic stenosis, pleurisy	Acute pleuritic pain	None	Last child 6 years ago	R.
44	47	20	8		Mitral stenosis and regurgitation	Bronchitis and œdema	5 months	Pregnancies uneventful. Quite well till hæmoptysis 5 months ago	R.
45	47	18	4	0	Mitral stenosis and regurgitation, bronchitis	Cough	3 years on and off	Married at 18; youngest child is 25	R.
46	47	None	14	1	Mitral stenosis and regurgitation, big liver	Dyspnœa and vomiting	4 days	Last pregnancy 2 years ago	R.
47	47	11	2		Mitral stenosis and regurgitation, bronchitis, big liver	Œdema and cough	6 weeks	Last child 20 years ago	R.
48	47	None	6	1	Mitral stenosis	Œdema and palpitations	2 months	Married at 15; pregnancies uneventful	R.
49	48	16	9		Mitral stenosis and regurgitation; hæmaturia	Dyspnœa	6 months	Married at 19; pregnancies uneventful	R.
50	49	None	14 + 1 D.	1	Mitral stenosis and regurgitation, ascites	Œdema	2 years	Married twice. 8 and miscarriage by first husband; 6 and 1 still-born at 7 months by second	R.
51	50	„	11		Mitral stenosis and regurgitation	Palpitations and œdema	3 years on and off	Last child 7 years ago; patient has been a widow for 5 years	R.
52	50	„	9		Mitral stenosis	Dyspnœa and œdema	6 years off and on	Pregnancies uneventful	R.
53	51	„	14		Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Anasarca	3 years	„ „	R.
54	53	14	1		Mitral stenosis and regurgitation	Dyspnœa	2½ years	Child born many years before	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
55	53	None	17	—	Mitral stenosis and regurgitation, tricuspid regurgitation, ascites	Dyspnœa and œdema	1 year	Pregnancies uneventful	R.
56	54	7	2	6	Mitral stenosis, bronchitis, extreme cyanosis	Dyspnœa	1 month	„ „	R.
57	55	15	14	—	Mitral stenosis and regurgitation, bronchitis	Dyspnœa and œdema	1 year	Last child 15 years ago	D.
58	56	20	14	—	Mitral stenosis, ascites	Cough and œdema	10 weeks	Married at 20, and had her children quickly and without heart trouble	R.
59	60	15	10	—	Mitral stenosis	Dyspnœa and œdema	1 year	There was no trouble with pregnancies, except that the first and last labours were prolonged. The physical signs of heart disease were known 30 years before; failure was recent	R.
60	58	16	6	—	Mitral stenosis and regurgitation	Ditto	3 years	Pregnancies uneventful	R.
61	50	None	3	—	Mitral stenosis, aortic regurgitation, ascites	Dyspnœa	9 months	Sent to an infirmary a wreck; in all probability died soon after	D.
62	64	16	1	—	Mitral stenosis and regurgitation	Dyspnœa and cough	1 year	Child born soon after marriage at 23	R.
63	69	None	9	2	Mitral stenosis, pleurisy	Cough and chest pain	3 years	Pregnancies uneventful	R.
64	71	„	4	—	Mitral stenosis	Palpitations	6 months	„ „	R.
65	22	10	1	0	Mitral stenosis and regurgitation, acute rheumatism	Rheumatism	None	Child born a year before, without heart symptoms	R.

	2	15	1	0	Mitral stenosis and regurgitation, acute rheumatism	Rheumatism	None	Child born 5 months before, without heart symptoms	R.
	3	10	2 + 1 D.	0	Mitral stenosis and regurgitation, aortic regurgitation, acute rheumatism	„	„	Last child 14 months ago. Has never had cardiac symptoms since pericarditis at 13 years	R.
	5	10	2	0	Mitral stenosis and regurgitation, acute rheumatism	„	„	Pregnancies natural	R.
	5	20	2	0	Mitral stenosis and regurgitation, acute rheumatism	„	„	„ „	R.
	7	Child-hood	6	1	Mitral stenosis, acute rheumatism	„	„	Miscarriage 1 month ago; no cardiac symptoms	R.
	28	14	1	0	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Angina (1 year)	„	Child born without trouble	R.
72	30	7	3	—	Mitral stenosis, acute rheumatism (5th attack)	Rheumatism	„	Pregnancies natural	R.
73	30	None	0	2	Mitral stenosis, general debility for 2 years	Debility	„	Last miscarriage 8 years ago	R.
74	31	Child-hood	3	1	Mitral stenosis and regurgitation, pneumonia	Pneumonic	„	Abortion 2 months ago, pneumonia followed; there were no cardiac symptoms	R.
75	35	5	5	0	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, acute rheumatism (4th attack	Rheumatism	„	Was known to have bruits at 12; has never had heart failure; last child 7 months ago	R.
76	36	15	4	—	Mitral stenosis and regurgitation, pleurisy	Pleuritic	„	Pregnancies natural	R.
77	36	9	3	—	Mitral stenosis, diabetes mellitus	Diabetic	„	„ „	R.
78	37	Child-hood	5	0	Mitral stenosis, movable kidney	Pain in loin	„	„	R.

Case Number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
79	37	None	7	1	Mitral stenosis, hemiplegia (sudden embolism)	Hemiplegia	None	Last child 2 years ago without trouble	R.
80	37	13	1	0	Mitral stenosis, diabetes mellitus	Diabetic	„	Child born 5 years ago	R.
81	37	15	1	—	Mitral stenosis, acute rheumatism	Rheumatism	„	Pregnancy natural	R.
82	40	None	2	—	Mitral stenosis, carcinoma of liver	Malignant	„	Last pregnancy 3 years ago	Worse
	40	„	3	0	Mitral stenosis and regurgitation, chronic osteoarthritis	Chronic joints	„	The chronic joint trouble (? septic synovitis) dated from a labour 2 years before; there had been no cardiac symptoms	R.
84	41	15	5	—	Mitral stenosis and regurgitation, acute rheumatism and simple stricture of œsophagus	Dysphagia	„	There had been no heart symptoms; she came in for simple stricture of œsophagus, and developed acute rheumatism in the ward	R.
85	44	14	7	—	Mitral stenosis, cerebral embolism, acute rheumatism	Hemiplegia	„	Last pregnancy was 6 years ago; there had been no cardiac symptoms; the hemiplegia was recent	R.
86	47	Childhood	4	—	Mitral stenosis, phthisis	Acute abdominal pain	„	Pregnancies uneventful; there had never been cardiac symptoms	R.
87	51	None	10	—	Mitral stenosis (old and fibrous) found p. m., admitted for perforated gastric ulcer, the mitral disease was unsuspected	Abdominal	„	Ditto	D.
88	56	18	8	2	Mitral stenosis, hystero-epilepsy	Hysterical	„	Ditto	R.

89	28	14	1		Mitral stenosis, lobar pneumonia	Pneumonic	None	Heart disease known since 14; no cardiac symptoms	R.
90	30	20	3	1	Mitral stenosis and regurgitation, ascites	Palpitations and œdema	3 months	No heart symptoms till 3 months ago; bruits known before marriage; pregnancies uneventful	R.
91	31	16	5	0	Mitral stenosis and regurgitation, big liver, ascites, double pleural effusion	Dyspnœa, ascites	6 months acute, 15 yrs. chronic	Has had dyspnœa since she was 16, when she was known to have heart disease; she married in spite of this, and has had 5 pregnancies without increase in symptoms; two of the children were short of full term, but lived; the acute symptoms definitely did not date from the last pregnancy	R.
92	33	5	3		Mitral stenosis and regurgitation	Dyspnœa and precordial pain	Acute	Was known to have heart disease at 13. The pregnancies caused no cardiac symptoms	R.
93	41	12	4	2	Ditto	Ascites and bronchitis	7 weeks	Has had dyspnœa and palpitations off and on since 13; she had no increase of symptoms during child-bearing	R.
94	41	16	4		Mitral stenosis and regurgitation, aortic regurgitation	Dropsy	Recent	Has had dyspnœa off and on since 16; she had no increase of symptoms during child-bearing; she was married at 19	D.
95	42	Childhood	8		Mitral stenosis and regurgitation, anasarca	Dyspnœa and dropsy	8 months	The last pregnancy was 3 years ago. She was married at 22. The bruits had been known to exist for 10 years. She bore her children without cardiac symptoms, but transient hemiplegia occurred 3 days after last labour, 3 years ago	R.
96	43	None	1		Mitral stenosis	Dyspnœa	Acute lately	She has had dyspnœa on exertion as long as she can remember; the child was born 25 years ago without any trouble	R.
97	69	19	1		Mitral stenosis and regurgitation	Precordial pain and dyspnœa	Recent	Cardiac bruits known since 19	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
98	24	8	1	0	Mitral stenosis and regurgitation, pericarditis, ascites	Pericarditic	Recent	The only pregnancy was 5 years ago, without trouble	D.
99	28	8	1	—	Mitral stenosis and regurgitation, infective endocarditis	Dyspnœa and weakness	Gradual onset for 1 year	The only pregnancy was 9 years ago, without trouble	D.
100	28	None	1	3	Mitral stenosis and regurgitation, infective endocarditis, thromboses	Œdema and dyspnœa	2 months	Married 8 years, no recent pregnancy	D.
101	28	„	2	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, ulcerative endocarditis	Hemiplegia, acute 3 months ago, vomiting	Diagnosed as gastric ulcer 3 months ago, no cardiac symptoms	Pregnancies uneventful	D.
102	32	10	3	—	Mitral stenosis and regurgitation, infective endocarditis	Pyrexia and joint pains	Recent	„ „	D.
103	32	Childhood	5	—	Mitral stenosis and regurgitation, anasarca	Dropsy and dyspnœa	Getting worse for 1 year	Married at 16; last labour some years before admission, without difficulty	D.
104	33	None	2	0	Mitral stenosis and regurgitation, big liver, etc., infective endocarditis	Dyspnœa	11 months	Last pregnancy was 3 years ago, without trouble. The mitral stenosis found p. m. was extreme	D.
105	35	„	7	—	Mitral stenosis, pericarditis, pneumonia, the mitral stenosis was unsuspected, but was found p. m.	Pneumonic	Acute	No cardiac symptoms; pregnancies uneventful	D.

106	36	None	4	1	Mitral stenosis, big liver, etc.	Dyspnœa	A few months	Last child 8½ years ago; husband died 6 years ago	D.
107	36	„	4		Mitral stenosis, aortic regurgitation, infective endocarditis	Dyspnœa and œdema	4 weeks	Pregnancies uneventful	D.
108	37	Childhood	4		Mitral stenosis, pleurisy, big liver, œdema, etc.	Dyspnœa, dropsy	2 years, recent	Pregnancies uneventful; last some years ago	D.
109	37	17	1	1	Mitral stenosis and regurgitation, pericarditis, anasarca	Œdema and ascites	Gradual onset for 2 years	Last pregnancy 13 years ago	D.
110	37	16	0	1	Mitral stenosis, pleuritic effusion	Dyspnœa and œdema	On and off for 4 years, acute a few months	The pregnancy was several years before	D.
111	38	14	6		Mitral stenosis, lobar pneumonia, empyema	Pneumonia	None before admission	Last child 9 years ago	D.
112	38	Childhood	1		Mitral stenosis and regurgitation, aortic regurgitation, pleuritic effusion	Dyspnœa and œdema	1 month	Married at 18. Had child without trouble	D.
113	39	„	2		Mitral stenosis and regurgitation, ascites	Anasarca and orthopnœa	2 years	Had had very many attacks of rheumatism before 20. Pregnancies uneventful	D.
114	40	19	3		Mitral stenosis and regurgitation, big liver, ascites	Dyspnœa and anasarca	A cardiac wreck for the last 4 years	The pregnancies were uneventful, and long preceded the heart failure	D.
115	40	17	10	0	Mitral stenosis, aortic stenosis, big liver, infarcts spleen and kidneys, lungs	Dyspnœa and hæmoptysis	Off and on 6 years, anasarca 1 month	Was married at 20. The last pregnancy occurred before the onset of severe hæmoptysis, though there had been slight hæmoptysis without heart failure previously	D.
116	40	15	6	1	Mitral stenosis and regurgitation, infarcts, ante-mortem thrombi	Dyspnœa and anasarca	Getting worse, 2 years	Pregnancies uneventful	D.
117	41	None	2		Mitral stenosis and regurgitation, aortic regurgitation	Precordial pain, œdema	4 months 1 month	The children were twins 21 years ago. The husband died soon after marriage	D.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
8	43	14	1	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, infective endocarditis, adherent pericardium	Rheumatic pains	Recent	The child is 19 years old	D.
119	43	None	4	Several	Mitral stenosis, tricuspid stenosis	Hemiplegia	Sudden embolism	Pregnancies uneventful	D.
120	44	„	13	—	Mitral stenosis and regurgitation, aortic regurgitation, adherent pericardium, infarcts in kidney and spleen	Dyspnœa	Sudden onset 3 months ago	„	D.
121	44	7	2	—	Mitral stenosis and regurgitation, aortic regurgitation, tricuspid stenosis	„	2 years, on and off	Pregnancies uneventful, early in married life	D.
122	44	20	3	—	Mitral stenosis and regurgitation, adherent pericardium	Palpitations	3 months	Last child 8 years ago	D.
123	45	Girlhood	6	0	Mitral stenosis and regurgitation, extreme cyanosis, œdema	Dyspnœa and œdema	12 years off and on, present attack began 1 month ago	Last pregnancy preceded first cardiac symptoms by years	D.
124	46	Childhood	7	—	Mitral stenosis and regurgitation, aortic disease, infective endocarditis, big liver, etc.	Œdema and dyspnœa	1 year	Husband has been dead over 6 years; pregnancies uneventful	D.

125	49	None	7		Mitral stenosis and regurgitation, big liver, etc.	Ditto	5 years	Pregnancies uneventful	D.
126	49	Childhood	8+1 D.	0	Mitral stenosis, ascites, infective endocarditis	Ditto	8 months	Last child 11 years ago	D.
127	49	None	5		Mitral stenosis, thrombosis renal and radial arteries and aorta	Acute pains	Acute	Pregnancies uneventful	D.
128	51	„	14		Mitral stenosis and regurgitation, adherent pericardium	Acute pain in chest	„	Pregnancies uneventful; the mitral stenosis was extreme	D.
129	52	12	2		Mitral stenosis and regurgitation, aortic stenosis and regurgitation, big liver, ascites, pleural effusions	Dyspnœa and œdema	Recent	Pregnancies uneventful	D.
130	52	None	11	2	Mitral stenosis, tricuspid regurgitation, ascites	Anasarca	6 weeks	„ „	D.
131	57	18	9	2	Mitral stenosis, œdema, etc.	Cough, œdema of legs	On and off 7 years 2 weeks	Pregnancies uneventful; on one occasion twins	D.
132	58	None	7+3 D.		Mitral stenosis and regurgitation, ascites, etc.	Anasarca	1 year	Pregnancies uneventful	D.
133	61	„	0	4	Mitral stenosis, quite unexpected, but found p. m. There had been no bruit, kidneys healthy	Dyspnœa and weakness, œdema	2 years, recent	„ „	D.
134	61	14	2	3	Mitral stenosis, aortic stenosis, tricuspid stenosis, pulmonary stenosis	Dyspnœa and weakness	2 years	„ „	D.
135	71	None	11		Mitral stenosis found p. m., no bruit during life, kidneys sound	Œdema and bronchitis	5 months	„	D.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
118	43	14	1	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, infective endocarditis, adherent pericardium	Rheumatic pains	Recent	The child is 19 years old	D.
119	43	None	4	Several	Mitral stenosis, tricuspid stenosis	Hemiplegia	Sudden embolism	Pregnancies uneventful	D.
120	44	„	13	—	Mitral stenosis and regurgitation, aortic regurgitation, adherent pericardium, infarcts in kidney and spleen	Dyspnœa	Sudden onset 3 months ago	„	D.
121	44	7	2	—	Mitral stenosis and regurgitation, aortic regurgitation, tricuspid stenosis	„	2 years, on and off	Pregnancies uneventful, early in married life	D.
122	44	20	3	—	Mitral stenosis and regurgitation, adherent pericardium	Palpitations	3 months	Last child 8 years ago	D.
123	45	Girlhood	6	0	Mitral stenosis and regurgitation, extreme cyanosis, œdema	Dyspnœa and œdema	12 years off and on, present attack began 1 month ago	Last pregnancy preceded first cardiac symptoms by years	D.
124	46	Childhood	7	—	Mitral stenosis and regurgitation, aortic disease, infective endocarditis, big liver, etc.	Œdema and dyspnœa	1 year	Husband has been dead over 6 years; pregnancies uneventful	D.

125	49	None	7	—	Mitral stenosis and regurgitation, big liver, etc.	Ditto	5 years	Pregnancies uneventful	D.
126	49	Childhood	8 + 1 D.	0	Mitral stenosis, ascites, infective endocarditis	Ditto	8 months	Last child 11 years ago	D.
127	49	None	5	—	Mitral stenosis, thrombosis renal and radial arteries and aorta	Acute pains	Acute	Pregnancies uneventful	D.
128	51	„	14	—	Mitral stenosis and regurgitation, adherent pericardium	Acute pain in chest	„	Pregnancies uneventful; the mitral stenosis was extreme	D.
129	52	12	2	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, big liver, ascites, pleural effusions	Dyspnœa and œdema	Recent	Pregnancies uneventful	D.
130	52	None	11	2	Mitral stenosis, tricuspid regurgitation, ascites	Anasarca	6 weeks	„ „	D.
131	57	18	9	2	Mitral stenosis, œdema, etc.	Cough, œdema of legs	On and off 7 years 2 weeks	Pregnancies uneventful; on one occasion twins	D.
132	58	None	7 + 3 D.	—	Mitral stenosis and regurgitation, ascites, etc.	Anasarca	1 year	Pregnancies uneventful	D.
133	61	„	0	4	Mitral stenosis, quite unexpected, but found p. m. There had been no bruit, kidneys healthy	Dyspnœa and weakness, œdema	2 years, recent	„ „	D.
134	61	14	2	3	Mitral stenosis, aortic stenosis, tricuspid stenosis, pulmonary stenosis	Dyspnœa and weakness	2 years	„ „	D.
135	71	None	11	—	Mitral stenosis found p. m., no bruit during life, kidneys sound	Œdema and bronchitis	5 months	„	D.

B. *Those who had been Pregnant, and did relate Cardiac Symptoms to a Pregnancy or Labour.*

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
136	24	None	2	1	Mitral stenosis and regurgitation, ? tricuspid stenosis	Palpitations	4 months	We are not certain of the relation, but suspect it	R.
137	26	„	4	2	Mitral stenosis and regurgitation, ascites, etc.	Ascites	1¼ years	Married 9 years. We suspect the condition was made worse by child-bearing	R.
138	33	„	6	—	Mitral stenosis, bronchitis	Bronchitis	16 years off and on	She dates her trouble from small-pox at 16. She had her first child 12 years ago, the last 9 days ago. She has had bronchitis and dyspnœa badly with each pregnancy, recovering between. The present attack has been her worst, and dates from soon after labour, 9 days ago	R.
139	37	15	12	—	Mitral stenosis and regurgitation	Dyspnœa	2 months	Eleven pregnancies were uneventful; dyspnœa came on 10 days after her twelfth labour, 2 months ago	R.
140	38	None	4	2	Mitral stenosis and regurgitation, anasarca	Œdema and dyspnœa	4 years	She had no symptoms of heart trouble until just after the last labour, an 8 months living child, 4 years ago	R.
141	39	17	4	3	Mitral stenosis and regurgitation, big liver, etc.	Ditto	6 years	We do not know for certain the relationship, but suspect heart trouble was made worse by pregnancies; she had been married 11 years	R.
142	39	None	6	2	Mitral stenosis, bronchitis	Cough	—	She had bad bronchitis each time she was carrying; no œdema	R.
143	40	14	6	—	Mitral stenosis, pulmonary regurgitation,	Œdema	11 years off and on	She dates her cardiac symptoms from soon after the birth of her second	R.

					ascites, etc.			child, 11 years ago; she has borne 4 children since, each time with but slight exacerbation of her symptoms	
144	46	18	11		Mitral stenosis and regurgitation, aortic stenosis and regurgitation, ascites	Palpitations, etc.	4 years	She was quite well until 4 years ago, having borne 10 children without trouble; she dates her symptoms from shortly after the birth of her eleventh child (a living 7 months infant), 4 years ago	R.
145	47	None	3		Mitral stenosis and regurgitation, pleurisy	Pleurisy	Heart trouble on and off 9 years	Last child 9 years ago; the two previous gave no trouble	R.
146	26	13	2		Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Dyspnœa	2 months acute	Was quite well till 3 month s after birth of first child, when she had acute dyspnœa; the second pregnancy was uneventful except for persistent dyspnœa, which became acutely worse again some while after labour	R.
147	25	None	2	0	Mitral stenosis and regurgitation, pleuritic effusion, old hemiplegia	„	On and off ever since a child	The last pregnancy was 2 years ago; there was no trouble with the previous child, nor indeed with the last, but the dyspnœa got gradually worse and worse after the labour; she was still alive 3 years later	R.
148	33	16	6		Mitral stenosis, tricuspid regurgitation	Œdema and precordial pain	8 weeks	No trouble with first 5 pregnancies, though heart disease was known from 16; 3 weeks before sixth child was born œdema of the legs began; after labour this went on to anasarca; she recovered	R.
149	21	None	1	0	Infective endocarditis on old mitral stenosis	Hæmoptysis, and splenic pain	6 weeks	No trouble with pregnancy or labour; is now 5 months pregnant; went out, still pregnant, against advice	Worse
150	23	12	4		Mitral stenosis and regurgitation, ascites, etc.	Dyspnœa	3 years, acute 3 weeks	The 4 children were born without trouble, but 3 weeks ago, 2 months after last labour, acute dyspnœa set in	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
151	24	Girl-hood	1	—	Mitral stenosis, bronchitis	Cough; no œdema	Recent	Was pregnant 5½ months on admission; she got much better and went out; relapsed, came in again, recovered, went out again, and went to term without further trouble	R.
152	24	None	0	0	Mitral stenosis	Dyspnœa and hæmoptysis	3 months	Was pregnant 5 months on first admission; got better on treatment, went out, relapsed, came in again, got better, went out again still pregnant	R.
153	24	16	1 d.	—	Mitral stenosis, aortic regurgitation	Dyspnœa (not bad)	Years	Married 12 months. Had been in and out of hospital seven times for heart disease before marriage. She was in bed in hospital 203 days; was then delivered of a dead 8-months fœtus, and went out 14 days after labour pretty well	R.
154	27	17	0	1	Mitral stenosis, ascites, tapped	Ascites	1½ years	She has been married 2 years. Ascites developed during first pregnancy and caused miscarriage. She has had œdema and ascites on and off ever since	R.
155	27	None	4 + 1 d.	—	Mitral stenosis	Dyspnœa, hæmoptysis	14 months, 6 months	She bore 3 children without trouble. The fourth was 4 years ago; 5 months before this labour she had a cerebral embolism with hemiplegia. She got better of this, and had no heart trouble till 14 months ago, when dyspnœa began; 7½ months ago she became pregnant again, and 1½ months later hæmoptysis started. Cough increased during pregnancy,	R.

								but she went almost to term, and had a living child weighing 6 lb. 8 oz., natural delivery. She went out fairly well	
156	28	16	4		Mitral stenosis and regurgitation, ascites, pleuritic effusion	Ascites	5 months	The first 3 labours were natural. Soon after the fourth child was born cardiac trouble began	R.
157	28	None	1 + 1 d.		Mitral stenosis and regurgitation, ascites	Dyspnœa and ascites	6 months	She had no trouble with first pregnancy, 6 years ago. Soon after the second, 6 months ago, ascites began and increased	R.
158	29	None	4	2	Mitral stenosis, aortic regurgitation, pleuritic effusion	Hæmoptysis, severe dyspnœa	3 years off and on, 1 month	The third full-term child was 3 years ago; she dates hæmoptysis from then. After that she had two miscarriages; a month ago she was delivered of her fourth full-term child, living, and has been in bed with severe dyspnœa since	R.
159	30	Childhood	2	0	Mitral stenosis and regurgitation, tricuspid regurgitation, etc.	Severe dyspnœa	11 months	There was no trouble with the first child; the second was born 11 months ago, and following labour the dyspnœa set in	R.
160	31	None	3	0	Mitral stenosis and regurgitation, œdema	Bronchitis, œdema	Some years off and on, 20 months	Was quite well till after first labour; bronchitis then set in, and recurred with each of the two pregnancies; the last labour was 20 months ago; œdema set in after this last labour. Infective endocarditis was suspected on last admission, on account of pyrexia; she went home worse	Worse
161	32	Girlhood	5	0	Mitral regurgitation	Hæmoptysis	Recent	She was in hospital at 18 for palpitations and dyspnœa. She married subsequently, and had 4 children without trouble. When 6 months pregnant of fifth child she had sudden hæmoptysis, lasting 4 days. There was no other cardiac trouble; she only lay up 4 days; she went to term naturally	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
162	33	None	4	—	Mitral stenosis, bronchitis	Dyspnœa and bronchitis	8 months, worse 1 week	Three pregnancies gave no trouble; early in the fourth dyspnœa and hæmoptysis set in; she went to term, and the child was born alive; the dyspnœa got worse after labour; she came to hospital for relief and recovered with rest in bed	R.
163	33	Childhood	7	1	Mitral stenosis	Dyspnœa	Many years	The first four children caused no heart symptoms; with fifth and sixth there was dyspnœa. She is now pregnant 7 months, having had hæmoptysis for 7 months; œdema set in at 7 months, and got worse to term. The child was born living naturally; there was a bad attack of dyspnœa on fourth day after labour; the mother responded to treatment, and went out moderately well	R.
164	34	20	7	1	Mitral stenosis and regurgitation, infarcts in spleen and lungs	Œdema and ascites	4 months	She dates her heart failure directly to her miscarriage 4 months ago, when 6 months pregnant. There was no trouble with any of the previous 7 children	D.
165	34	Childhood	2	0	Mitral stenosis, pleurisy	Pleurisy	None	She came in with a week's history of pleuritic pain when pregnant nearly to term. A pleuritic effusion was found. Labour at term was natural	R.
166	36	None	2	0	Mitral stenosis, tricuspid stenosis	Dyspnœa	4 months	No trouble with pregnancy till fourth month, when acute dyspnœa set in. She had several attacks of dyspnœa, but went to term, and was delivered	R.

								of living twins (boys) naturally. Two weeks after labour there was another very acute attack of dyspnœa; the patient rallied rapidly and went out apparently well	
167	37	None	5	1	Mitral stenosis and regurgitation, ascites, etc.	Orthopnœa and œdema	9 weeks	She was quite well during five former pregnancies, but had a miscarriage 9 weeks ago, since when she has not been well	R.
168	37	None	12	—	Mitral stenosis and regurgitation	Acute rheumatism	No real heart failure	She had no trouble at all with the first 12 children; when 4 months pregnant with the 13th she got very bad rheumatic fever, and was found to have signs of old mitral disease. She recovered and went out still pregnant	R.
169	38	20	6	—	Ditto	Œdema and dyspnœa	Many years on and off	She got dyspnœic during her first pregnancy, and has been bad with each subsequently. On two occasions labour was induced at the 8th month for heart failure, on one of which occasions p. p. h. was almost fatal. After her fourth child she was discharged "a wreck," but recovered at home, and bore two more children. The last of these was born without induction; it was a transverse presentation; version was performed; the mother and child both did well	R.
170	38	12	10	—	Ditto	Dyspnœa	·14 months	There was no trouble with first nine children; after the birth of the tenth, 14 months ago, dyspnœa set in, and has been getting worse and worse since	R.
171	41	16	5 + 1 D	2	Aortic disease and mitral stenosis	„	Recent	No trouble with former labours. When pregnant for eighth time, and near to term, dyspnœa began, followed by easy labour and recovery. The child was dead	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
172	43	18	13	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Œdema	5 months	12 pregnancies were uneventful; with the 13th cardiac symptoms began; œdema set in 2 months after labour, and grew worse. She recovered with rest in bed	R.
173	41	None	7	—	Mitral stenosis and regurgitation	Anginal pain	14 years	3 pregnancies were uneventful; after the fourth labour anginal attacks began. Notwithstanding these, she bore three more living children, the last six years ago. She is a chronic invalid.	Very ill.
174	25	None	1	—	Mitral stenosis, thromboses, anasarca	Dyspnœa	14 days	The child was born living 14 days ago; there were no symptoms till after labour	D.
175	38	„	8	—	Mitral stenosis and regurgitation, calcareous vegetations	„	11 weeks	Was quite well until after last confinement, 11 weeks ago; the first 7 pregnancies were uneventful	D.
176	31	„	8	—	Mitral stenosis, pleuritic effusion	Anasarca, precordial pain, dyspnœa	7 weeks + many years on and off	She had cardiac symptoms shortly after second pregnancy and was short of breath through all the subsequent ones; the first was natural, the last was 7 weeks ago	D.
177	31	„	5	1	Mitral stenosis and regurgitation, aortic stenosis, infarcts in lungs	Dyspnœa and œdema	1 year	She came in pregnant and got better under treatment; she went out and went to term naturally; she came in again a few weeks afterwards. She dated her heart symptoms to the miscarriage 1 year ago	D.

178	30	17	1	0	Mitral stenosis, tricuspid stenosis, aortic stenosis, infarcts in lungs, gastric ulcer	Anasarca, dyspnœa, and hæmatemesis	Some months	The cardiac symptoms came on early in the only pregnancy, but she rested and went to term; the child was small, living; she collapsed 10 days after labour, a few days before admission; she got worse and worse, and died	D.
179	25	None	2	2	Mitral stenosis, infective endocarditis, various infarcts	Œdema and weakness, and acute hemiplegia	Recent + some years	The first labour at term was natural; then followed two miscarriages, and there were cardiac symptoms with each; the last labour at term was 10 months ago, without much trouble, but the patient has never been well since; the progress was downhill continuously	D.
180	23	„	3		Ditto	Chorea	Recent	There had been no previous chorea; the three children were born without trouble. When pregnant fourth time, she developed chorea at sixth month and aborted 21 days afterwards; she went rapidly downhill and died 23 days after the abortion	D.
181	3	12	5		Mitral stenosis and regurgitation, adherent pericardium, ascites, etc.	Cough Œdema	9 years 2 years	The first 4 children were born without trouble; the fifth was born alive at term 3 months ago naturally; œdema of legs and ascites came on one week after labour; the patient went rapidly downhill	D.
182	20	14	1	0	Mitral stenosis and regurgitation, infective endocarditis, pericarditis	Œdema	2½ years	Symptoms of heart failure came on early during the only pregnancy, 2½ years ago; the cardiac symptoms were so bad that labour was induced at the eighth month; the child lived. The mother recovered a little, but was a chronic invalid, and finally developed malignant endocarditis	D.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
183	28	None	4	0	Mitral stenosis, tricuspid regurgitation	Dyspnœa	Some months	She "had never been ill in her life" until, when 4 months pregnant of the fourth child, symptoms of dyspnœa and cough came on; after rest and digitalis in hospital she got better and went home. She returned at term, and had a living child easily; the mother did well at first, but a few days after getting up she developed further heart symptoms, and rapidly went downhill and died	D.
184	24	16	1	—	Mitral stenosis and regurgitation, bronchitis	Dyspnœa and œdema	18 months	Heart failure began during the pregnancy, but acute symptoms did not arise until a living child had been born at term. Since then she had been in and out of hospital 5 times in a year, never really recovering compensation	D.
185	40	None	4	4	Mitral stenosis, infarcts in kidneys	Dyspnœa	5 months	She had always been well, except that 10 years ago she was in hospital for albuminuria during pregnancy. Four labours and 3 miscarriages were without cardiac symptoms; the latter date from a miscarriage at the 3rd month, 5 months ago	D.
186	28	Childhood	1	—	Mitral stenosis, tricuspid stenosis, aortic regurgitation	General failure	2 years	She was quite well till the child was born, 2 years ago; heart failure set in soon after labour, and she has never been well since	D.
187	28	None	1	—	Mitral stenosis, hemiplegia, infarcts, tricuspid vegetations	Palpitations and hæmoptysis	5 years	Palpitations and hæmoptysis have recurred during the last five years. The only child was born living at the	D.

								7th month, 8 months ago, and the cardiac symptoms became much worse. She has gone downhill ever since	
188	32	17	2		Mitral stenosis and regurgitation, hemiplegia	Œdema	3 years on and off	The first child was born normally. The symptoms date from soon after the birth of the second child, 3 years ago	D.
189	38	6	1		Mitral stenosis, infective endocarditis, pleuritic effusion, various infarcts	Dyspnœa and hæmoptysis	7 months	The child was born naturally 9 months ago. Two months later dyspnœa and hæmoptysis set in; the heart symptoms went from bad to worse	D.
190	41	8	6+ 1 D.		Mitral stenosis and regurgitation, infective endocarditis	Œdema, dyspnœa, acute	9 months 2 weeks	There was no trouble till the last child was born, 2 years ago. Soon after she had hemiplegia. No other cardiac symptoms followed until 9 months ago, when œdema appeared; she became acutely dyspnœic 2 weeks ago and died in a few weeks	D.
191	43	8	2		Mitral stenosis and regurgitation, vegetations, œdema, hæmoptysis	Dyspnœa, œdema	1¾ years 1 month	The first child brought no heart trouble. Three months after the birth of the second, 1¾ years ago, the patient became dyspnœic. She was able to do her work until 1 month ago, when œdema came on, and she died soon after admission. It is doubtful if this can really be attributed to the pregnancy	D.
192	48	Girlhood	8	4	Mitral stenosis and regurgitation, general heart failure	Dyspnœa	10 years	The patient directly dates symptoms to a labour 10 years ago. She has since been pregnant 3 times. The eldest child is 25, the youngest 6. She has never been well since the last was born, though she has done her work on and off till recently	D.
					c. *Cases Married, but never Pregnant.*				
193	25	18	—	—	Mitral stenosis and regurgitation	Rheumatism	None	Married 3 years.	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
194	26	None	—	—	Mitral stenosis and regurgitation	Dyspnœa and precordial pain	2 years	Married recently. Heart troubles started before marriage	Worse
195	26	Girl-hood	—	—	Mitral stenosis, bronchitis	Œdema and cough	5 weeks	—	D.
196	29	None	—	—	Mitral stenosis, tricuspid regurgitation	Dyspnœa and weakness	6 years	Married 9 years	D.
197	31	16	—	—	Mitral stenosis and regurgitation, bronchitis	Cough and precordial pain	2 months	Married 11 years	R.
198	34	None	—	—	Mitral stenosis and regurgitation, pulmonary regurgitation, ascites, etc.	Œdema and ascites	„	Married 8 years, and has been out of health on and off ever since	R.
199	34	„	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Dyspnœa and œdema	4 months	—	R.
200	35	16	—	—	Mitral stenosis, general failure	Dyspnœa	18 months	Has been in Guy's Hospital more than a dozen times. She recovers quickly, but soon relapses. She is a widow	R.
201	36	7	—	—	Mitral stenosis, anasarca	Dyspnœa and ascites	1 year	Had cerebral embolism 9 years ago. Married 18 years	D.
202	36	None	—	—	Mitral stenosis and regurgitation, tricuspid regurgitation	Orthopnœa and œdema	17 years	Married 8 years. A chronic hospital inmate	R.
203	39	„	—	—	Mitral stenosis, epithelioma of œsophagus	Dysphagia	None	Married 9 years. Mitral stenosis, unsuspected, found p. m.	D.
204	41	4	—	—	Mitral stenosis and regurgitation, double aortic disease	Dyspnœa	Months	—	D.
205	55	12	—	—	Mitral stenosis, hæmatemesis	Dyspnœa and cyanosis	28 years on and off	—	D.

D. *Unmarried cases.*

206	20	6	—	—	Mitral stenosis	Dyspnœa, hæmoptysis	2 years	—	R.	
207	20	None	—	—	Mitral stenosis, aortic stenosis	Dyspnœa and palpitations	2 months	—	R.	
208	20	,,	—	—	Mitral stenosis	Dyspnœa	3 years	—	R.	
209	21	Child-hood	—	—	Mitral stenosis, acute rheumatism	Precordial pain	None	—	R.	
210	21	19	—	—	Mitral stenosis and regurgitation, acute rheumatism	Dyspnœa	2 years on and off	Hemiplegia due to cerebral embolism occurred just before admission	R.	
211	21	12	—	—	Mitral stenosis and regurgitation	Dyspnœa	Acute	—	R.	
212	21	Girl-hood	—	—	Mitral stenosis and regurgitation, aortic stenosis, acute rheumatism	Precordial pain	3 months	—	R.	
213	21	12	—	—	Mitral stenosis and bronchitis	Cough and dyspnœa	7 years	—	R.	
214	21	None	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Precordial pain	Acute	—	R.	
215	21	10	—	—	Mitral stenosis and regurgitation, bronchitis	Cough and pain in chest	2 weeks	—	R.	
216	21	10	—	—	Mitral stenosis and regurgitation, anasarca	Dyspnœa and œdema	Recent	—	R.	
217	21	7	—	—	Mitral stenosis and regurgitation	Pain in side, œdema	,,	—	R.	
218	22	14	—	—	Mitral stenosis and regurgitation, paracentesis abdominis	Precordial pain, ascites	1 year	—	R.	
219	22	10	—	—	Mitral stenosis and regurgitation	Dyspnœa	Recent	—	R.	
220	22	10	—	—	Mitral stenosis and regurgitation, large liver, etc.	Œdema	1 month	—	R.	

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
221	22	None	—	—	Mitral stenosis and regurgitation, bronchitis	Dyspnœa and œdema	6 months	Was often admitted afterwards. A chronic invalid	R.
222	22	11	—	—	Mitral stenosis and regurgitation	Acute rheumatism	None	—	R.
223	23	11	—	—	Mitral stenosis and regurgitation, infective endocarditis	Hæmaturia	Recent	Went home to die	Worse
224	23	12	—	—	Mitral stenosis, epilepsy	Fits	None	—	R.
225	23	None	—	—	Mitral stenosis and regurgitation, rheumatic nodules	Weakness	Months	—	R.
226	23	Childhood	—	—	Mitral stenosis, hæmatemesis	Hæmatemesis	None	—	R.
227	23	14	—	—	Mitral stenosis and regurgitation	Œdema	5 months	—	R.
228	23	14	—	—	Ditto	Dyspnœa	Recent	—	R.
229	23	Childhood	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	„	4 years	—	R.
230	23	16	—	—	Mitral stenosis and regurgitation, pericarditis	Dyspnœa	3 months	—	R.
231	23	None	—	—	Mitral stenosis and regurgitation, exophthalmic goitre, Raynaud's disease	Nervousness	None	—	R.
232	23	16	—	—	Mitral stenosis and regurgitation, bronchitis	Cough and dyspnœa	4 months	—	R.

233	24	8	—	—	Mitral stenosis and regurgitation, gastritis	Gastric pain and vomiting	None	—	R.
234	24	7	—	—	Mitral stenosis and regurgitation, acute rheumatism (3rd attack)	Rheumatism	„	—	R.
235	24	19	—	—	Mitral stenosis and regurgitation, gastritis	Gastric pain	„	—	R.
236	24	None	—	—	Mitral stenosis, ganglion on wrist	Ganglion	„	—	R.
237	24	9	—	—	Mitral stenosis and regurgitation, nutmeg liver	Dyspnœa and œdema	Years	—	R.
238	24	16	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Dyspnœa	„	—	R.
239	25	9	—	—	Mitral stenosis and regurgitation, ascites	„	2 months	—	R.
240	25	None	—	—	Mitral stenosis and regurgitation	Œdema	1 year	Palpitations for 7 years	R.
241	25	16	—	—	Ditto	Precordial pain and œdema	Recent	—	R.
242	25	None	—	—	Ditto	Palpitation	1 year	—	R.
243	25	„	—	—	Ditto	Dyspnœa and œdema	4 years	—	R.
244	26	20	—	—	Mitral stenosis and regurgitation, pleuritic effusion	Ditto	1 year	There was slight cerebral embolism 1 year ago	R.
245	26	None	—	—	Mitral stenosis and regurgitation, pericarditis	Ditto	10 months	—	R.
246	27	7	—	—	Mitral stenosis and regurgitation	Œdema	2 weeks	—	A wreck
247	27	12	—	—	Mitral stenosis and regurgitation, aortic regurgitation	Bad dyspnœa and cough	Years	Has been in and out of hospital nearly a dozen times	

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
248	27	7	—	—	Mitral stenosis and regurgitation, aortic stenosis	Dyspnœa and palpitations	7 months	—	R.
249	28	10	—	—	Mitral stenosis and regurgitation	Œdema	2 years	—	R.
250	28	16	—	—	Mitral stenosis, chronic osteoarthritis	Deformed joints	None	—	R.
251	28	12	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Pleuritic effusion	Acute	—	R.
252	28	Childhood	—	—	Mitral stenosis, tricuspid regurgitation	Dyspnœa and œdema	1 year	—	R.
253	28	None	—	—	Mitral stenosis and regurgitation, cerebral embolism	Hemiplegia	None	—	R.
254	29	11	—	—	Mitral stenosis and regurgitation, aortic regurgitation, big liver	Orthopnœa	4 years	—	R.
255	30	10	—	—	Mitral stenosis and regurgitation, aortic regurgitation	Hæmoptysis	Recent	—	R.
256	30	6	—	—	Mitral stenosis	Precordial pain	4 years	—	R.
257	31	18	—	—	„ „	Hæmoptysis	None	—	R.
258	31	14	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Dyspnœa	1 year	—	R.
259	32	None	—	—	Mitral stenosis and regurgitation, big liver, etc., ascites	Orthopnœa	6 years	—	Worse

260	32	12	—	—	Mitral stenosis and regurgitation, pleurisy, typhoid fever	Enteric	None	—	R.
261	32	None	—	—	Mitral stenosis	Dyspnœa, Hæmoptysis	6 months	—	R.
262	33	„	—	—	Mitral stenosis and regurgitation, bronchitis	Dyspnœa	1 year	—	R.
263	33	16	—	—	Mitral stenosis and regurgitation	Pleurisy	None	—	R.
264	34	7	—	—	Ditto	Dyspnœa	Years	Known to have had heart disease at 15.	R.
265	34	None	—	—	Mitral stenosis, transverse myelitis	Paraplegia	None	—	R.
266	35	„	—	—	Mitral stenosis, carcinoma of breast	Dyspnœa	11 years	—	R.
267	35	5	—	—	Mitral stenosis, appendicitis	Appendicular	None	—	R.
268	35	16	—	—	Mitral stenosis and regurgitation, tricuspid regurgitation	Dyspnœa	9 years	Known to have had heart disease at 14.	R.
269	35	Childhood	—	—	Mitral stenosis and regurgitation, aortic regurgitation	„	3 years	—	R.
270	35	None	—	—	Mitral stenosis	Precordial pain	8 months	—	R.
271	36	„	—	—	„ „	Cough and weakness	1 year	—	R.
272	37	„	—	—	Mitral stenosis, acute rheumatism, mania	Insanity	None	—	R.
273	37	16	—	—	Mitral stenosis, cerebral embolism	Hemiplegia	6 years	—	R.
274	38	Girlhood	—	—	Mitral stenosis, gastric ulcer	Hæmatemesis	None	—.	R.
275	39	20	—	—	Mitral stenosis, mad with delusions	Hæmoptysis	11 years, on and off	—	R.
276	40	None	—	—	Mitral stenosis, aortic regurgitation	Dyspnœa	6 weeks	—	R.
277	40	19	—	—	Mitral stenosis, tricuspid regurgitation, bronchitis	Dyspnœa and cough	3 years	—	R.

Case number.	Age.	Age at which rheumatism or chorea.	Number of children.	Number of miscarriages.	Main diagnosis.	Symptoms for which admitted.	Duration of cardiac failure.	Details.	Result.
278	40	None	—	—	Mitral stenosis, pelvic tumour, no operation	Dyspnœa	Many years	—	R.
279	43	„	—	—	Mitral stenosis and regurgitation, aortic stenosis	„	Years	—	R.
280	45	Childhood	—	—	Mitral stenosis and regurgitation	Dyspnœa and œdema	4 months	—	R.
281	47	20	—	—	Mitral stenosis and regurgitation, big liver, etc.	Dyspnœa and pain	Years	—	R.
282	48	None	—	—	Mitral stenosis and regurgitation, big heart, bronchitis	Ditto	1 year	—	R.
283	60	„	—	—	Mitral stenosis and regurgitation	Dyspnœa and cough	1 month	—	R.
284	21	None	—	—	Mitral stenosis and regurgitation, aortic regurgitation	Dyspnœa	1½ years	—	D.
285	23	9	—	—	Mitral stenosis, pericarditis	„	1 year	—	D.
286	23	None	—	—	Mitral stenosis, infective endocarditis, infarcts	Malaise	Recent	—	D.
287	23	16	—	—	Mitral stenosis and regurgitation, acute endocarditis	Dyspnœa	7 years	—	D.
288	23	None	—	—	Mitral stenosis, pericarditis, infective endocarditis	Dyspnœa and pain	4 months	—	D.
289	24	12	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation	Angina pectoris	6 years	—	D.

290	26	None	—	—	Mitral stenosis (old), infective endocarditis	Dyspnœa	2 years	—		D.
291	26	„	—	—	Mitral stenosis, pericarditis, pleurisy exophthalmic goitre	Joint pains	None	—		D.
292	28	Childhood	—	—	Mitral stenosis, tricuspid stenosis, dropsy	Dropsy	3 years	—		D.
293	29	15	—	—	Mitral stenosis, pericarditis, pleuritic effusion, infarcts	Dyspnœa	Recent	—		D.
294	33	None	—	—	Mitral stenosis, infective endocarditis, infarcts	Sudden hemiplegia	„	—		D.
295	38	„	—	—	Mitral stenosis and regurgitation, big liver, infarcts	Dyspnœa	2 years	—		D.
296	40	Childhood	—	—	Mitral stenosis and regurgitation, adherent pericardium	„	Recent	—		D.
297	42	None	—	—	Mitral stenosis and regurgitation, tricuspid stenosis, anasarca	Dropsy	„	—		D.
298	44	„	—	—	Mitral stenosis, big liver, ascites, pericarditis, pleuritic effusion	„	„	—		D.
299	44	12	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, adherent pericardium	Dyspnœa	Years	—		D.
300	41	19	—	—	Mitral stenosis and regurgitation, aortic stenosis and regurgitation, infective endocarditis	„	4 months	—		D.

DISCUSSION.

Sir DYCE DUCKWORTH thought that Dr. French had done good service in bringing forward the facts he had gathered from that excellent storehouse of them at Guy's Hospital. The question as to the desirability of marriage in cases of heart disease was a very important one, and had enlisted his interest in the course of practice as a physician. He might state at once that he was in the habit of forbidding matrimony to young women suffering from mitral stenosis, although he was bound to add that his advice was, as a rule, not taken. Alluding to the greater frequency of this condition in women, to the fact of its dependence on previous rheumatic endocarditis, and to the special risks entailed owing to the natural plethora of pregnancy and the mechanical pressure, he conceived the risk to be so considerable as to justify abstention from maternity. Dr. French had, however, shown by statistics that the risks were less grave by far than was commonly taught and believed. After all, statistics did not prove everything, and each case required to be studied as to age, soundness of constitution, and the prospects of future comfort and suitable environment. Women with old rheumatic heart-disease he thought more liable than others to transmit a vicious tendency in this direction to their offspring. The condition of mitral stenosis was much more serious than that of mitral reflux, and the latter condition might be consistent with viability to the natural term. In spite of Dr. French's statistics and views, it would still remain difficult to sanction matrimony, and all that that state entailed, for young women with mitral stenosis.

Dr. HERMAN said the paper was a most valuable and important one. He had long thought, taught by clinical experience, that the monographs on pregnancy with heart disease, by Macdonald and others, put the dangers of this complication far too high. This was because, as the authors of this evening's paper said, the monographs were based on selected cases, cases which had been reported because with pregnancy there was trouble from heart disease. Nevertheless these monographs had been compiled with great ability and care, and therefore the writers of text-books on midwifery could not neglect them, and thus these exaggerations appeared in one text-book after another. The able paper they had just listened to would, he hoped, cause them to disappear. The authors had also, he thought, disposed of the fictions that mitral disease caused sterility and that it caused abortion. Although in the majority of cases of mitral stenosis with good compensation the patients went through pregnancy and labour perfectly well, yet there were a few in which, although compensation was adequate while the patient

was not pregnant, yet in the last two months of pregnancy compensation began to fail. In such cases he had seen wonderfully great and rapid improvement follow the induction of premature labour. He had seen a patient unable to lie down from breathlessness up and about a fortnight after the induction of labour. He thought the best practice was to do this as soon as signs of failure of compensation appeared. He agreed with the authors in thinking that the dogmatic "No" as to marriage was unjustifiable. To forbid marriage was beyond the doctor's province. If a patient consulted a doctor as to marriage, all the doctor had to do was to explain to the patient what he thought would be the effects upon her health. If, knowing what those effects were likely to be, she yet chose to marry, that was her business, and not the doctor's. In the case of heart disease the present paper showed how small the risk was, although some increased risk in the event of pregnancy did exist. It was so small that he thought that if the circumstances of a contemplated marriage were in every other respect all that they should be, the patient should be advised to accept the small risk.

Dr. J. T. GARDNER (Chelsea) remarked that he had had a large midwifery practice extending over more than a quarter of a century, and during that time had had to deal with several cases of labour complicated with mitral stenosis. He had always in bad cases, as soon as labour had definitely set in, put the patient under chloroform, dilated, and delivered with forceps, and in every case the patient had had no bad symptoms. With regard to the statement quoted by Dr. French that one authority had said that women suffering from mitral stenosis were often sterile, he thought such a condition might in some measure be due to medical advice, and quoted a case in which a lady when young had suffered from rheumatic fever, in which the heart was seriously involved. She had fallen in love and consulted her medical man, who advised her not to marry, and told her if she did and became pregnant she would certainly die in her confinement. This advice was not followed and the couple married, and religiously used various methods for preventing conception. In spite of these precautions, however, she got in the family way and her husband consulted him (the speaker) and asked him what was to be done as he felt much distressed and considered himself, after what had previously been stated, in the light of her murderer. He advised him to relieve his mind of all anxiety, to let her go to full time, and simply keep her under supervision. This was done, and as soon as labour had actually set in chloroform was administered, the os dilated and forceps applied, and the case did well. Now, as in this case the patient had been told she would certainly die if she had a child, so in other cases if the same advice was given probably in case of marriage preventives would be used and the case would apparently be sterile,

and perhaps that would give rise to a false impression that sterility was associated with mitral stenosis. In his experience he had never noticed that the two conditions were so associated.

Dr. GIBBES quite agreed with the deductions of the authors, for the more he saw of pregnancy in mitral stenosis the more he was convinced that the accepted statistics were wrong and the less he dreaded its results in that disease. He believed that even cases of marked loss of compensation could be safely piloted through child-birth if treatment were commenced at an early period of pregnancy. He, however, went farther than this, for he believed that in certain cases pregnancy could be utilised to restore compensation, and quoted two illustrative cases. First, a young married lady who suffered from mitral stenosis previous to her marriage was confined in November, 1900, without showing any loss of compensation. In March, 1901, she contracted diphtheria, and miscarried in the following month, being then three months pregnant. Compensation failed consequent on the diphtheria; in spite of all treatment it could not be restored. At the end of 1903 she again became pregnant, and the physiological cardiac hypertrophy consequent on that condition fully restored compensation. She passed through her confinement and puerperium without any heart failure, nor has she had any signs of it since. The second case was somewhat similar. The patient was confined with her first child in January, 1903, without any loss of compensation, but contracted typhoid fever in July of the same year, and failure ensued. Treatment greatly improved the heart, but only restored compensation up to a certain point. He then recommended that she should have another child, and she was confined in September, 1905. The results were quite as satisfactory as in the former case, and the patient stated quite recently that she felt as well as she did before her marriage. He considered that great care should be taken in the selection of cases, and should not recommend pregnancy in any case of mitral stenosis unless there had been a previous parturition without any heart-failure, because he thought that gave a reliable basis upon which to form a prognosis. He had also recommended it in a third case with equally good results, and should not hesitate to do so again provided the case was a suitable one. He considered that heart-failure in mitral stenosis more frequently resulted from pregnancy following some intercurrent disease or some debilitating cause, such as over-lactation, than from the pregnancy *per se*.

Dr. POYNTON said that he must apologise to the meeting if he turned the path of the discussion a little to one side for a moment. He wished to put on record some statistics which he thought simply and clearly explained the frequency of mitral stenosis in women. In 350 consecutive cases of rheumatism in childhood he had found 228 were female and 122 were males.

This preponderance of female children was a recognised fact. He also found that heart disease was as frequent in the female as in the male children. It followed, therefore, that at the age of twelve there would be more females than males with rheumatic heart disease. He also found that he had among these 350 cases 25 fatal ones—15 males, 10 females; that is, 10 in 228 females had died of acute rheumatism, and 15 of the 122 males. In his opinion these numbers expressed the general law that acute rheumatism was more acutely fatal in the males and more chronic in type in the females. After puperty the strain on the man's heart, especially among the poor, in whom rheumatism was so rife, was, by nature of his employment, greater than on the woman's, and so in adult life even more females were met with suffering from rheumatic heart disease than males. But, as he had already remarked, the form of heart disease in females was more chronic, and the common type of chronic rheumatic heart disease was mitral stenosis, and thus it was that so many cases were met with in women. The second point he would like to speak upon was suggested in Dr. French's most interesting paper, by his allusion to the occurrence of fungating endocarditis in some cases of his series. Where Dr. French had said that the authors fancied that possibly pregnancy might have had some influence in producing this type of endocarditis he himself had fell in agreement with them. He would now speak of the entire question of rheumatism and pregnancy. Rheumatism he believed to be an infection secondarily in importance in this country to the infection of tuberculosis, and he believed that the general tendency of pregnancy and the puerperium was to intensify the virulence of the rheumatic infection. With Dr. Paine before this Society he had demonstrated that the micro-organism which could produce simple endocarditis was also able to produce fungating endocarditis. Further, pregnant animals were, in their experience and that of Dr. Vernon Shaw, particularly liable to severe and fungating endocarditis when infected during pregnancy. He believed, then, that rheumatic endocarditis in pregnancy was liable to become fungating in type. Chorea, too, was more malignant under those circumstances, and owing to the kindness of Sir Cooper Perry and Dr. French, he had recently with Dr. Gordon Holmes demonstrated a diplococcus in the central nervous system of such a case, a point of considerable interest which would be published in detail shortly. Then, lastly, he thought that some of those severe forms of arthritis, rheumatoid in type and following the puerperium in rheumatic women, were in reality malignant rheumatic arthritis. It was then, he thought, an important point for consideration in prognosis whether these married women were suffering still from repeated attacks of subacute rheumatism, or whether the rheumatism had been quiescent for

years and had only left the stamp of its early reign in the form of mitral stenosis.

Dr. VICTOR BONNEY, whilst agreeing in the main with the conclusions which the authors had drawn, thought that puerperal women the subject of old-standing valvulitis should certainly be regarded as peculiarly liable to acute infective endocarditis in the event of puerperal sepsis. He had himself seen three cases in whom death from puerperal sepsis had been associated with acute streptococcal valvulitis. In all these three cases the organism found in the valves was proved to be present in the uterus also; they therefore did not belong to the class of acute rheumatic valvulitis to which Dr. Poynton had drawn attention. On the other hand, he recalled a case in which acute infective valvulitis developed some weeks *before* the onset of labour. Unfortunately, no bacteriological examination of the valves was made, but this might well be such a case as Dr. Poynton had described. He felt most strongly that in patients the subjects of cardiac disease very special precautions should be taken to include the possibility of puerperal sepsis. The poorer patients should go into a lying-in hospital.

Dr. GRIFFITH said that the paper was a valuable contribution to our knowledge of the subject and an excellent corrective to the opinions which all obstetricians must form of the great gravity of the cases which usually come under their notice. The cases to which the obstetrician is called to advise are mostly those in which there is some great heart-failure. You find the patient advanced in pregnancy, sitting up in bed in great distress, cyanosed, with considerable œdema, and sometimes hæmoptysis, and in these very grave cases, undoubtedly aggravated by the advanced pregnancy, a favourable prognosis, not only as to safe delivery but of eventual recovery, which may, however, be rapid and far more complete than might be expected, cannot with certainty be given until several weeks have elapsed, when the heart has had time to settle down to its previous normal condition to which it has been accustomed. These cases of varying degrees of severity are naturally those that impress the mind of the obstetrician. Dr. Ingram, senior resident medical officer at Queen Charlotte's Hospital, collected for him the following information about the cases under care during the years 1902, 1903, 1904: The total number of women delivered in these three years was 4171, of whom 28 were found to have marked cardiac disease; 2 were aortic, both recovered; 14 mitral regurgitation, with 2 deaths; 12 mitral stenosis, with or without regurgitation, 1 death. The latter was a 1-para with heart dilated and the lungs œdematous. She died forty-five minutes after delivery. The two cases of regurgitation which died, one a 10-para, the labour precipitate, death ten minutes afterwards. The third case, a 6-para, the child born in a cab; general œdema with increasing incompetence, died the nineteenth day.

Mr. HICKS, in reply, said that as to the question of induction of labour in heart cases, it seems that most authorities are against induction of premature labour during an acute attack of dyspnœa, because labour must necessarily throw more work upon an already distressed heart. He agreed with Dr. Herman that induction, if carried out, should be done after compensation had been established by suitable medical treatment. When this paper was commenced the authors thought that the occurrence of infective endocarditis during the puerperium would be more frequent than at other times, but could not find sufficient evidence to support their view. They begged to thank the fellows of the Society for the kind way in which they had received this paper.

Dr. HERBERT FRENCH also replied. He agreed with Sir Dyce Duckworth that the children of a mother who had mitral stenosis were liable to suffer from rheumatic affections, and that many of them might develop heart disease. This tendency in the children, however, was probably not greater when the mother had mitral stenosis than when the mother had had acute rheumatism without developing a valvular lesion. It would be impossible to prevent all persons who had had acute rheumatism from getting married on this account, and therefore this could not be used as a real argument against the marriage of a woman who had mitral stenosis, who had survived the age of twenty without showing signs of failing compensation. He thanked Sir Dyce Duckworth for the kind way in which he had referred to the "accumulated stores of wealth in the Guy's Hospital 'Reports.'" He thanked Dr. Herman for his cordial appreciation of the paper, and for his remarks as to the necessity for re-investigating many statistical points that were based upon fallacies, but were so often blindly copied from book to book. He was interested in the remarks of Dr. Poynton and Dr. Bonney upon the bacteriology of rheumatism and chorea, and the suggestion that pregnancy increased the virulence of the *Diplococcus rheumaticus*. In regard to the incidence of fungating endocarditis, however, he was afraid that Dr. Poynton had mistaken him. As far as could be judged from the cases in the paper, the incidence of fungating endocarditis at the end of mitral stenosis in women was *not* appreciably greater in women who had borne children than it was in women who had not been married. He thanked Dr. Griffith for adding statistics from Queen Charlotte's Hospital; he felt that these afforded the strongest support to the conclusions drawn in the paper. Dr. Griffith's cases were as much *selected* as were MacDonald's; the cases were only discovered to have mitral disease because they had cardiac symptoms. There was no record as to how many of the other cases (between 4000 and 5000) at Queen Charlotte's Hospital had mitral disease, because there were apparently no records of

the heart condition, except when symptoms led to its particular examination. It was possible, or even probable, that some at least of the other cases had mitral stenosis and had no trouble with pregnancy or labour; and yet the mortality amongst the virtually selected bad cases was much less than the 64 per cent. given by MacDonald. Several of these bad cases, moreover, had had no fewer than ten or eleven children previously without trouble. He also thanked the other speakers for their support. He only regretted that several questions had not been raised which he had hoped would be discussed. Amongst these were the question of the behaviour of the blood-pressure in pregnancy and labour, with and without pregnancy respectively; and the question as to whether uterine hæmorrhage should or should not be encouraged after delivery in mitral stenosis cases. Some books suggested that it should be encouraged as a means of relieving the heart in bad cases. Dr. French would have wished to hear the views of others on this point, but he himself was strongly opposed to it. He felt that uterine hæmorrhage was so difficult to control that it was in every case best to minimise it to the utmost; venesection being easy to control, he thought that relief to the heart, if necessary, should be given by letting blood from a peripheral vein, but never purposely from the uterus. He thanked the meeting for the very kind way in which his report of a laborious investigation by himself and Mr. Hicks had been listened to, received, and discussed.

APPENDICITIS AND GANGRENE OF THE VERMIFORM APPENDIX CONSIDERED AS SEPARATE DISEASES

BY

JOHN D. MALCOLM, F.R.C.S.EDIN.

SURGEON TO THE SAMARITAN FREE HOSPITAL

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AT the meeting of our Society held on March 14th, 1905,[1] I urged that there is a form of mischief which hitherto has invariably been described as an appendicitis, but which may be more correctly regarded as a separate disease both in its origin and in its effects.

In elaborating this view I will first relate very briefly six clinical histories showing different phases of an inflammation of the vermiform appendix, beginning in its mucous membrane and extending outwards.

CASES OF APPENDICITIS BEGINNING IN THE MUCOUS MEMBRANE.

CASE No. 1.—A man, aged 25, had three slight attacks of appendicitis within a year. In the most severe he stayed in bed two days and had pain for a fortnight. He was not then in this country, and as he had to live abroad

[1] "Discussion on the Subsequent Course and Later History of Cases of Appendicitis After Operation," 'Med.-Chir. Trans.,' vol. lxxxviii, p. 482.

I removed his appendix on his first visit home, in 1900. It lay in the angle between the ileum and cæcum and was so soft and so completely buried in adhesions that I had much difficulty in finding it, but otherwise it showed no sign of disease. The patient recovered and has remained well.

CASE No. 2.—A married woman, aged 22, had a long history of pains attributed to ovarian irritation and uterine catarrh. She lived in India, and on two occasions, after being apparently cured, her symptoms returned on her arrival in the East. Thinking that these relapses were due to the climate, I advised her to remain a few months in England when she had been under my care for the third time. Some weeks later I saw her in a typical attack of appendicitis, with a well-defined, tender swelling in the cæcal region. This gradually but completely disappeared, leaving no trace even of tenderness. The pain was the same that the patient had long been accustomed to, only more severe than usual. When convalescence was complete I removed the appendix, which was not adherent and showed no sign of disease, even on microscopic examination. The operation was followed within a couple of months by a marked improvement in the patient's health, and, although she returned to India, she remained free from her old trouble when last heard of, some four years later.

These cases are examples of a catarrhal appendicitis, the inflammation in the first extending to the peritoneum. Recovery, except for the persistent adhesions in one patient, was apparently complete, but there was an obvious tendency to relapse in both instances.

CASE No. 3.—A woman, aged 48, had two attacks of appendicitis with an interval of about three months. I removed her appendix after the patient was supposed to have fully recovered from the second illness, and when there was only a very slight tenderness on pressure over

the cæcal region. There were some old adhesions, but for the most part the appendix was free. About half an inch at its base was of normal size, the rest having quite twice its proper diameter, and being very soft and like a big worm. There was a constriction near the cæcum, and the passage of a probe through it caused a gush of thin, muco-purulent fluid, but when laid open the mucous membrane showed no ulceration. The enlargement was entirely due to distension, not to thickening of the walls. The patient recovered, and remains well. The fact that she appeared to be healthy when her appendix was in the condition described is very important. The absence of tension explained the freedom from symptoms.

Case No. 4 was that of a lady, married, aged 25, who had two attacks of severe pelvic inflammation with eight months between, the first being attributed to appendicitis and the second to salpingitis. I operated eight weeks after the temperature caused by the second illness subsided, when it was thought that the patient had recovered. The appendix was in contact with the right ovary, and firmly adherent to everything it touched. A small abscess, not larger than a pin's head would fill, communicated with its lumen. The appendix and the adhesions containing the abscess were removed, and the patient made a good recovery.

Case No. 5.—The patient's age was 33. She had suffered for many years from attacks of pain, often with fever, and always attributed to salpingitis. I first saw her in a very severe attack, when the whole contents of the lower abdomen seemed to be glued together. Recovery appeared to be so complete that the patient was sent to the seaside, where she considered herself very well, but on returning to London she had another attack of fever and pain, lasting three days. I opened the abdomen ten days later, and, in addition to ovarian mischief, found an abscess nearly as big as a pigeon's egg connected with the

appendix, which was in the middle line of the abdomen just above the pelvic brim. The abscess wall was formed by the posterior layer of abdominal peritoneum and by a coil of ileum and its mesentery, which were folded down over the displaced appendix. I removed the whole disease by resecting about twelve inches of the lower end of the small intestine with its mesentery, and the patient made a good recovery. The proximal part of the appendix was patent, so that, as in the last case, the abscess was draining into the cæcum.

These two histories show that a patient may appear to be cured even when an intra-peritoneal abscess exists. It is important to note that the improved condition was accompanied by a discharge of the abscess contents into the cæcum. In Case No. 6 [1] a very soft abscess to the inner side of the back of the cæcum and containing foul pus was opened, extra-peritoneally, on the ninth day of illness and was drained by rubber tubes. The discharge remained offensive, and there were severe hæmorrhages on the third and sixth days after the operation. On the seventh day the wound was re-opened, but no bleeding point was discovered, and the position of the appendix was not defined. Some small black sloughs were observed on the raw surfaces. The abscess cavity was widely opened and packed with gauze, the discharge became sweet in three days, and the sloughs gradually separated. Healing by granulation was then rapid and recovery was complete. Much mucus, which must have come from the appendix, escaped for a time, but there was no stay in the progress of healing, so that the communication with the cæcum must have been free. This accounted also for the softness of the abscess before it was evacuated. I shall point out later that possibly in this case the abscess did not arise from an inflammation beginning in the mucous membrane.

The conditions described in these records, perhaps excepting the sixth, arise from two causes acting together,

[1] Read before the Clinical Society February 23rd, 1906, and published in the 'Clinical Journal' April 11th, 1906.

namely an obstruction of the lumen of the appendix and an inflammation of its mucous membrane, each of which when once developed tends to produce the other and to aggravate its effects.

A chronic catarrhal inflammation may arise in the mucous membrane of the appendix, and may terminate in an organic stricture. If the process begins at the tip the whole mucous membrane may be converted into cicatricial tissue without obvious symptoms. In the course of operations for other diseases I have removed several appendices, the external appearances of which were not healthy, and in which this process had made considerable progress, although the histories did not indicate that there had been a previous appendicitis. But when the inflammation is accompanied by obstruction in the proximal portion of the tube, a characteristic attack of appendicitis results.

The importance of obstruction and of distension as causes of pain and fever, arising from inflammatory mischief in the appendix, cannot be over-estimated. The appendix is like every other part of the intestine as regards the fact that a catarrhal inflammation in it is painless, so long as the mucous surface is not stretched and there is no resistance to contractions of its wall. Hence, it is not too much to say that pain from catarrhal inflammation of the mucous membrane of the appendix does not arise without a partial or a temporarily-complete occlusion of its lumen. Similarly, a catarrh without retention of secretions rarely, if ever, causes fever.

Sometimes a chronic dilatation arises, and the appendix becomes practically an abscess cavity, as in Case No. 3. But, under pressure, an ulcerative process is apt to occur, and it may penetrate the wall. When an inflammation of this kind extends to the peritoneum it is always preceded by the formation of adhesions between the opposing layers of that membrane. Hence, an abscess so formed, although sometimes it may extend rapidly, does not burst into the general peritoneal cavity, except as a consequence of injury. The movements of the bowels may occasionally give rise to a sufficient strain or pressure to cause a

rupture, but this is seldom the case, especially if the patient is kept quiet in bed.

The micro-organisms in the abscess may induce a simple enlargement, extending indefinitely in the direction of least resistance; but Cases No. 4 and No. 5 above related show that even after an abscess has formed outside the appendix, if the obstruction is relieved, and if drainage is efficient, the inflammatory symptoms may completely subside, whilst in Case No. 4 the abscess had almost healed by granulation.

In other cases secondary abscesses may form by metastasis in near or distant parts, and in still others a local sloughing effect may be induced.

Gangrenous Changes in the Wall of the Appendix.

All the foregoing cases are easily understood as the results of inflammatory and obstructive conditions in the appendix. On the other hand, there are cases of mischief in this tube which cannot be so explained. A collection of pus may be found communicating freely with the peritoneal cavity and associated with a diffuse peritonitis. Moreover, the appendix may, and frequently does, rupture without any evidence of abscess formation or the slightest sign of an effective effort on the part of the tissues to localise the disease by the formation of adhesions. The following history is instructive in this connection.

Case No. 7.—A widow, aged 71, was seized by a slight pain about the region of the middle of the ascending colon, well above the normal position of the vermiform appendix, in the afternoon of a day in the spring of 1905. She consulted her doctor, but thought so little of the illness that he had difficulty in persuading her to go to bed for examination and to stay in bed until his next visit. Except for the pain, and tenderness in the same position, nothing abnormal was discovered. The pain, though slight, was persistent, and towards afternoon of the

following day the temperature began to rise very gradually. I saw the patient thirty hours after the illness began. No opiate had been given, and the pain was still insignificant, but there was a slight resistance over the ascending colon, the rest of the abdomen being quite soft and very little, if at all, distended. The rectum contained fæces, and the bowels had not been moved for two days. An interval of this duration between the evacuations was, however, not unusual. The temperature had gradually risen to 100° F., the pulse was beating between 80 and 90 to the minute, and the general aspect of the patient did not indicate that she was seriously ill. No history of a previous attack was obtained. I recommended the administration of an enema and said that when the bowels were cleared, if the patient continued to have pain and resistance over the tender part, the question of exploring the abdominal cavity would have to be considered.

The enema acted, but vomiting set in during the night, and next morning the patient was very ill, her abdomen being distended and hard all over, whilst she was exhausted by constant retching. The pulse had risen from 90 to 130 to the minute, whilst the temperature was only 100·6° F., and there was still no great pain. It was obvious that an operation offered the only hope of saving the patient's life, but this was strongly opposed for a time. Forty-four hours after the pain began I removed the appendix, which lay outside the middle of the ascending colon. It was not adherent, but was immediately surrounded by loose, flaky lymph. There were 2 or 3 oz. of slightly turbid fluid lying in the loin pouch. The intestines were greatly distended, and were emptied by means of incisions which were carefully closed. The loin pouch was drained. After the operation the abdomen rapidly became distended again, and the patient died early the next morning. There was no examination of the body after death.

The appendix had three small, round, well-defined gangrenous patches in its wall, the largest not more

than three eighths of an inch in diameter. These were not shrunken, nor surrounded by a swollen "angry" area, and they were in normal position with regard to the rest of the tube, so that there was no rupture. The appendix was not enlarged, it contained no stercolith, and there was no occlusion of its lumen.

The Evidence in this Case that the Gangrenous Patches formed before the Symptoms developed, and that the Symptoms were not those of Appendicitis, but those of Peritonitis.

It is certain that the gangrenous patches found in this case were not due to a sthenic inflammation terminating in the formation of a slough. Such an inflammation would be accompanied by a steadily advancing fever with a progressive rise of temperature and pulse before the gangrenous patches would form, and the tissues around the patches, and especially those between the patches, would be congested and œdematous. The whole neighbourhood would be obviously inflamed. In the case under consideration the highest temperature was 100·6° F., and the rapid pulse was fully accounted for by the constant vomiting and the generally enfeebling conditions. The other symptoms were those of a slight peritoneal irritation, causing paralysis of the intestine, and there was no evidence of an inflammation of the wall of the appendix, except of its serous coat.

If these dead patches, as seems certain, were not the results of a sthenic inflammation terminating in death of tissue, their origin must be sought for in some other process.

There are four conditions in which a local death of tissue may be observed, unaccompanied by symptoms of any kind.

(1) In senile gangrene necrotic changes may take place without pain or fever.

(2) In the stomach and duodenum a death of patches of tissue may occur, and the first indication of this

change may be a profuse hæmorrhage or the symptoms of a perforation of the part.

(3) In the wall of an ovarian tumour there is occasionally seen a considerable area which is evidently dead. It is of a greyish colour, sometimes of large size, perhaps six or eight inches across, usually of very irregular shape, with a well-defined line of demarcation which separates the surrounding vascular healthy part from that which has been deprived of its blood-supply. This condition always occurs at a distance from the pedicle of the tumour and, I believe, only in large cystic growths, so that it is now less commonly observed than formerly, when the operative treatment of ovarian tumours was often delayed. The condition is not accompanied by any general disturbance, and there are no apparent evidences of irritation when it is discovered.

(4) In fibroid uterine tumours a change, to which the name "necrobiosis" has been applied, is not infrequent. Mr. John S. Fairbairn has examined nineteen cases,[1] and he considers that "the characteristic change is one of necrosis." "Cultures were taken from five specimens, and in all cases were sterile."[2] In three of these cases there was no pain, in six there was no tenderness, and, as a rule, "there was little or no rise in the temperature."

The causes of a local death of tissue are not definitely known. The fact that the subjects of diabetes are especially liable to gangrenous changes would seem to indicate that an alteration in the tissues is concerned. In a fibroid uterine tumour the necrosis seems mainly dependent on an arrest of the vascular supply to the part. In two cases of this kind which I exhibited at the Obstetrical Society[3] the condition followed immediately on delivery of the pregnant uterus, and in both cases it seemed to me certain that interference with the blood-supply to the

[1] 'The Journal of Obstetrics and Gynæcology of the British Empire,' August, 1903, p. 133.

[2] *Loc. cit.*, p. 124.

[3] 'Obstet. Soc. Trans.,' 1894, p. 200; 1905, p. 15.

tumours and pressure on them were the chief causes of the change.

It is very obvious that the blood-supply is cut off in the case of a dead patch in the wall of an ovarian tumour, and this is probably the most important factor in its production. In senile gangrene also the death of tissue is usually attributed to abnormal vascular conditions.

In cases of perforating gastric or duodenal ulcer the gangrene has been attributed to a digestion of the tissues by the secretions, and the perforations have been called "peptic" ulcers; but it is certain that a solvent action of this kind must be preceded by a modification of the characters of the tissue acted upon, otherwise none of us could possibly live. The question of septic causes arises in connection with these perforations, and it is also practically certain that some change must occur in the tissues before micro-organisms can invade them. It seems to me, therefore, that in all these cases an alteration in the vascular or nervous supply, or in the structure of the tissues is the primary cause of the necrotic change.

The exact origin of a gangrene formation is, however, not material to my argument. The important point is that, in all the conditions referred to, the local death occasionally takes place so painlessly and insidiously that it is not accompanied by any signs or symptoms except those which *follow* the necrosis.

It is obvious that a gangrenous patch so forming in the wall of an ovarian tumour can only become infected by micro-organisms circulating in the vessels or passing through the Fallopian tubes or through damaged tissues. All the cases of necrotic fibroids examined bacteriologically by Mr. Fairbairn were also sterile. The dead tissues might therefore exist almost indefinitely in these cases. In senile gangrene and in gastric and duodenal affections, on the other hand, the necrosed parts must become septic sooner or later. Nevertheless, in those cases in which a perforation of the stomach occurs, and symptoms of this complication are the first indications of mischief, it is

certain that the slough not only forms, but also becomes separated before giving rise to clinical evidences of its presence. This necessarily involves the lapse of an appreciable period of time, possibly even two or three days, during which a necrotic patch is present without symptoms. Obviously the same changes may occur, and a gangrenous patch may exist, with a similar temporary absence of symptoms, in the wall of the vermiform appendix. But if the whole thickness of this wall is affected, it must be a mere matter of time before septic influences will pass through the dead part or the contents of the appendix will escape by separation of the slough.

These considerations lead me to believe that in the appendix now under discussion three gangrenous patches developed before the pain began, and all the evidences of mischief *followed* their formation. First, some irritating micro-organisms gained admittance to the peritoneal cavity through the slough and caused an effusion from the serous surface, whilst later there was a local exudation of lymph, caused probably by some other microbes. There were not, however, sufficient grounds for forming an opinion as to how long these processes had been going on. The fact that the lumen of the appendix was not obstructed is very important. This and the consequent absence of distension fully account for the freedom from serious pain and from all symptoms except those of an asthenic peritonitis. The fact that the symptoms of a gangrene formation may be so definitely separated from those of an inflammation beginning in the mucous membrane of the appendix is very instructive, and enables us to explain many conditions that are otherwise obscure.

Inflammation of the Appendix and Gangrene occurring together.

It is obvious that if a gangrenous patch may develop in the wall of the appendix without causing any symptoms whatever until pathogenic organisms affect the perito-

neum by passing through the dead tissue, such a patch may also form in association with a true appendicitis—and, indeed, gangrene of the appendix is generally associated with inflammation of its mucous membrane. When this is the case, the indications of a necrotic change and those of an appendicitis develop more or less concurrently, and the clinical picture exhibits a variety of combinations of symptoms, consisting of signs attributable to one or the other of these pathological states. The symptoms of appendicitis varying with its severity, whilst those of gangrene vary with the period of the inflammatory attack at which the death and separation of tissue take place. Again, both sets of symptoms vary with the state of the appendix itself, especially as regards occlusion of its lumen, and also with the particular pathogenic organisms most actively at work.

Case No. 8.—It is over ten years since I was asked to see this patient, whose age was 46, and who had suffered for some fifteen years from abdominal troubles that were attributed to indigestion and ovarian irritation. She was seized with intense pain in the abdomen and vomiting one morning at 5 a.m. Treatment was without benefit, and, at a consultation held between the general practitioner and a well-known gynæcologist during the evening of the first day of the attack, it was decided that I should be asked to be in readiness to operate if there was no improvement during the night. There was little rise of temperature or pulse, and the symptoms were thought to point to intestinal obstruction as the cause of mischief. The patient was not any better next morning: no flatus or fæces had passed from the bowel, the abdomen was full, but not greatly distended, tenderness was not localised, and there was no marked fever. I operated twenty-eight and a half hours after the onset of pain. The appendix was not adherent but was surrounded by a considerable quantity of thin, milk-like fluid. The small intestines were in parts completely collapsed and in parts distended. I punctured the

transverse colon, letting out much flatus through a cannula and relieving the intra-abdominal tension. The appendix was removed, the abdomen was washed out with saline fluid, and the patient lived eight days, but the bowels only showed signs of power when strong purgatives and enemata were given, becoming quiescent in the intervals and at last ceasing to respond to any stimulus. At the autopsy a general adhesive peritonitis without suppuration was found. The site of the puncture of the colon was not discovered, and there was no leakage at the place from which the appendix had been taken.

There was a small gangrenous patch about a quarter of an inch in diameter near the tip of the appendix and exactly resembling those seen in Case No. 7. There was no swelling round the dead patch, and the appendix was not ruptured nor enlarged. It did not contain a stercolith and there was no evidence that its lumen had been obstructed.

In this case also the symptoms were not those of a sthenic inflammation, but rather those of an irritation causing an exudation of slightly turbid serum into the peritoneal cavity. A localised paralysis of the intestine followed and the phenomena of obstruction were induced. The pain was probably due to a transient appendicitis or to an appendical colic such as the patient seemed to have suffered from before, but on this occasion the pain was aggravated by the presence of a gangrenous patch and by traction on the tissues around it. Except in the acute onset of the disease this case was in every essential detail an exact counterpart of Case No 7.

It may be concluded that in these two cases if the patients had not been operated on, and if they had lived long enough, the sero-purulent fluid would have become purulent and the patches of gangrene would have separated. Thus a collection of pus communicating with the appendix and with the general peritoneal cavity, but perhaps more or less localised by adhesions, would have developed. When such a condition is found at an operation or after

death, unless the steps leading up to it are traced, the most obvious explanation is that a suppurative inflammation of the mucous membrane of the appendix has extended beyond its walls and has ruptured into the general peritoneal cavity. These two histories show, however, that this is not the only possible method of development of the condition, and if it is considered how seldom a localised abscess bursts into the peritoneal cavity except from an injury, it seems to me that these ill-defined abscesses must more frequently arise from the presence of a gangrenous patch.

Further Evidence of the Development of Gangrene of the Appendix without Symptoms except those which follow the Death of Tissue.

In the exhaustive work on 'The Appendix and its Diseases,' published by Dr. Howard A. Kelly and Dr. E. Hurdon, there is definite evidence that the first recognisable pathological change may be the formation of a gangrenous patch in the wall of the appendix, and that this may be unaccompanied by any symptoms except those which *follow* its development.

These authors emphasise the extraordinary suddenness with which symptoms of lesions of the vermiform appendix may develop, and they assert that sometimes "there is reason to believe that the first acute symptoms are due to beginning peritonitis, the result of perforation, gangrene, or a virulent infection. Intense agonising pain at the onset is often due to a perforation."[1] In another passage they say "that in the present condition of our knowledge it is impossible to estimate how rapid the progress of an appendicitis will be. In one case of Finney's a hospital nurse was seized with her first attack of pain shortly after coming on duty in the morning, and the operation, performed within three hours of the apparent onset, showed the appendix gangrenous on one side and ready to per-

[1] *Loc. cit.*, p. 408.

forate. In another case of the same surgeon's the patient, a young physician, operated upon within six hours of the initial complaint, was found to have a spreading peritonitis, and there was every reason to believe that the very first pain he felt was occasioned by the perforation: both cases recovered."[1]

Such cases strongly support my contention that a gangrenous patch may form in the wall of the appendix, and may exist for a time without symptoms of any kind, and that, therefore, the death of tissue is not due to an inflammatory process.

Spontaneous Recovery from Localised Gangrene of the Appendix.

It is difficult to understand how a dead patch in the wall of a hollow viscus can prevent an escape of infective organisms until it has become so loosened that a gross perforation suddenly takes place, but the two following cases illustrate a condition which, I think, has not been described, and which seems to throw light on the pathology of rupture of the appendix. They clearly show that a formation of a gangrenous patch in the wall of the appendix is not necessarily a fatal occurrence.

Case No. 9.—A woman, aged 58, had an attack of abdominal inflammation, which kept her in bed twelve days, in July, 1905. Otherwise she had been very healthy, and both before and after the illness of last year the bowels moved daily and gave no trouble. On January 9th, 1906, she went to bed quite well, and early on the 10th she was seized with intense abdominal pain. There was then constipation, the abdomen gradually enlarged, and Dr. Duncan Menzies informed me that the temperature rose to 102·8° F. on the 12th. I saw the patient on January 13th, when it was impossible to define any intra-abdominal condition on account of the intestinal distension

[1] *Loc. cit.*, pp. 502, 503.

and there was no abnormal dulness. The patient complained of pain on pressure on both sides, but the pain was felt in the cæcal region whichever side was pressed upon. The cervix uteri was atrophied and the rectum was full of fæces. It was decided to give the patient an enema and to operate immediately if any aggravation of symptoms followed. After the patient had been taken to the Samaritan Free Hospital an enema was administered and it acted well. The temperature fell to 99° F. next morning, and under treatment by gentle laxatives and enemata the abdominal distension subsided. No definable swelling was felt at any time. A fortnight later the abdomen was nearly flat and there was only a very slight tenderness in the right iliac region. Nineteen days after the illness began I opened the abdomen, and after a little search found the appendix well within the pelvic brim and universally adherent. The adhesions were, however, quite soft, and with the fingers I had no difficulty in separating them and bringing the appendix out of the incision. It had a large opening about the junction of its middle and distal thirds, the mucous membrane being freely exposed. There was no sign that any appreciable amount of fluid had escaped. After the appendix was removed several coils of small intestine were found much matted together by recent adhesions which were very readily torn through. I carefully disentangled the coils, and in doing so I came upon two somewhat more firmly attached than the others, but still quite easily separated. On each there was an elongated granulating surface, the two making an area which had evidently been fitted on the opening in the appendix. The granulations were cut off and the raw surface on each coil was cleaned and turned in by a few Lembert sutures. Beyond the granulating surfaces the adhesions had been so slight that the separated parts showed everywhere an apparently healthy surface. The abdomen was closed without drainage, the patient made a good recovery, and she has continued well.

The appendix was not dilated and was patent through-

out. It contained no fæces and no foreign body. Two perforations were found close together, one small, round and about an eighth of an inch in diameter, the other of oval shape and nearly half an inch long. The edges showed healthy granulating tissue, and it was obvious that there had been a loss of substance (see Fig. 1).

It seems to me that in this case also the gaps in the wall of the appendix were due to a death of tissue, and not to an inflammation of the appendix beginning in its mucous membrane. There was a complete absence of any visible pus, and the fact that the adhesions were so easily separable seems to me inconsistent with the view that they were caused by an inflammation sufficiently severe to ulcerate through the wall of the appendix.

On the other hand, the conditions were fully accounted for if a gangrenous patch formed in the wall of the appendix, and if the micro-organisms which escaped excited an adhesive peritonitis, or the mere presence of the dead tissue caused the adhesions. The gangrenous part on separating could then be cast off only into the lumen of the appendix, and the place it had occupied would necessarily become surrounded by a granulating surface. It is possible that the openings in this appendix might even have healed, and the slight intestinal adhesions might have separated, if the patient had been allowed to go home, and if no further gangrene-formation had taken place.

On this view it is obvious that the symptoms of the gangrene were those of inflammation of the peritoneum and of the surfaces from which the gangrenous patches separated, the actual death of tissue apparently causing no disturbance. Clearly the inflammation excited was not clinically distinguishable from an inflammation beginning in the mucous membrane of the appendix until the parts were exposed. Why in one case a serous exudation should be induced as a consequence of gangrene-formation and in another an adhesive inflammation, is an interesting question which need not be discussed now.

It is very remarkable that a patient, apparently quite well, and taking ordinary doses of purgatives without ill effects, should have a gross perforation in her appendix, lightly closed by adherent small intestine. The pathological condition was, however, almost exactly reproduced in the following case.

CASE No. 10.—A very healthy-looking woman, aged 49, was admitted to the Samaritan Free Hospital on February 26th, 1906. Three months earlier she had a sharp attack of pain in the right side and was in bed three days. There was no constipation, and before the illness now under consideration the bowels always acted regularly. Mr. A. C. Ransford informed me that on February 7th the patient was seized suddenly with pain, rigidity in the cæcal region, and vomiting, followed by constipation. The sickness stopped after twenty-four hours, but the pain continued for several days. The temperature rose to over 101° F., and fell to normal on February 12th. After two days it rose again to 102°, and it was between 101° and 102° for a week. Then the whole condition improved, and on admission three days later the temperature was 99° and the pulse 100. The bowels were easily moved. There was a very hard, rounded, well-defined swelling, apparently about two inches in diameter, immediately internal to the right anterior superior iliac spine. This subsided quickly, being scarcely felt after four days, the temperature and pulse being then normal. The patient seemed particularly insensitive to pain even when the swelling was freely manipulated.

I opened the abdomen on March 6th, twenty-seven days after the illness began, and a week after it seemed to cease. The omentum was lightly adherent in the angle between the cæcum and the lateral abdominal wall. On removing it and separating the parts more deeply, about a drachm of clear mucus was released. This came out of the appendix. The latter was removed, its enucleation being fairly easy. The stump and its surroundings were

thoroughly cleansed, and a gauze drain was inserted. The patient made an uninterrupted recovery.

The appendix was dilated in this case, there being a partial constriction about three quarters of an inch from its cæcal end. Near the tip there was a hole in its wall surrounded by granulation-tissue, and apparently the opening had been closed by peritoneal adhesions exactly as in Case No. 9. There was an obvious loss of tissue at the point of perforation, and this, with the fact that the lumen was distended with mucus and not with pus, whilst the adhesions were so easily separated, seemed to prove that the conditions found were not caused by a suppurative process. There had, of course, been time for the slough to become disintegrated. In this case the appendix lay outside the cæcum, and there were extensive, although not strong, adhesions around it.

A very important point in connection with these two cases is that in each, if further pressure had arisen within the appendix, the adhesions would have been very easily broken down. In the last case, unless the force had been very great, the extent of the adhesions and the pressure of the cæcum against the abdominal wall would probably have prevented a rupture into the peritoneal cavity and an abscess would have formed. Unless the perforation showed a sloughy edge, there would then have been nothing to indicate how the abscess originated, whether in an inflammation extending from the mucous membrane or after separation of a gangrenous patch. In Case No. 6 above related, the abscess might very well have developed in this way. In Case No. 9, in which the small intestine was adherent, in all probability a very slight increase of pressure within the appendix would have led to a complete separation of the adhesions, and the conditions found after death in the following case would have arisen.

Case No. 11.—A short, stout woman, aged 37, who had been a hard drinker for at least three years, was seized

by intense pain all over the abdomen, with vomiting and diarrhœa, after a big supper of veal and ham. Her medical attendant was called next morning, and he told me that then the abdomen was not distended, but was tender all over. The skin was cold and moist, the pulse was beating from 70 to 80 to the minute, and the temperature was not raised. At 9 a.m. half a grain of morphia and a hundredth of a grain of atropine were administered hypodermically. At noon the pulse was 140 and the temperature 103·5° F., the pain was easier, but the abdomen was slightly enlarged and very hard. The vomiting and diarrhœa had stopped. Another half grain of morphia was injected, without any atropine. At 10 p.m. the pulse was 130, the temperature was not recorded, but the patient was free from pain or tenderness. Early next morning the nurse reported that the pulse was very feeble and that stercoraceous matter had been vomited, but the vomit was not preserved for inspection. At 6 a.m. the pulse was of fair quality, beating 130 to the minute, and the temperature was 100° F. I saw the patient at 9.30 a.m., about thirty-six hours after the illness began, and when no sedative had been given for twenty-one and a half hours. She then felt, and was said to appear, very much better. She had a fair pulse of 130 and the temperature was 100° F. The bowels had been moved by enema, flatus had passed freely and repeatedly, the abdomen was said to be much smaller, and was quite soft and mobile. I could detect no tenderness except a little on pressing on the neck of the uterus, which had been curetted some months earlier.

In consultation it was agreed that the patient had been suffering from some irritation within the bowel, due to indigestible food, and that she was recovering. I did not see her again, but afterwards I was told that the condition remained much the same until early next morning, when flatus ceased to pass downwards. Vomiting followed, the pulse became very rapid, the temperature rose to 103·5° F., and death followed at about 5.30 p.m.

The practitioner in charge of the case had formed a very unfavourable opinion of the patient's ability to bear operative interference, and in this view I think he was right.

A post-mortem examination was made. The cavity of the appendix was enlarged, and there were two openings in its wall through which a considerable quantity of fæcal material had escaped into the peritoneal cavity. There were some strong adhesions around the appendix, but the perforations opened freely into the peritoneal sac without any indication of a formation of recent adhesions. The bigger rupture was round in shape, which showed that there had been a loss of tissue, and on its edges there was a filmy slough, which must have formed and been in process of separation before the patient died. I do not think that the bowel contents found in the pelvis after death in this case could have been the cause of the initial symptoms, and could also have been there for three days, in the middle of which time definite evidences of an improving condition were observed.

On the other hand, the symptoms may be fully accounted for in the following way. The patient had an inflammation of the mucous membrane of the appendix, with retention of the contents of this tube, the symptoms being aggravated by the fact that two gangrenous patches existed in its wall. Relief was obtained by a natural cure of the appendicitis, with the escape of its contents into the cæcum, shortly before I saw the patient. At that time the parts were sealed off by slight adhesions. Later the sloughs in the wall of the appendix separated, the adhesions broke down, and the pelvis became flooded with fæces, from which condition the patient rapidly died.

The presence of stercoliths is a factor in these cases which I have not mentioned. A foreign body must tend to precipitate the formation of a gangrenous patch, whether the tissues are inflamed or not, but the cases recorded show that a necrotic change may take place without this complication.

Conclusions as to the Results of Gangrene-Formation.

I have shown that gangrenous patches forming in the appendix may bring about at least three well-defined conditions which are easily understood and are quite independent of inflammation beginning in the mucous membrane, although this may also be present.

First.—There may be (as in Cases No. 7 and No. 8) an escape into the peritoneal cavity of slightly irritating organisms before the patches begin to separate. These may give rise to a spreading sero-purulent exudation, and to a paralysis of the intestine, which is the direct cause of urgent symptoms and of death.

Second.—The adjacent peritoneum (as in Cases No. 9 and No. 10) may become adherent to the appendix over the gangrenous patch, before the latter separates, and a temporary, perhaps even a permanent, cure, with disintegration and discharge of the slough through the appendix, may follow.

Third.—Some such sealing off of the mischief may occur, and when the gangrenous patch separates the adhesions (as in Case No. 11) may suddenly give way, and the abdominal cavity becomes flooded with intestinal contents.

It seems certain that (*fourth*) in some of these cases of gangrene (Nos. 7 and 8, for instance) a collection of pus, only partially shut off from the general peritoneal cavity or free in it, may develop, and that in others (No. 10) a completely localised abscess may arise.

As the pathology of these cases of gangrene is so different from that of inflammation of the appendix beginning in its mucous membrane, I would strongly urge that the two conditions ought to be clearly differentiated from a scientific point of view, and as much as possible in practice.

I have never seen, and I do not think I have read of, a case of serous exudation into the peritoneal cavity

associated with an unruptured "gastric ulcer," but the other effects of gangrene which I have described may be found in connection with the stomach exactly as with the appendix.

Whether an inflammation of the appendix is ever sufficiently severe to terminate in gangrene in a way comparable to the formation of the core of a carbuncle is very doubtful. Such an inflammation in the appendix would probably kill the patient before it produced local death. The condition generally described as a gangrenous appendicitis is therefore more accurately attributed to an appendicitis with gangrene.

The Numbers of these Cases of Localised Gangrene in the Appendix.

I do not think it is generally recognised that cases of gangrene of the appendix are very common. That they are, in one sense, rare is beyond dispute, for many practitioners of large experience have never met with a case. The general practitioner and the surgeon are, however, apt to get very different notions regarding the numbers and importance of these conditions. The former sees, proportionately, a very few cases of appendix mischief in which a consideration of immediate surgical treatment is required. The surgeon sees only these few in the acute stage. But when even a single case is met with, and also when these cases are considered from the point of view of the incidence of mortality their importance is beyond all question.

Dr. Kelly and Dr. Hurdon found that out of 4028 autopsies in three hospitals there were 86 cases in which death was due directly or indirectly to acute inflammatory disease of the vermiform appendix,[1] and out of these 86 deaths "in 29 cases there was acute gangrenous appendicitis with single or multiple perforations. In two of these

[1] *Loc. cit.*, p. 211.

a gangrenous appendix had entirely sloughed away from the cæcum." [1]

"In 25 cases inspection of the abdominal cavity at the time of the autopsy revealed no sign of any tendency towards limitation of the inflammatory process to the immediate vicinity of the appendix, nor was there anything pointing to a previous abscess in the region of it. In 29 cases it was evident that there had first been a localising process resulting in an abscess, either completely or incompletely walled off, and that subsequently a leakage had taken place from this abscess, causing infection of the peritoneal cavity and, finally, a general peritonitis." [2]

I have shown, however, that it may be a matter of extreme difficulty at an operation or at an autopsy to decide whether certain conditions are due to a rupture of an abscess or to a diffuse peritonitis becoming partially limited. The percentage of deaths attributable to gangrene may therefore be greater than that stated. But even if cases of perforation of the appendix, without any tendency to limitation of the consequent peritonitis, represent all those of gangrene, and if they occur only in 25 out of 86 deaths from appendix mischief, the importance of this condition is obviously very great.

Diagnosis and Treatment.

If we could make an exact and early diagnosis between the signs and symptoms of inflammation of the appendix beginning in its mucous membrane and those of the gangrene formation which occasionally occurs in its wall, the treatment would be much simplified; but the differentiation between the two may be very difficult.

Apart from certain rare conditions—*e. g.* cancer, etc.—cases of mischief in the appendix may be divided, clinically, into four groups, namely—

(1) Those in which signs of inflammation of this tube arise and subside completely within a week or ten days;

[1] *Loc. cit.*, p. 212. [2] *Loc. cit.*, p. 212.

but in which sometimes, (1 *a*) if the lumen remains occluded, the symptoms develop into those of an abscess.

(2) Cases in which signs of an appendicitis partially subside, and are followed after an "interval of repose" by symptoms of gangrene-formation; but in which sometimes, (2 *a*) if the lumen remains closed, the symptoms of appendicitis merge into those of gangrene.

(3) Those in which signs of acute perforation develop at once, death following within forty-eight hours.

(4) Those in which the first sign of danger is due to paralysis of the intestine following an asthenic inflammation caused by micro-organisms entering the peritoneal cavity through a gangrenous patch.

It must not be forgotten that there are intermediate conditions, and that in Cases No. 9 and No. 10, above recorded, a gangrenous formation gave rise to symptoms simulating those of an appendicitis so exactly that they were not separable clinically.

The only cases which may be watched with little anxiety are those of Group (1), in which the illness begins with mild but decided febrile symptoms, and there is a well-defined local swelling, all the abnormal conditions subsiding after a week or ten days. Every variation from this, the commonest type of appendicitis, should be carefully noted. But even if the temperature does not fall decidedly, and the local swelling increases and becomes an abscess, the patient's life will probably be saved.

Cases belonging to the other three groups should be operated on as soon as the condition of gangrene-formation is diagnosed, and Finney's cases, above referred to, show how successful an operation promptly performed may be.

In cases of acute perforation (3rd group) the pain is intense, frequently localised, and accompanied by tenderness of the appendix region. Collapse may be profound. Vomiting, a rapid pulse, and a normal or low temperature will probably be observed. Such conditions indicate clearly the necessity for operative interference.

Cases belonging to the second group are so common as

to suggest that the formation of a gangrenous patch and the development of an appendicitis are frequently related in such a way that the signs of the inflammation tend to subside very shortly before those of the gangrene-formation develop. In these cases the diagnosis is often very difficult.

When a necrotic patch forms in the course of an appendicitis, the only immediate indication of its presence may be that the pain is accentuated on account of the traction on the tissues adjacent to the dead area. An unusually intense initial pain or a sudden severe exacerbation of pain in the course of an appendicitis may therefore be a symptom of the most serious import.

Later in the history of the gangrene-formation, but perhaps early, or it may be very late, in the course of the appendicitis, evidences of a spreading inflammation of the peritoneum may arise. Constipation and intestinal distension are apt to accompany any inflammatory condition in or near this membrane, and, when slight in degree and associated with evidences of a well-localised inflammation, they do not necessarily indicate great danger. But when the distension is out of proportion to the evidences of local mischief, when it steadily increases, and when there are no signs of intestinal activity, the bowel wall is probably becoming paralysed, and this is the most surely fatal complication of an abdominal lesion.

Moreover, the mere persistence of intestinal distension favours the development and spread of peritonitis, and therefore opiates should never be given in these cases unless they are absolutely necessary on account of the acuteness of the pain, and then the smallest dose likely to be efficient should be injected hypodermically.

The administration of a purgative may clear away many symptoms suggestive of appendicitis and effect a complete cure. If the abdomen is not distended, if the patient is not very sick, and if the disease is an inflammation of the mucous membrane of the appendix, a dose of castor oil, given very early in the illness, will probably do good, and

if it acts well it will facilitate recovery. But, when appendix mischief is suspected, if a purgative is given the surgeon must be prepared to follow up the treatment by an immediate operation, should this become necessary.

When the symptoms are severe, especially if there is great pain, marked distension, much sickness, or decided collapse, it is better to avoid purgatives. They are contra-indicated in cases of gangrene of the appendix, and there are many conditions in which the symptoms of gangrene of this part are closely simulated, and in which, also, aperients should not be given. But a consideration of these cases does not come within the limits of this paper.

If there is intestinal distension, if the rectum is full, and if appendicitis without abscess-formation is diagnosed, an enema should be administered, and the surgeon must be prepared, in this case also, to open the abdomen immediately if more serious symptoms develop as a consequence of the treatment. On the other hand, if a gangrene formation or an abscess is believed to be present, it is safer to operate first and give the enema afterwards.

When a purgative or an enema acts efficiently, if the general symptoms are relieved, a moderate increase of fever following the treatment is not necessarily an indication of danger; it is often caused by a disturbance of peritoneal adhesions which is of no importance unless an abscess or a gangrenous patch exists.

A rapid pulse, and especially a high pulse-rate in proportion to the temperature, frequently indicates that a low form of peritoneal inflammation, and probably some intestinal distension, have arisen. A sudden fall of temperature may be due to the fact that relief has been obtained by a natural discharge of the appendix contents into the cæcum, in which case, if there is no other mischief, all the adverse symptoms will quickly subside. But if a fall of temperature is not accompanied by a general improvement, and if it is associated with more pain or an increased pulse-rate, or is followed by a greater abdominal distension, the conditions probably indicate that the peritoneum has

become involved in a diffuse irritation by the separation of a gangrenous patch.

An absence of a localised swelling, when there is little or no intestinal distension, shows that the disease is not a simple appendicitis, but it must be remembered that the appendix is not always in the usual position. Rigidity of the abdominal wall does not necessarily indicate more than the presence of a tender area beneath the fixed muscles.

The fourth group of cases, which was illustrated typically by the seventh and less exactly by the eighth case, recorded above, will always be apt to mislead the surgeon. It is well nigh impossible to lay down rules of treatment in such a case as No. 7, so that the surgeon may interfere sufficiently early to insure success without recommending many unnecessary operations. Fortunately, a gangrenous formation generally gives rise to acute symptoms. Case No. 7 would have had more chance of recovery if treated by a purge early in the illness so as to force the symptoms and indicate quickly the necessity for an operation. This is the treatment I would adopt if I had another patient in whom I believed that similar conditions existed. Nothing can be gained by watching such a case.

The differential diagnosis between the two conditions under consideration is, however, so uncertain, and there is so much risk in waiting for definite evidence of the exact nature of a case, that it becomes an urgent question as to whether the prospects of individuals would be prejudiced, if all cases of appendix mischief were operated upon immediately after the attack developed. There is no doubt that, *in a first attack* of an inflammation of the appendix spreading from its mucous membrane, an operation for the removal of this part would be one of the most successful in surgery if it were performed always within some twenty-four hours of the onset of the illness, before septic mischief penetrated its wall.

But if an operation is undertaken during a severe inflammatory process, when the appendix is buried in old adhesions, the difficulties and dangers of the procedure

may be very great. These cases would, of course, be practically eliminated if all were operated on early, or in the first interval, a course which would lead to the saving of many lives.

Danger would still arise, however, in unrecognised chronic cases becoming acute, and in those in which operation would be refused during an interval, and thus even the most experienced surgeon may be placed on the horns of a dilemma, knowing that if he operates and finds many old adhesions he can only remove the appendix with a very great risk to the patient, who may be in no fit state to undergo a serious operation, whereas if he does not operate infective mischief may rapidly get such a hold on the peritoneum that there will be no chance of success from any treatment.

Hence, in the cases under consideration, it is more than usually true that each individual patient must be treated according to his symptoms. The majority of cases of appendix mischief recover without operation and the surgeon is not consulted; but assuming that there are sufficient grounds for definitely diagnosing an appendix lesion, it seems to me that in all cases beginning very acutely or in the course of which acute symptoms develop, it is wise to recommend an immediate operation. Of course a little time must be allowed for making a diagnosis, and if for any reason an operation is not undertaken in a case of acute abdominal disturbance, the advice given by Mr. Charters Symonds should be followed, whenever it is possible to do so, namely to make a second visit in from four to six hours,[1] when a more exact opinion as regards the condition present may perhaps be formed. Frequently it is wise to order the administration of an enema in the interval.

When there is a doubt as to the details of diagnosis the case must be considered with great care, and probably

[1] 'An Address on the Individual Value of the Symptoms in Perforative Appendicitis, more especially as regards Operation,' John Bale, Sons and Danielsson, 1898, p. 48.

more harm will be done by unwisely avoiding an operation than by a too active treatment, provided, of course, that the procedure is carried out with reasonable discretion and consideration.

The following case suggests that it may be desirable very occasionally to cut down on the cæcal region in order to make sure that a gangrene of the appendix and an open rupture into the peritoneal cavity do not exist. If no rupture is found, the surgeon will decide whether to proceed with the removal of the appendix or not. If the patient is already very ill, and if the appendix is buried in firm adhesions it may be wiser to leave it, only making an exit for the pus, in case an abscess develops.

Case No. 12 was that of a lad, aged 18, who had a severe illness lasting a month, with much abdominal pain and a high temperature, when he was six years old. There was no further evidence of abdominal mischief until, at the age of eighteen, he had a severe pain which passed off in a few hours. A fortnight later he felt very uncomfortable, and on the following day had an attack of acute pain in the appendix region. On the third day there were definite local signs—rigidity, fulness, and tenderness, with pulse 130 to the minute, and temperature 102·2° F. The abdomen was opened, the ileo-colic valve was located, and a firm mass behind the small bowel indicated the position of the appendix. The surgeon who was operating thought it wiser, however, not to attempt its removal because of its close attachment to the bowel, the inflamed and softened condition of the parts and the state of the patient. An iodoform gauze tampon was therefore inserted to drain the area exposed. The patient recovered, and the wound healed without the formation of any collection of pus. This illness occurred abroad, and I was asked by Sir Constantine Holman to see the patient when he arrived in London some weeks later. The abdomen was then decidedly enlarged, and there was much trouble from flatulent eructations. The bowels moved, however,

when a laxative was administered, and the general condition was improving.

It was decided that the appendix should be removed, but the operation was postponed for a time. Eight months after the first operation, when the patient's health was in every respect good, I excised the appendix, which was buried in adhesions behind the cæcum. The abdomen was closed without drainage, and the operation was followed by a complete recovery. A point of interest (see Fig. 2) in this case was the fact that five or six lymphatic glands, some of them half an inch in length, were clumped together close to the appendix. So many glands in this position are quite unusual, and it would appear that they had been produced as a defence to the general system against the invasion of bacteria.

The appendix was acutely bent about half an inch from its distal end, whilst the proximal end was narrowed, so that I could not pass even a bristle through it. Between the bent and the strictured parts the canal was distended by a yellow, glutinous, muco-purulent material.

The result of the first operation in this case was disappointing to all concerned, but possibly the local loss of blood did good and prevented more serious mischief. It is practically certain that if the illness had been caused by a first attack of appendicitis an easy excision would have been effected, and the operator had to settle a very difficult problem when he decided not to remove the appendix. There is no doubt that his decision was a wise one, for the operation which I performed would have been extremely formidable if the circumstances had not been favourable. Certainly it would be better occasionally to undertake two operations, as in this case, than to delay interference and miss the opportunity of curing a patient with a gangrenous patch, or to persevere with an operation in order to obtain an immediate cure under desperate conditions, when a safer although less brilliant method is available.

DISCUSSION.

Mr. ALBAN DORAN believed that in many cases a solitary gangrenous patch in the wall of the appendix was due to acute local inflammation caused by the pressure of a hard fæcal concretion. He described a case where localised inflammation from this cause was very marked; the patient had suffered from two most characteristic attacks. There was no trace of any inflammatory change outside the appendix nor in the adjacent pelvic and abdominal organs. Gangrene might well have occurred in this case, though perforating ulcer would have been more probable. Mr. Doran noted that in this case the mesentery of the appendix was infiltrated with fat, which formed two distinct pedunculated outgrowths like appendices epiploicæ; yet the patient was thin. Perhaps the fat represented a degenerative change and interfered with the blood-supply of the appendix. He had noted deposit of fat with outgrowths in the mesosalpinx in association with ovarian dermoids and papilloma.

Mr. C. B. LOCKWOOD thought that at least 85 per cent. of the cases of appendicitis began in the mucous membrane. As to the assumed variety that began in the peritoneum, strong evidence would be required that no ulceration of the mucous lining was present. It was probable that infective bacteria found their way from the lumen of the appendix through such superficial ulceration, and these might give rise to the gangrene. He could not recognise a spontaneous gangrene. Rising pulse-rate, temperature, and leucocytosis were indications by which the earlier stages of appendicitis might be detected.

Mr. ASLETT BALDWIN said that they had all probably had their attention drawn to cases of strangulated hernia with gangrene of the bowel, where resection had been done and an end-to-end anastomosis performed through apparently healthy bowel, but the patient had died and at the autopsy gangrene of both ends of the intestine had been found. He thought this was probably due to invasion of the bowel-wall by virulent micro-organisms which caused rapid necrosis. He thought these necrotic patches in the appendix had a somewhat similar origin. Owing to some cause such as inflammation, pressure, or injury, the mucous membrane was damaged, virulent organisms entered the wall of the appendix, and necrosis took place at once, the symptoms being slight or unnoticed because the nerves of the part were dead and its vessels blocked, and the peritoneum outside intact;

not till organisms began to pass through the peritoneum, or the peritoneum necrosed and a perforation took place, were symptoms caused which directed attention to the condition.

In reply, Mr. MALCOLM said that in his paper he had carefully avoided giving any opinion as to the cause of the gangrene in these cases. He had described it as *apparently* spontaneous. He did not know its cause, but thought that, as Mr. Haward and Mr. Doran had suggested, it might be due to vascular changes, the nature of which were also obscure. He could produce no evidence from his own cases for or against this view. On the other hand, the gangrene might be due to an action of micro-organisms, but even then it seemed that it was not necessarily accompanied by inflammation other than that which followed the death of tissue. The question was an exceedingly difficult one, and Mr. Lockwood had done so much valuable work on the subject that it was with diffidence that the speaker discussed it before him. Mr. Lockwood had, however, mentioned the important fact that when a gangrenous patch in the vermiform appendix was examined it contained many kinds of micro-organisms, and the majority of appendices investigated had been at least a few hours, and often many hours, in a diseased condition. It was the initial changes that would throw light on the question at issue. In a case mentioned in the paper and fully published in the 'Clinical Journal,' April 11th, 1906, after an appendix abscess was opened the clinical signs indicated that the patient's condition was satisfactory, when suddenly on the third day there was a profuse hæmorrhage, which recurred on the sixth day. On opening up the wound small black patches of necrosed tissue were found on the raw surfaces. These were gradually cast off. They presented all the naked-eye appearances of a pure culture of an organism on a nutrient medium. Evidently a localised destruction of tissue had been produced. It might be inferred that the same organism had eaten into some considerable vessel and caused the bleeding. It seemed to the speaker doubtful whether such an action could occur in undamaged tissues, and in support of the view that there was always a history of mischief preceding gangrene-formation he might say that in the seventh case recorded, although the patient positively denied any previous illness of the kind, it was stated afterwards that she had occasionally complained of abdominal pain. Even then, however, it was quite clear that the final illness was quite different from any previous one. The author's contention was not concerned with the exact nature and cause of the slough, but with the fact, as he believed it to be, that, whether after evidence of chronic or repeated mischief or without any recognised preceding history, a patient might be seized with an illness the initial lesion of which, so far as could be ascertained,

was the formation of a gangrenous patch, and all the symptoms of which could be best explained as following and depending on this phenomenon. He would like Mr. Lockwood and those who agreed with him to consider in future whether some of their cases could not be explained in this way better than in any other.

FIG. 1.

Case No. 9.—Appendix removed when the patient was apparently well. There were two perforations, the larger being nearly half an inch long. These were closed by lightly adherent peritoneum. There was no abscess cavity.

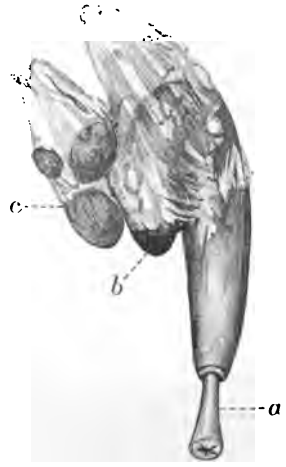


FIG. 2.

Case No. 12.—Appendix removed during interval. A, constriction; B, tip; C, glands. Other glands were detached during the operation.

Bale and Danielsson, Ltd.

SUBMUCOUS EXCISION OF DEVIATIONS AND SPURS OF THE NASAL SEPTUM,

WITH A REPORT OF 30 OPERATIONS

BY

StCLAIR THOMSON, M.D., F.R.C.P., F.R.C.S.

Received April 3rd—Read June 26th, 1906

It is generally agreed that operations on the nasal septum have not been amongst the most satisfactory in rhinology.[1]

Occasionally a limited spur may be chiselled or sawn through, or a ledge on an undeviated septum may be shaved off, and symptoms are thus relieved. A deviation, limited entirely to the cartilaginous septum, is sometimes met with, with no concomitant spur on it. Then a crucial incision at the most convex point, or a U-shaped incision made around it, will allow of the parts being moulded into the middle line, so as to free the obstructed nostril.

[1] "That many spurs have been removed unreservedly and without benefit to the patient is apparent to any careful observer connected with a large clinic where such results come to his knowledge. Not only am I warranted in saying that in many instances no good has obtained from their removal, but would further affirm that absolute harm has been done by creating a dry, 'scabby' condition of the septum, which is a constant source of irritation to the patient." (Harmon Smith, 'The International Journal of Surgery,' December, 1904.)

But the cases suitable for these operations form a minority amongst the abnormalities of the septum which require treatment.

Deviations of the septum are only too frequently sigmoid in shape—either in the vertical or horizontal plane—so as to cause some obstruction in both nostrils, and in the majority of cases part of the bony septum has to be removed (Krieg 52·3 per cent., Boenninghaus 68 per cent.). The septum, in fact, is too large for the space available for it between the floor and the roof of the nose, and one of our greatest difficulties has been its resiliency, which even the operations of Asch and Moure have only partly overcome. A simple deviation of the cartilage, or an uncomplicated spur, is much less frequently met with than various combinations of the two. These cases have proved a *bête noire* to rhinologists, and in the most marked forms (*i. e.* with more or less complete obstruction of one nostril) we have hitherto had no operation which could satisfactorily correct them.

Design of the Operation.

I do not at present intend to discuss the varieties of septal deformities, nor the indications for operative treatment, but propose to describe an operation which can be warmly recommended as entirely satisfactory for even the most marked deformities. The design of this operation is to excise all obstructing cartilage and bone, with any projecting spurs or ledges, while preserving intact the mucous membrane on each side. The results, both immediate and remote, are all that could be desired; for the resiliency of the deformity is entirely overcome, the obstructing outgrowth can never re-form, the patency secured exceeds that obtainable by any other proceeding, scabbing or crusting of discharge is avoided, and the preservation of the mucosa on each side secures rapid return to a normal condition.

Preparation.

The patient should be prepared by avoiding alcohol and any excess of diet or tobacco for three days beforehand. The operation is done under local anæsthesia, but an aperient should be given the evening beforehand. These precautions greatly help to avoid any bleeding during the delicate operation to be described. The patient can have an ordinary meal (breakfast or lunch) just beforehand. The vestibules—the only really septic parts of the nasal chambers[1]—are cleansed with spirit soap, and if a moustache is present, it should be thoroughly washed.

Anæsthesia.

Inch wide strips of sterilised ribbon gauze are soaked in adrenalin chloride containing 10 per cent. of cocaine and applied along the septum on each side, tucking them well up towards the roof of the nose in front and down to the floor. It may be impossible to get the gauze far in on the obstructed side at first, but after a few minutes the anæsthetic and vaso-constrictor action of the mixture will generally allow of a fresh piece being introduced more deeply. It is important to wait at least fifteen or twenty minutes to secure complete analgesia and full hæmostatic effect. If, then, the anterior end of the septum is still found to be sensitive, a pledget of cotton-wool soaked in 20 per cent. cocaine should be inserted for another five minutes, or some powdered hydrochlorate of cocaine may be applied on a minute damp swab. When the septum is found to be blanched and insensitive a fresh piece of soaked gauze is left along the concave side, while a small portion of dry gauze is packed along the floor of the opposite nostril to collect any drops of

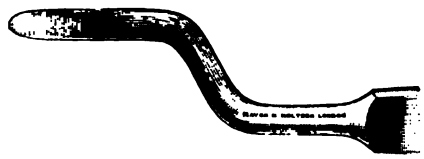
[1] StClair Thomson and R. T. Hewlett, "The Fate of Micro-Organisms in Inspired Air," 'Lancet,' January 11th, 1896; "Micro-Organisms in the Healthy Nose," 'Med.-Chir. Trans.,' vol. lxxviii.

blood which may run backwards. Small pledgets of gauze or cotton-wool should be at hand for mopping the wound, and a couple of retractors may be useful in holding open the nostril.

Position.

The operation is best done with the patient horizontal on a couch or operating table, with the head and shoulders well raised. The surgeon is armed with a Kirstein electric head-lamp or a frontal searchlight, although he can also operate successfully with an ordinary forehead reflector.

Fig. 1.

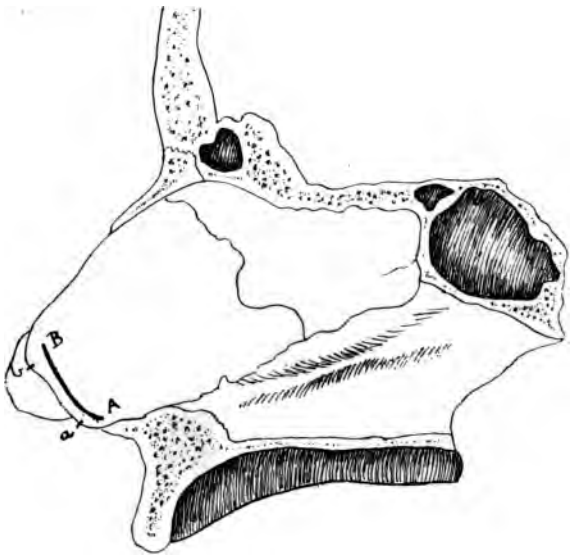


First Incision.

Tilting up the end of the nose with the thumb of the left hand, and inserting the left forefinger into the patent nostril, an incision is made through the mucous membrane of the septum on the convex (the obstructed) side. It may be made with an ordinary bistoury, but a much shorter instrument mounted on a bayonet handle and cutting all round the point will be found more satisfactory (Fig. 1). The incision lies half a centimetre behind the junction of the skin and mucous membrane, and mainly parallel to the septum cutaneum, but it may have to curve away from it at each extremity (Fig. 2). It should be started near the floor and then be carried high up, well into the attic of the nose. This incision, in its whole extent, does not only cut through the mucous membrane and perichondrium, but should go deep enough to cut into the cartilage. With practice this incision can be carried

through the muco-perichondrium and the entire thickness of the quadrilateral cartilage at one cut, but without puncturing or wounding the mucosa of the opposite (concave) side. During the proceeding the operator's left forefinger serves as a useful guide and check, by feeling the rounded tip of the knife as soon as it has traversed

FIG. 2.



The incision is made, on the convex side, through muco-perichondrium and cartilage, from *A* to *B*. If the free end of the quadrilateral cartilage is displaced from behind the septum cutaneum, and presents in one nostril, then the incision is made from *a* to *b*.

the cartilage (Fig. 3). In those cases where the lower end of the quadrilateral cartilage is displaced from behind the septum cutaneum into one of the nostrils—which it more or less blocks—the incision is made directly over the exposed extremity (Fig. 2). If this extremity presents in the open (concave) nostril, the septum cutaneum is first tilted across it so that the cut can still be made from the convex surface. If this is impossible, the projecting

cartilage must be dealt with through a separate incision from the concave side (Cases 28 and 30). Afterwards the procedure is the same.

Raising the Convex Flap.

With a sharp elevator the muco-perichondrium is carefully separated and raised along the posterior edge of the

Fig. 3.

Making the incision from the convex side, while the forefinger of the left hand acts as a guard in the opposite nostril.

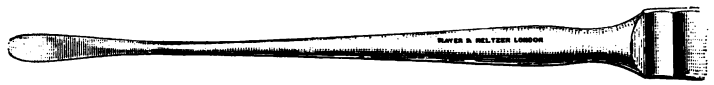
incision. Difficulty arises if the raspatory passes in between the mucous membrane and the perichondrium, instead of completely underneath the latter. Once freed along its whole length, a dull-edged detacher is used (Fig. 4), and if a good start has been made it is very easy to separate the muco-perichondrium clearly away from the cartilage. The dead white, slightly roughened surface of the latter

should be distinctly visible, and should not be coated with any soft, smooth, or pinkish perichondrium. The stripping up of the convex surface is carried upwards and backwards—where it is easily reflected—as well as downwards, where progress is apt to be arrested by its close adhesion to a cartilaginous spine or bony ledge. If possible, the limits of the convexity should be well passed.

Incision through the Septal Cartilage.

The next step is to cut through the cartilage at the site of the incision, but without incising the mucous membrane of the concave side. If the cartilage has not already been completely cut through, it will, at least, have been scored with the bayonet-knife in the original incision. The

Fig. 4.



Dull-edged perichondrium detacher. The blade is thin and slightly curved.

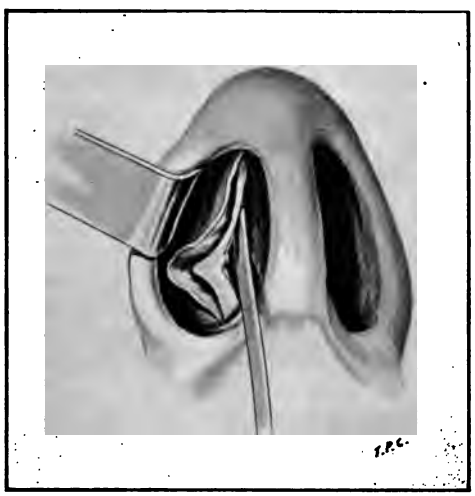
rounded tip of the knife is inserted into this groove and worked to and fro, taking great care not to button-hole the mucous membrane on the concave side. The tip of the left forefinger in the opposite nostril assists by feeling the end of the knife as soon as it has traversed the cartilage. The latter is thus cut through in the same extent as the first incision (Fig. 2).

Raising the Concave Flap.

The sharp elevator is now introduced from the convex side, through the incision in the cartilage, and insinuated between it and the muco-perichondrium lining the concavity. Once started, the operator takes the dull-edged separator, and by carefully hugging the septum all the

time, and observing the same precautions as in raising the convex flap, the membrane lining the concavity can be completely undermined (Fig. 5). But the most troublesome moment is when we reach the depth of the concavity, especially in those cases where a sudden hollow with steep edges is encountered, a condition which I can best describe by comparing it to the inside of a saddle (Fig. 19 *c*). To

FIG. 5.



The muco-perichondrium has been raised from the convex side of the septum, and the cartilage has been cut through (from *A* to *B* in Fig. 2). The dull-edged detacher is shown separating the mucous membrane from the concavity of the deflection.

avoid a button-hole at this point a good plan is first to free the mucous membrane well above and below it. If a puncture does occur, it is better not to go on working at that spot, but to leave it until separation has taken place all round it. The point of the instrument can be watched as it manœuvres below the mucosa in the concavity. The separation is carried on until the membrane has been stripped up all over the concavity, and also over any secondary convexity, if the deviation is sigmoid-shaped.

Excision of the Septal Cartilage.

The deviated and denuded septum is now exposed in a pocket whose walls are formed by the detached mucous membrane on each side, and whose mouth opens into the obstructed nostril. The next step is to excise the deviated portion through this opening. The field of operation can

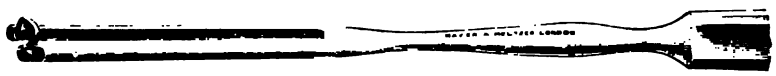
Fig. 6.

Semi-diagrammatic drawing of a transverse section of the nose, viewed from above. The deviated septum has been divided in front, and its muco-perichondrium has been stripped up on each side. The nasal speculum is introduced through the convex nostril, and a blade is inserted on each side of the septum, between it and its mucous covering.

be well exposed by the help of Killian's long nasal speculum. We are so accustomed in this country to Thudichum's speculum that I have had one made with blades two inches long to serve the same purpose. Used through the obstructed nostril, a blade is inserted on each side of the denuded septum, between it and the separated muco-perichondrium (Fig. 6). With a good electric searchlight it is

easy to see if the mucous membrane on each side has been sufficiently stripped off. If not, we must return to the

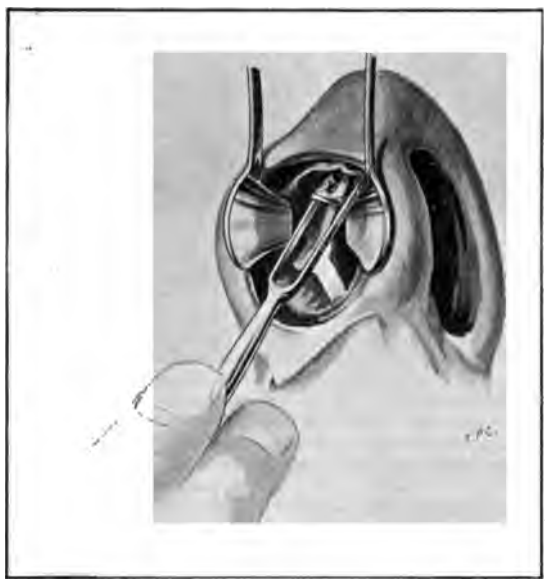
Fig. 7.



Ballenger's swivel septum knife.

raspatory. I have never had to regret removing too much of the septum, and it is much better, if possible, to separate the mucous membrane as far as will be required before commencing the excision of the septum.

Fig. 8.



The method of employing Ballenger's swivel septum knife for cutting out the cartilaginous deviation.

This can be done with a stout pair of narrow scissors, such as Heymann's, supplemented by punch forceps. But this part of the operation is quickly, safely, and completely

carried out by using Ballenger's swivel septum knife [1] (Fig. 7). This is placed astride the anterior, cut surface of the cartilage, pushed upwards and backwards below the roof of the nose, until it comes in contact with the ethmoid; then the cutting surface is directed downwards and backwards to the angle between the perpendicular plate of the ethmoid and the vomer; and, finally, it is pulled forwards along the upper margin of the vomer (Fig. 8). The excised cartilage is lifted out. In this way the main part of the deviation is removed *en bloc*. Some of the pieces thus removed measure one inch by one and a half inches (Fig. 19 *b*).

The empty pocket between the two separated and flaccid mucous membranes is now wiped free of any blood in it, and the two sides allowed to fall together—mucous membrane with mucous membrane. This should hang perfectly plumb in the middle line, and on looking into the formerly obstructed nostril one can see the previously invisible middle turbinal, the whole length of the inferior turbinal (often ill developed from pressure), the anterior wall of the sphenoidal sinus, the levator palati muscle, and the posterior wall of the naso-pharynx.

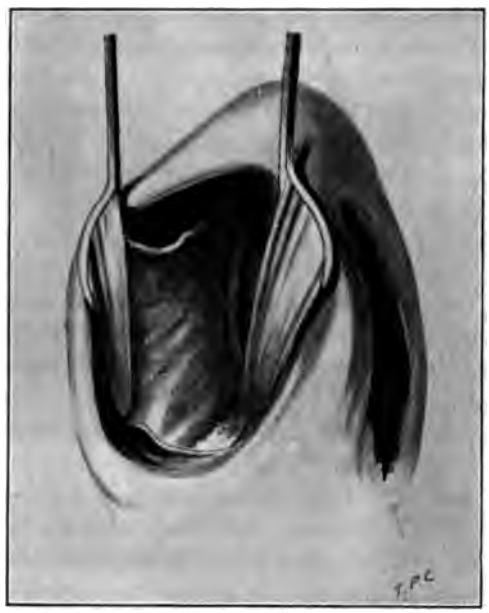
If this view is not quite free, or if any projection is still seen on the septum, the two mucosæ are again separated by the long nasal speculum, and more of the septum is shaved off with Ballenger's septum knife or Ingals' cartilage knife, or clipped away with punch forceps. In doing this portions of the vomer and of the perpendicular plate of the ethmoid are removed. A specimen is shown in which more than forty bits were thus clipped away, even after a bony spur and a large piece of cartilage had been excised. It is well to remember that the fleshy curtain will hang between the upper and lower margins of the gap left in the septum. These margins, therefore, must both be in the middle line, otherwise the membranous septum stretched between them will be oblique or to one side (Fig. 12).

[1] 'The Laryngoscope,' vol. xv, June, 1905, No. 5, p. 417.

Excision of Bony Spurs and Deviations.

If, as is only too often the case, the deviation is accompanied by a bony spur or ledge, the operation is started as already described. Much difficulty is encountered in

Fig. 9.



The deviated septum has been removed. The two flaps of mucoperichondrium are held apart by the blades of the nasal speculum. In the pocket between them are seen the lower edge of the remaining portion of quadrilateral cartilage, and the free edge of the perpendicular plate of the ethmoid passing downwards to the angle where it meets the vomer. Below, and in front of this, is seen the nasal spine of the superior maxilla.

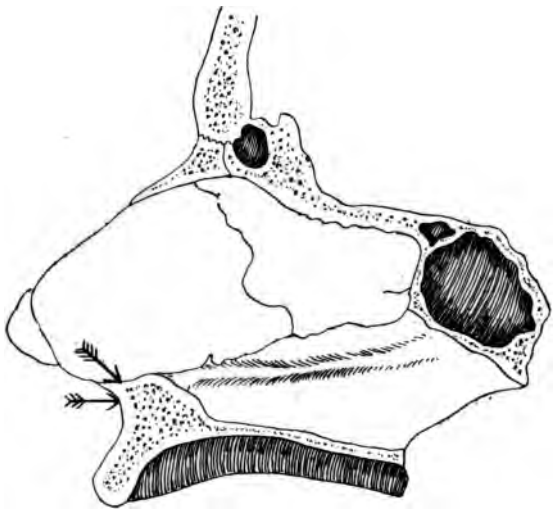
raising the mucosa from an acute, prominent spine, especially if it presses into the opposite inferior turbinal. Killian says that "whoever attempts to separate the mucosa around these corners will perforate as a rule."

It is also frequently a very tedious matter to lay bare any thickening or deviation of the nasal process of the

superior maxilla, or the chondro-vomerine articulation—the usual sites of bony obstructions. Here the periosteum is not only intimately adherent, but also coats over the bone, between it and the nasal quadrilateral cartilage. In such cases freer access is obtained after the removal of the cartilaginous deviation (Fig. 9).

Once well exposed, the maxillary spine is attacked with strong punch forceps or chisel, and as pieces of it are prised up they are twisted off with forceps (Fig. 10). A

FIG. 10.



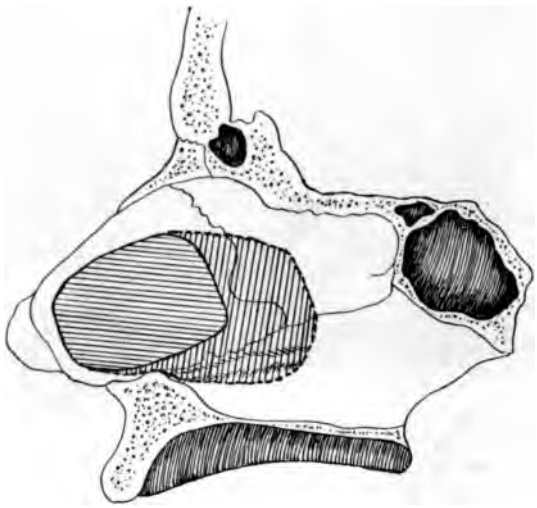
The arrows indicate the points where the chisel may be applied when exostosis of the nasal maxillary spine requires removal.

bony spur on the vomer has sometimes to be followed back nearly to the posterior choana (Case 21), and the vomer is often so curved over into the obstructed nostril that it lies parallel and close to the floor of the nose. A great deal of the success of an operation depends on the complete removal of these spurs and ledges of bone, and this part of the operation, in many instances, is both the most necessary and the most difficult. Not infrequently the removal of part of the quadrilateral cartilage is little

more than the preliminary step to the main object in view.

Success depends on carefully separating the muco-periosteum from the maxillary spine (if prominent), and then removing the latter so as to bring any vomerine deformity into view. The perichondrium must be separated from each side of the vomer right down to the floor of the

FIG. 11.



The area surrounded by a dark line and shaded by horizontal lines indicates the size and situation of the cartilaginous deviation removed with Ballenger's swivel septum knife. The area shaded with vertical lines, and surrounded with a dotted line, consists of cartilage and bone, which are removed with punch forceps and chisel.

nose. Deformities of the vomer ascend as the deeper regions of the nasal cavity are reached, and, fortunately, the vomer is apt to be thinner just below any exostosis. Hence, if the bone is chiselled or punched just below a projection, it is at once freed and can be lifted or twisted out.

When a completely vertical and smooth fleshy septum has been thus secured, and the formerly obstructed nostril is seen to be quite free, the pocket is carefully wiped out

with sterile gauze, and care is taken that no chips of bone or cartilage are left in between the two flaccid mucosæ (Fig. 11).

Stitching the Wound.

The original wound is now closed with one or two stitches. A very small Trélat needle is armed with finest cleft-palate silk (No. 000), and while an assistant holds the nostril open with a retractor the edge of the posterior flap is seized with a small pair of dissecting or toothed forceps, and then traversed with the threaded needle from behind forwards. The needle is carried in the same way through the anterior edge of the wound, one end of the silk is pulled out with a fine hook, the needle is then withdrawn, carrying the other end, and the stitch is tied. Care, of course, is taken that the edges of the wound are properly affronted. One or two stitches may be required.

The Dressing.

The formerly obstructed nostril is now lightly packed with pencils of dry sterilised cotton-wool, well smeared with simple vaseline. One or two plugs in the opposite side may be introduced. The nose should not be plugged tightly, our object being simply to keep the two mucous membranes in apposition. In some cases I have done without any plug (Nos. 3, 4, 9, 10, 11, 14).

After-Treatment.

The patient rests quietly for the remainder of the day, sips some iced drink, and keeps an iced cloth across the bridge of the nose. A little blood-stained oozing is best met by ice-water ablution to the face and neck. I have never had any secondary bleeding requiring attention. Cotton-wool, dipped in cold boracic lotion, is used for wiping out the blood which dries in the vibrissæ and causes discomfort to the patient.

Next day the plugs are partly or entirely removed, and a smaller one may be left for another twenty-four hours. The patient can go out or resume his work. The septum may look somewhat swollen and the nose be more or less obstructed for a few days. During this time he must not blow his nose, but should suck any blood-stained mucus backwards into the naso-pharynx and then hawk it up. Relief from the obstruction can be obtained by spraying the nose with liquid vaseline, or introducing a piece of menthol and boric ointment into each nostril morning and evening.

At the end of three or four days the swelling of the fleshy septum subsides, and the stitches are removed. In seven to ten days the patient begins to enjoy the benefit of the operation, but it is often only after three weeks that the full advantage of it is established.

After-Condition.

It is frequently asked if cartilage is re-formed between the two mucous flaps. Two of my cases (Nos. 2 and 3), which were operated on two and a half years ago, have recently been examined, and although some solidification has taken place in the fleshy septum, it is still seen to quiver like the sail of a boat when the patient sniffs quickly through one nostril.

K. M. Menzel was able to submit a piece of the fleshy septum to histological examination two and a half months after the quadrilateral cartilage had been resected.[1] Both flaps of mucous membrane were intact and united together by connective tissue, but there was no trace of re-formation of cartilage. This is what we would expect from the researches of Paget on the processes of repair.[2] He pointed out that there are no instances in which a lost portion of cartilage has been restored, or a wounded portion repaired, with new and well-formed permanent

[1] 'Archiv f. Laryngologie,' Bd. xv, 1904, S. 54.

[2] 'Lectures on Surgical Pathology,' London, 1863, p. 195.

cartilage. Even the preservation of the perichondrium does not secure the re-formation of cartilage, as is shown by a case of wounded thyroid cartilage which Paget examined several years after complete healing. A layer of tough fibrous tissue united the gap, but there was no appearance of a renewed growth of cartilage. Similar results were arrived at by Redfern in incised wounds of the articular cartilages of dogs.[1] Paget points out that in membraniform cartilages that have a perichondrium the healing process is probably in some measure modified, a reparative material being furnished, at least in part, from the perichondrial vessels. Hence the importance, in this operation, of carefully preserving the perichondrium, not only in facilitating the technique, but also in contributing to a firmer, fibrous, fleshy septum.

Occasionally, while delighted with the free air-way through the formerly obstructed nostril, the patient complains that the side which used to be his best is no longer so free. This is due to the fact that compensatory hypertrophy of the inferior turbinal had taken place in the only acting nostril. When the formerly concave septum is rendered vertical, the passage is proportionately narrowed (Fig. 12). This can be corrected subsequently by removing some of the redundant turbinal.

Some of the difficulties apt to be met with may be briefly referred to:

Insufficient illumination is one that can be provided against.

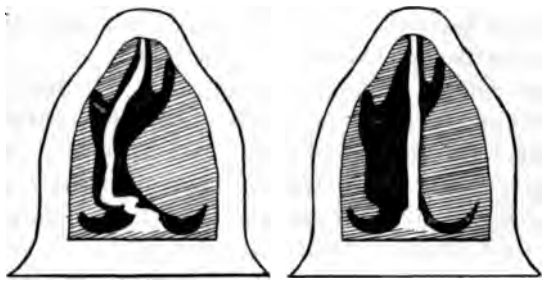
Anæsthesia.—Many operators advise a submucous injection of cocaine and adrenalin. Killian employs four drops of adrenalin in 2 c.c. of a ½ per cent. solution of cocaine. One c.c. of this is used on each side, and fifteen minutes are allowed to elapse to secure its full effect.[2] I have found that the making of this injection is apt to

[1] 'Abnormal Nutrition in Articular Cartilages,' Edinburgh, 1850. And "On the Healing of Wounds in Articular Cartilages," in the 'Monthly Journal of Medical Science,' Sept., 1851.

[2] 'Archiv f. Laryngologie,' Bd. xvi, S. 362.

unnerve the patient; it gives rise to palpitations and uncomfortable sensations; and it often starts a little troublesome bleeding at the point of injection. If the cocaine and adrenalin are applied to the surface, as I have described, the operation is remarkably painless. Athough the procedure is naturally uncomfortable, it is not more so than a prolonged dental treatment, and most patients have expressed more sympathy for the strain on the operator than complaint for themselves. In an uncomplicated deviation there is no pain. The disagreeable cases are those in which a bony ledge has to be chiselled

FIG. 12.



Diagrammatic transverse section of the nose. Shows the compensatory hypertrophy of the inferior turbinal in the unobstructed nostril. Part of this frequently requires removal after the septum has been straightened.

out a long way backwards; the pain of clipping and twisting out pieces of bone cannot be quite deadened with cocaine. Only two patients complained of the pain; they were very nervous subjects. All the others agree that it was trifling or entirely absent, and that they only regretted their unnecessary fears of anticipation. Five cases were operated on under chloroform. Four of these were the first I performed, before I had sufficient confidence in the effect of local anæsthesia. The fifth case (No. 18) insisted on chloroform.

Hæmorrhage presents no difficulty. In some cases only a few drops of blood are lost, and in none did any run backwards into the pharynx during the operation.

The incision.—In one case I tried the incision from the concave side, but found it so much more difficult that I abandoned it. The one incision is sufficient. In a few cases, with very sharp, low-lying spurs, I have found that I had, involuntarily, carried the lower extremity horizontally backwards, so as to resemble an "L" facing backwards.

Raising the perichondrium.—The importance of this has been referred to. In two cases (Nos. 25 and 29), as will be seen from the specimens, I found I had separated the mucous membrane, but left the thin white perichondrium attached. No puncture was made, and no harm resulted, but it is important to avoid this difficulty.

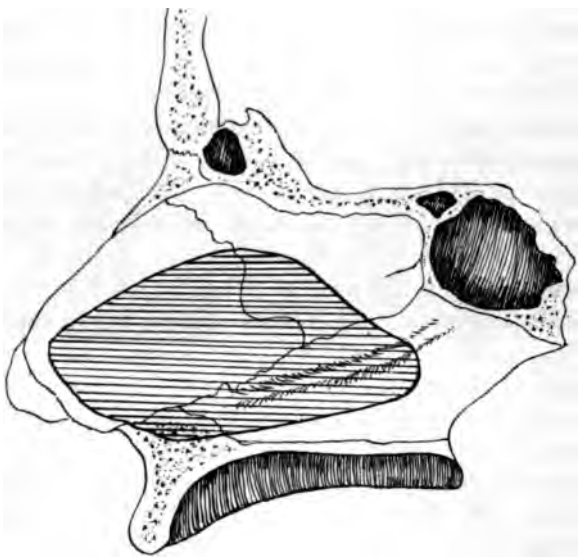
Avoiding perforations.—This difficulty is avoided if one muco-perichondrium can be raised intact. Even if both flaps are punctured, a perforation only occurs when the openings are *vis-à-vis*. Although undesirable, a perforation causes no annoyance if it occurs far back. I find that the margins are smoothly healed, and no crusting takes place in them. It is more important to avoid a perforation anteriorly, where dust is apt to keep up irritation. Hence the care requisite in cutting through the cartilage, and the advantage of stitches, if the concave flap should happen to get button-holed.

Removing the septum.—This has been greatly facilitated since employing Ballenger's swivel knife. It is helpful to remember that the quadrilateral cartilage is very thin in front, but that it may be as much as 5 mm. in thickness far back. The perpendicular plate of the ethmoid is as thin as paper, and very brittle. The vomer is apt to be thickest at its junction with the quadrilateral cartilage. The nasal maxillary spine is not only very stout, but it bleeds readily.

Previous operations.—These may greatly increase the difficulties. In one case (No. 16) an adhesion between the convexity and the inferior turbinal, left by treatment, had first to be separated; and then, in undermining the flap on that side, I found that the cartilage had been

quite cut through in one point by a previous operation (Fig. 19, *a*). Although the mucous membranes of the opposite sides of the septum were stuck together in this area, I succeeded in separating them. In another case (No. 19), where the same complication had been left, the mucous membrane of the convexity was torn in separating it from that of the concavity (the intervening cartilage having been "shaved off" in previous treatment). No

FIG. 13.



The shaded area indicates the extent of bony and cartilaginous septum usually requiring removal.

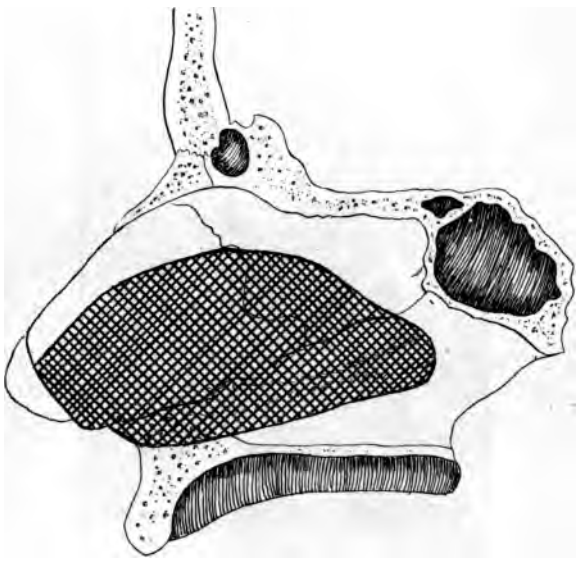
perforation was left, but the healing was delayed by scab-formation.

Stitches.—In my earlier cases much time was spent over the stitches, and I experimented with various needles and needle-holders before adopting the one recommended. Some operators have abandoned stitches owing to the time and trouble entailed, the tendency to tear the flaps, and because a plug is sufficient to keep them in place. I find that the stitches described can be readily inserted, allow

of lighter packing, and secure healing by first intention. I have tried some cases (Nos. 2, 19, 20) without any, and found that granulations were apt to spring up between the edges. Finally, if the concave flap is punctured anteriorly, stitching is most important to avoid a button-hole.

The objections which may be raised against this operation can be stated and answered as follows:

FIG. 14.



The shaded portion indicates the extent of cartilage and bone removed in marked deformity, with deflection of the free end of the quadrilateral cartilage into one nostril, as in Case 21.

(1) *That the excision of a large part of the septum may lead to flattening or deformity of the nose.*—This objection is groundless. We know that the end of the nose does not fall in, even when a large perforation has been made in the septum. Saddle-nose deformity is usually brought about by the retraction of inflammatory scar-tissue (generally syphilitic or after external traumatism), or when the whole septum is destroyed. In the above operation a strip of the septal cartilage is always left

above, beneath the crest of the nose, and generally another strip below behind the septum cutaneum. It is because of this that the method is called in Germany the *Fensterresektion*. A "window" is taken out of the cartilaginous and bony septum, but the window-frame all round is left intact. Even this is not necessary, for the cartilaginous septum was removed in several of my cases (Nos. 8, 17, 18, 20, 21, 28, 30) right down to its free

FIG. 15.

From Case 8. Displacement of the free end of the quadrilateral cartilage into one nostril.

border, and yet the tip of the nose has not collapsed (Fig. 14). Indeed, this operation is quite the best for the deformity known as "displacement of the septum into one nostril." Fig. 15 shows this condition in a girl aged 15, in whom the operation was done in December, 1904, and there is now no external disfigurement (Fig. 16). On the contrary, the external appearance of the nose is always improved by the operation. It is difficult to show this

in photographs, as an improvement in appearance often depends on very slight alterations, but all my patients are satisfied that the appearance of the nose has been altered for the better (Figs. 17 and 18). Finally, there is the convincing proof that in none of my thirty cases has there been any falling-in or disfigurement, although two of them were operated on two and a half years ago.

(2) *That the operation entails greater risks from any*

FIG. 16.

Case 8, after operation.

subsequent blow on the nose.—This objection has been met by the experience of Otto T. Freer in four of his cases where severe blows, causing epistaxis and occurring even within a week of operation, did not result in any damage to the fleshy septum, nor to the external appearance of the nose.[1]

(3) *That the operation is long and tedious.*—In cases limited to the cartilage, the deviation can be excised and

[1] 'Annals of Otology, Rhinology, and Laryngology,' June, 1905.

the operation completed in twenty minutes. But when bony spurs and ledges are met with, most writers agree that we require an hour, and many of them vaguely add "and even more." [1]

In my earlier cases I have spent three hours over the operation, but now less than half that time is sufficient. Time is often taken up in waiting for fresh applications of cocaine and adrenalin to act, and the operation is prolonged if one flap happens to be button-holed. It is highly important not to get two button-holes *vis-à-vis*, as a permanent perforation is then inevitable. If one mucosa

FIG. 17. FIG. 18.

FIG. 17.—Case 21. A pencil mark has been made on the skin of the nose to show the deformity before operation.
FIG. 18.—Case 21. Shows improved external appearance after operation.

is separated intact, we can proceed more boldly and quickly with the other.

Besides, it is well to remember that "les opérations succédent d'autant mieux qu'elles sont moins nécessaires."

[1] "The average time for my operation is at least three quarters of an hour to an hour." Otto T. Freer, 'Annals of Otology,' June, 1905.

"The one and one half hours required." Leon E. White, 'Boston Medical and Surgical Journal,' April 21st, 1904.

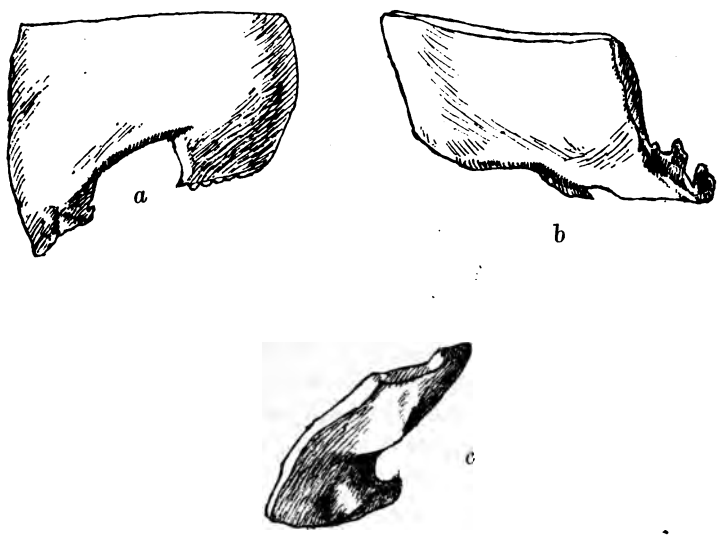
"When bone needs removal, the operation is long, from one to two hours." A. Coolidge, Jun., 'Boston Medical and Surgical Journal,' February 2nd, 1905.

"The operation may take as long as two and a half hours." Felix Cohn, 'The Laryngoscope,' xiv, July, 1904, p. 556.

"The operation lasts from one to three and a half hours." Stepanov 'Revue hebd. de Laryngologie,' xxv, 1904, ii, No. 31, p. 143.

This operation is especially suitable for forms of septal deformity which are the most severe, and therefore the most in want of operation. Some surgeons may snatch a fleeting reputation for celerity by treating the slight cases only. I began by reserving this operation for very bad cases, and in view of the satisfactory results have lately extended it to the milder ones. Beginners are also apt to

FIG. 19.



Life-size drawings of removed portions of deviated quadrilateral cartilage. *a*. From Case 16. Shows defect in cartilage from a previous operation, in which the prominent portion had been shaved off. *b*. From Case 13. Shows the thickness of a large deviation. *c*. From Case 21. Shows the saddle-shaped deformity of a very irregular deviation.

be content with an incomplete operation, one which simply frees the obstructed nostril. But when the shrinkage of the soft parts induced by the cocaine has passed off, it will be found that the patency is never so good as at the time of operation; and the results are unsatisfactory unless all obstructions are completely removed so as to leave a straight passage, open right back to the naso-pharynx and from the olfactory cleft above to the floor of the nose

below. Incompleteness of removal must not be sacrificed to rapidity, particularly in this operation, for it would be extremely difficult, and in some cases quite impossible, to separate the two mucous membranes at a later period for further treatment. (Compare Cases 16 and 19.)

(4) *That the operation requires special skill.*—The technique is a little difficult to acquire.[1] Perforations appear to be inevitable in the earlier cases of every one. Thus, Freer had six in his first fifteen cases, but only five in his last 101. In the synopsis of cases which I append it will be seen that perforations occurred in four of my first seven patients. Twenty-six cases have now been completed without this drawback. This illustrates the progress made by practice.

Writers are agreed that the operation is not a simple one. Thus, in one of the latest text-books, Zarniko writes, "As all operators who know it will confess, the *Fenster-resektion* of the septum belongs to the most extremely difficult intra-nasal operations."[2]

Both celerity and certainty are secured by practice, and the method and instruments I now recommend have made the operation considerably simpler, so that this objection is one that will have less force as the operation evolves further.

(5) *The operation is unsuitable for children.*—From my own experience I would say that it is not a suitable operation for children or young people much under seventeen years. Before that age the nasal chambers are so small that the technical difficulties are greatly increased, and it is possible, though not very likely, that it might prevent the full development of the nose. Besides, it would have to be carried out under a general anæsthetic. Killian advises that, as a general rule, children younger than twelve

[1] "In submucous resection . . . *a great deal more technical skill and dexterity* are demanded which many who treat the nose will probably never have the patience to acquire." L. H. Pegler, 'Brit. Med. Journ.,' November 4th, 1905, p. 1202.

[2] 'Die Krankheiten der Nase,' 1905, p. 300.

are not fit subjects for this operation. Otto T. Freer, however, is of opinion that the operation is proper for children at all ages, although with them the deformity tends to recur unless every vestige of it has been removed. E. Mueller has performed the operation successfully in three children under ten; one of them, indeed, was only six years old.[1]

(6) *The armamentarium is large and expensive.*—This was an undeniable objection when I first practised this operation. Freer's complete outfit contains over twenty instruments. Killian's has the objection that different instruments are required for the right and for the left nostril.

By combining the good points in the instruments of various operators I have been able to reduce and simplify those absolutely necessary. Those I advise all act in a straight line, which allows of finer and more accurate work than those fitted with a shank at the so-called "nasal angle." They can be used on either side of the septum.

Doubtless in time further improvements will be made and will greatly help in popularising the operation. At present my list of instruments is as follows:

(1) Ordinary Thudichum nasal speculum.

(2) Long Thudichum nasal speculum.

(3) A sharp bayonet-handled knife, cutting for a quarter of an inch all round the point, for dividing the mucous membrane and quadrilateral cartilage.

(4 and 5) Sharp and dull-edged separators. I agree with Freer that these should be thin-edged and narrow, so as to work round sharp angles and into deep concavities.

(6) Ballinger's swivel cartilage knife.

(7) Hartmann's punch forceps with solid male blade.

(8 and 9) Hammer and chisel.

(10 and 11) Needle and a fine hook.

(12) Freer's or Jansen-Middelton forceps.

The **advantages** of this operation may be summarised as follows:

[1] 'Archiv f. Laryngologie,' Bd. xv, 1904, s. 312.

(1) No general anæsthetic required.

(2) No hæmorrhage.

(3) Absence of pain and shock.

(4) No reaction. The post-operative temperature seldom rises above 99° F.

(5) Absence of sepsis, with its possible extension to ears, sinuses, or cranial cavity.

(6) No splints required and no plugs after forty-eight hours.

(7) Rapid-healing, without crust formation.

(8) No risk of troublesome adhesions.

(9) Short after-treatment.

(10) Speedy establishment of nasal respiration.

(11) Suitability for all deformities of cartilage or bone in the septum requiring treatment.

(12) The space gained is not only that resulting from a vertical septum, but the extra room secured by removal of the cartilage, which is sometimes one eighth of an inch in thickness.

(13) No ciliated epithelium is sacrificed.

(14) Accuracy of result can be depended on, and the prognosis is, therefore, the more definite.

(15) Improved appearance of the nose externally.

The **contra-indications** of submucous resections:

(1) Elderly people are so accustomed to their nasal obstruction, and its secondary consequences are generally so fully established, that the benefits would be much less marked than earlier in life.

(2) The question of its indication for children has been considered under the section of "Objections" (page 26).

(3) Serious or progressive organic disease. This does not apply to healed tuberculosis. In Case No. 11 the patient had been advised to consult me after leaving a sanatorium. The operation was performed ten months ago; the result was entirely satisfactory, and lately the patient reported that he was keeping well and free from symptoms.

(4) Active syphilis.

(5) Lupus. A case of healed lupus of the larynx had a marked deviation into one nostril and displacement of the lower end of the cartilage into the opposite. I put her name on my waiting-list of patients, but when admitted a few months later apple-jelly infiltration had commenced on each side of the septum. The operation was therefore cancelled.

(6) The operation should be postponed if the patient shows any symptoms of influenza or acute or infectious catarrh.

The **special indications** of this operation would appear to be :

(1) Cases where it is desirable to establish normal nasal respiration and remove mouth-breathing, with its numerous consequences.

(2) Correction of the disfigurement caused by the lower end of the quadrilateral cartilage projecting into one nostril.

(3) Cure of reflex neuroses of nasal organ.

(4) Relief of Eustachian catarrh.

(5) Facility of treating nasal polypi and affections of the accessory sinuses. In two cases (Nos. 2 and 3) the polypi could not be attacked until the septum had been straightened, and in one of these the ethmoidal labyrinth required free removal. As with this operation a deviation can be followed high into the roof of the nose, it is particularly indicated when drainage or treatment of the frontal or anterior ethmoidal cavities is required (Case 25).

History of the operation.—It is difficult to settle the paternity of this operation. An entire article on this point has recently beon contributed by Suckstorff, who traces the principles of it back to Heylen in 1847.[1]

For those who wish to refer to the matter, I have added in an appendix some of the bibliography. As at first designed the mucous membrane on one side was removed together with the septal deformity, leaving only the mucosa of the opposite side to act as a septum. This entailed a

[1] 'Archiv für Laryngologie,' Band xvi, 1904, S. 355.

long convalescence, during which crusts formed and required careful attention. When healed, the surface did not leave the even, moist, slippery surface secured by the present method.

As I have described it, the operation is in most respects similar to the one carried out by Professor Killian.[1]

Conclusion.

The increasing satisfaction with this operation, which has come with extended practice, has encouraged me to prefer it in the majority of septal deformities calling for interference. It is possible in some cases to avoid operation on the septum by directing attention to other points in the nose. For spurs and ledges in a more or less vertical septum—a rare condition—this operation is unnecessary. Deviations, if limited to the cartilaginous septum, may be partially corrected by the more easily executed operations of Asch and Moure.[2]

But for all other forms of deviation, and for combinations of spurs with deviations, the operation above described will be found the most satisfactory.

Epitome of first Thirty Cases.

Case 1.—Captain I. C—, aged 35. Complained of obstruction of both sides of the nose for ten years; some anosmia. Has an attack of bad earache on right side, followed by discharge, about twice a year. Nasal voice. Large deviation occluding right nostril, with tip of nose tilted to left. Weight, 8 st. 9 lb.

October 5th, 1903.—Operation. Submucous injection of cocaine and adrenalin. Chloroform. A button-hole

[1] 'Archiv für Laryngologie,' Band xvi, 1904, S. 362.

[2] "Few, if any, of the Asch operations result in a perfectly smooth outline of the septal surface, and in quite a number of instances subsequent operation for the removal of spurs or spines is necessary." Harmon Smith, 'The International Journal of Surgery,' December, 1904.

was made on concave side. Gauze plugs. Duration of operation, one hour and twenty minutes.

The button-hole for the first week appeared to be filled up by mucous membrane of opposite side, but at the end of that time it was seen that a small puncture must also have occurred on the convex side, and as these openings were *vis-à-vis* the perforation was permanent.

November 13th.—Septum in middle line; margin of perforation healed, and as it is far back in nose it causes no symptoms. Free respiration through both nostrils. Friends notice his nose is straighter. Sense of smell "distinctly better." Weight 9 st., which it has not been for some years.

Case 2.—Mr. F. D. B—, aged 29, sent by Dr. Sangster for nasal obstruction, snoring, and disturbed sleep for ten years. No ear trouble.

Voice thick and nasal. Deviation and spur in right nostril, which is so occluded that no air passes through it during inspiration or expiration. He can only get a little air in by sniffing hard and expel it by raising the right ala nasi with his finger. Sense of smell very slight, no cacosmia.

Some polypi were first removed on the right side.

Operation.—November 4th, 1903. Chloroform. Submucous injection of cocaine and adrenalin. No perforation, though the right flap was somewhat damaged as the bony spur lay so close to floor of nose. After removal of obstruction more polypi came into view on right side and were removed. Attempts to stitch wound failed; plugs of iodoform gauze both sides.

Duration of operation, two hours.

May 6th, 1904.—Patient shown at Laryngological Society of London (*vide* 'Proceedings') with fleshy septum quite vertical in middle line and the result pronounced to be "ideal."

March 1st, 1906.—The patient sleeps quietly through the night with his mouth closed; the voice and sense of

smell are improved. The external nose is, if anything, slightly improved in appearance. The patient states that it feels "quite firm," but though the septum is vertical and looks firm, it still quivers on sniffing.

Case 3.—Mr. A. C. S—. aged 26. Complained of always being blocked in the nose, although his adenoids had been removed at the age of sixteen, and he had recently had his nose cauterised.

Deviation and spur in left nostril, buried in the inferior turbinal, and occluding all view of the middle turbinal. Nasal maxillary spine very marked in right nostril. Patient can never blow his left nostril, which he, therefore, has to clear by hawking out through his mouth. Mouth-breather at night and on any exertion. Chronic pharyngitis and laryngitis.

Operation.—December 5th, 1903. Chloroform. Submucous injection of cocaine and adrenalin. Spur had to be followed far back along vomer, and much time and labour were required to remove the right maxillary nasal process. A puncture occurred in the deepest point of the concavity, but was quite filled up by the intact convex flap. Three silk stitches, no plugs.

Duration of operation, three hours.

Subsequently, as patient complained of obstruction in the right (the formerly most patent) nostril, the lower border of the hypertrophied inferior turbinal was removed. After removal of the obstruction on the left side some pus and polypi came into view and a carious condition of the ethmoid had to be attended to.

May 6th, 1904.—Patient was shown at the Laryngological Society (*vide* 'Proceedings').

March 1st, 1906.—The fleshy septum still quivers on inspiring quickly, but is quite straight in the middle line. Free nasal respiration. Sleeps with mouth closed. No pharyngitis. Friends notice improved appearance of nose.

Case 4.—N. K—, referred to me by Dr. Percy Lewis,

was a boy, aged 13, on whom I should have preferred to defer operation, had it not been that his admission to the Royal Navy was threatened by his being a mouth-breather. This was due to complete blockage of the right nostril by a deviation with a sharp spur on it.

Operation. December 31st, 1903. Chloroform by Dr. Bousfield. No plugs. Two stitches. A perforation the size of a small bean was left, but a perfectly clear air-way was secured.

CASE 5.—Norman H—, aged 19. Very crumpled septum, from a blow which had depressed the cartilaginous part of the bridge of the nose.

April 19th, 1904.—Operation under cocaine and adrenalin applied on surface. Perforation.

March, 1905.—Free nasal respiration. Perforation far back, with smooth edges, quite free from crusts and causing no inconvenience.

CASE 6.—Mr. H. S. D—, aged 20, a student in King's College. Injury to nose seven years previously. Constant mouth-breather. Snorer. Short-winded when running or dancing. Left nostril entirely occluded by large deviation and spur, so that no part of the inferior or middle turbinal is visible.

Attempt to operate from concave side, under chloroform, was not successful, owing to difficulty of working round such a deep depression.

August 30th, 1904.—Operation after application of cocaine and adrenalin. One puncture in concave flap was filled up by integrity of convex. One stitch. Light packing of cotton-wool and vaseline in left nostril.

September 5th.—Septum plumb in the middle line and verified by Dr. Bryan, of Washington.

March 10th, 1906.—Patient writes: "I do not snore now. I believe I sleep with my mouth closed. My wind is greatly improved. I believe the appearance of the nose is improved—*i. e.* it is much straighter."

Case 7.—Miss L. C—, aged 28, referred to me by Mr. W. Rose. Complete obstruction of left nostril by deviation and sharp spur.

October 19th, 1904.—Operation under cocaine and adrenalin, applied to surface only. On the right side the concavity was so deep that a perforation took place, which, unfortunately, was opposite a puncture over the prominent spur. Free respiration, and no annoyance caused by perforation.

Case 8.—Miss L. D—, aged 15 and 3 months. Complained of mouth-breathing and tenderness of "bone in right nostril." Mouth-breather, day and night. Free end of quadrilateral cartilage displaced into right nostril (Fig. 15).

October 7th, 1904.—Some adenoids removed.

December, 1904.—Resection under cocaine applied locally.

March, 1905.—Free respiration (Fig. 16).

Case 9.—E. W—, aged 25, a lay clerk in the cathedral, was sent by Mr. C. Wace, of Winchester. He complained of nasal obstruction and its interference with his singing. He had been treated elsewhere with "hot wires" and the removal of "pieces of bone" from his nose.

An antero-posterior sigmoid deviation rendered both nasal chambers very narrow. High-arched palate, chronic pharyngitis, and laryngitis. Some pus-secreting adenoids were first removed.

July 16th, 1904.—Operation. Superficial application of adrenalin and cocaine. Duration, one and a half hours. Two stitches. No plug. Removed septum found to be one eighth of an inch thick.

July 19th.—Returned home.

October 8th.—Mr. C. Wace reports "his nose is a great success, and he is most pleased. He has excellent breathing space."

March 4th, 1906.—Patient writes, "I have very little trouble in the way of catarrh, and the improvement in my voice is quite noticeable."

CASE 10.—Mr. N. P—, aged 19, a medical student, referred to me by Dr. G. A. Hamerton. Always blocked in the nose, and a constant mouth-breather. Diffuse deviation to the left, through which he inspired a very little with much difficulty; no view of inferior or middle turbinal on that side.

November 26th, 1904.—Application of cocaine and adrenalin. Concave flap punctured, but no perforation left, as the convex flap was intact. Two stitches; no plugs.

October 17th, 1905.—Clear view through left nostril to posterior pharyngeal wall. Can run a mile with mouth closed, and formerly could not do it even with mouth open. Sleeps with mouth closed. Volunteered statement that he feels increased capacity for mental as well as physical activity. The septum no longer flaps, and between the fingers it feels thickened.

CASE 11.—Mr. R. B—, aged 26, was sent to me by Dr. A. Bousfield in May, 1904, for nasal obstruction on both sides. I applied the cautery to the right inferior turbinal and removed the anterior end of the left.

In August, 1904, patient had hæmoptysis, and tubercle bacilli were found in sputum. He went to a sanatorium for five months; bacilli and temperature disappeared, and he then carried out an after-cure. As he was still a mouth-breather at night, and was subject to "sniffing catarrhs," he was advised to have his nasal obstruction more completely removed.

May 22nd, 1905.—Cocaine and adrenalin on surface. Duration of operation one hour and twenty minutes, chiefly occupied with nasal process of superior maxilla. Two stitches, no plug. The removed septum was very thick. No perforation. Restoration of free nasal respiration.

CASE 12.—J. M—, a male, aged 17, stated he could breathe freely through nose before receiving a blow on it five years previously. Is an engineer, and much exposed to dust.

Mouth-breather at night. Could not inspire at all through right nostril, owing to a large deviation with a long ascending spur on it. Complains of bad taste in mouth every morning.

June 3rd, 1905.—Cocaine and adrenalin on surface. The depths of the concavity were very acute-angled, and examination of the removed cartilage shows that part of the perichondrium was left on it at this point. No perforation; two stitches; plug twenty-four hours.

October 27th, 1905.—Patient shown to Clinical Society.

March 6th, 1906.—Sleeps quietly. No bad taste in morning. Free nasal respiration.

CASE 13.—Mr. A. E. W—, aged 32, complained of winter cough and expectoration, and mouth-breathing at night. Typical facies of neglected adenoids, high narrow nose, high arched palate, and crowded teeth. A small amount of adenoids was removed.

June 21st, 1905.—Cocaine and adrenalin applied superficially. A small puncture was made in furrow-like hollow of concave side, but no perforation occurred, as the convex flap had been peeled off intact. Large cartilage removed in one piece (Fig. 19 *b*). Deviated and thin ethmoid and vomer clipped away. Naso-maxillary crest chiselled off. Three sutures. Cotton-wool and vaseline plugs. Duration of operation, one hour and ten minutes.

October 27th, 1905.—Patient shown to Clinical Society.

March, 1906.—The septum is intact and plumb in the middle line; it still quivers when he inspires quickly. Free nasal respiration. Sleeps with mouth closed. No winter cough.

CASE 14.—Mr. F. W—, aged 25, referred by Dr. G. A. Hamerton. Complained of bleeding and crusting in right nostril, obstruction in left, inability to lie on right side,

and mouth-breathing at night. Could only inhale a trifling amount of air through left nostril, owing to large deviation and long, low spur. Large concavity on right side of septum, nearly all occupied by an abraded, bleeding ulcer. Above this concavity the septum is convex into the upper part of right nostril, and below there is a marked naso-maxillary process.

June 26th, 1905.—Cocaine and adrenalin applied to surface. A puncture occurred in the deepest part of concave flap. After clearing spur on left side a second limited spur was found far back on left side, imbedded in the inferior turbinal. An attempt to resect this submucously led to an oval puncture about half an inch long. But as these two punctures were not *vis-à-vis*, no perforation was left. The cartilaginous septum was easily removed, but the vomer was so hard that it required chisel and hammer, the ordinary bone forceps making no impression on it. Two stitches; no plugs. Duration of operation one and a half hours.

July 25th, 1905.—No epistaxis or crusting; can sleep on either side. Sleeps and cycles with mouth closed. Free nasal respiration, but it is now seen that more of the deviated vertical plate of the ethmoid above and of the nasal maxillary spine below might have been removed.

October 27th, 1905.—Patient shown to Clinical Society.

Case 15.—Mr. A. E. B—, aged 18, complained of nasal obstruction and his "dead voice," which threatened to interfere with his career as a student interpreter. Adenoids had been removed four years previously, and two years ago an operation had been performed on his nose, in both instances without relief. Trifling respiration through left nostril owing to deviation and ascending spur imbedded in inferior turbinal.

September 21st, 1905.—Cocaine and adrenalin to surface. No perforation. Very thick cartilage, and spur more marked as it went deeper. Two stitches. Vaseline plugs. Some blood-stained oozing for three days.

October 10th, 1905.—Quite free nasal respiration on both sides. Patient returned to Continent three weeks after operation.

Case 16.—Mr. A. C—, an actor, aged 23, complained of nasal obstruction for at least ten years. Mouth-breather at night; throat parched in morning; dead voice. Had attended the Throat Hospital five years previously and something was cut out of right nostril—without relief.

There was almost entire obstruction of right nostril, owing to a large deviation, with the lower edge of the quadrilateral cartilage overhanging the junction with vomer. A fleshy adhesion to outer wall concealed all view of the turbinals. On the left side the middle and inferior turbinals were hypertrophied, and there were some adenoid remains.

September 27th, 1905.—Under chloroform the lower margin of the inferior turbinal and the anterior end of the middle turbinal were removed on the left side, the adenoids were curetted, the adhesion on the right side was divided, and a celluloid plate inserted.

October 11th, 1905.—Operation under cocaine and adrenalin. In raising convex flap found that a portion of septal cartilage must have been completely cut out at time of his operation five years previously. When removed, the cartilage showed this to be the case (Fig. 19 *a*). Consequently, much difficulty in separating the two mucosæ, which were here adherent together. Maxillary nasal spine chiselled away. No perforation. Two stitches. Vaseline plugs on right side only.

October 25th, 1905.—Respiration free, and patient out of treatment, fourteen days after operation.

January 15th, 1906.—External appearance of nose much improved, being straighter in the middle line. Voice is more ringing and is never tired. Sleeps with mouth closed. Free respiration through right nostril, allowing inspection of inferior turbinal, front of middle turbinal, the whole length of the septum, the front of sphenoid, and

the posterior wall of naso-pharynx. The septum is vertical in the middle line, but still quivers on sniffing.

CASE 17.—E. H—, male, aged 17, had been rejected for the Royal Navy on account of mouth-breathing and complete obstruction of left nostril.

Constant mouth-breather. Sinuous deflection of septum, with anterior free border of quadrilateral cartilage projecting into left nostril.

October 12th, 1905.—Operation under cocaine and adrenalin. No perforation.

November 9th, 1905.—When written for to come up for inspection his mother replied, "Since the operation my son has passed into the Navy and is now on H.M.S. *Boscawen.*"

CASE 18.—Mr. W. P—, aged 20, was sent to me by Sir William Broadbent for post-nasal catarrh, obstruction in nose, and noisy, heavy breathing even when awake.

Has had three operations for adenoids, at ages of seven, fourteen, and fifteen. The pharynx was very scarred, with adhesions of posterior faucial pillars to posterior wall of pharynx; the uvula had been removed, and the soft palate pulled to one side by traumatic adhesions. There were still some slight adenoid remains. Both nasal chambers narrowed, and liable to block completely when he had a cold. The anterior free end of quadrilateral cartilage projected into left naris, while the right nostril was almost completely obstructed by deviation and spur.

November 10th, 1905.—Patient insisted on operation under chloroform, which greatly increased difficulty of operation owing to cough and much frothy mucus. Ballenger's swivel knife used for first time. Puncture of concave flap, but closed by integrity of right. Two stitches. Vaseline cotton plugs in each nostril.

November 28th, 1905.—No perforation. Free and noiseless breathing. Fleshy septum still flaps when sniffing.

Case 19.—G. K—, male, aged 25, had been unable to breath through right nostril for five years, consequent on a blow.

Had been operated on at Throat Hospital for septum, with removal of greater portion of both inferior turbinals. Experienced no relief, and was told that nothing more could be done for him.

Mouth-breather at night. Large deviation into right nasal chamber, extending high up, and allowing merest trace of respiration. Prominent maxillary nasal process in left nostril.

November 16th, 1905.—Operation under cocaine and adrenalin. In reflecting convex flap it was found, as in Case 16, that the central part of cartilage must have been cut out in previous operation, leaving the mucosa of one side of septum adherent to that of the other. It was found impossible to separate them, and consequently a large defect was left in the convex flap. No perforation resulted, as the concave flap was intact. No stitches; vaseline plug in each nostril. Duration of operation, one hour.

November 30th, 1905.—Up to this date some crusting took place in right nostril.

February, 1906.—Free nasal respiration; no crusting; no perforation.

Case 20.—Miss E. F—, aged 30, was sent to me by Dr. C. Vise, of Tunbridge Wells, as she always slept with mouth open, and it was apt to fall open during the day. She got tired when reading or talking, and as she had been told that her right lung was not well expanded was anxious to get freer nasal air-way.

The nose externally was twisted, with end directed to the left. Anterior free end of quadrilateral cartilage projected into left naris. Right side almost entirely occluded by deviated and low-lying, sharp spur, entirely preventing any view of the inferior or middle turbinal.

November 20th, 1905.—Operation under cocaine and

adrenalin. The patient was very nervous, and was the first who complained of pain, especially during the use of the chisel and hammer. Convex flap torn in front, so that no stitches could be inserted, but flaps kept in place with vaseline plugs.

January 15th, 1906.—No perforation; respiration free and equal on both sides; nose much straighter in middle line.

CASE 21.—Dr. L. W—, a London physician, was a mouth-breather at night and when exercising.

The anterior end of quadrilateral cartilage lay behind the septum cutaneum above, but then it appeared in the left nostril, and the lower extremity, instead of resting on the maxillary spine, lay alongside it, projecting into floor of left vestibule. Behind this the septum showed a large concavity, with a smaller, deeper one in centre ("inside of saddle" type). On right side, merest trace of respiration owing to large deviation being closely applied to outer wall, and obliterating any view of turbinals. It extended high up towards dorsum of nose. Below, it ended in a bony spur overhanging floor of nasal chamber. With posterior rhinoscopy the end of this spur could be seen extending nearly to the posterior free border of the septum.

November 25th, 1905.—Operation under cocaine and adrenalin. No puncture, although very difficult to work round the deep concavity (*vide* Fig. 19 *c*). Anterior free border of quadrilateral cartilage removed, as well as maxillary crest, part of vertical plate of ethmoid, and of vomer close back to posterior choana (Fig. 14). Two stitches; one vaseline plug in the left and two in the right side. When completed, the right nasal chamber was absolutely free right back to the naso-pharynx, and from the olfactory cleft above to the floor of the nose below. The left side looked a little narrowed by the mucosa which had been peeled out of the deep concavity and was now superabundant on a vertical septum.

November 27th, 1905.—No reaction; the patient resumed his professional duties.

February 10th, 1906.—Septum quite plumb in middle line. Patient delighted with restoration of free nasal respiration. Sleeps with mouth closed. The right side is much the freest, owing to redundancy of mucosa on left side and the compensatory hypertrophy which had taken place in left inferior turbinal (Fig. 12). Part of this was therefore removed. Improved appearance of nose externally (Figs. 17 and 18).

Case 22.—W. S—, male, aged 21.

December 7th, 1905.—Usual operation under cocaine.

The notes and specimen of this case were lost.

Case 23.—Mr. T. McN—, aged 25, was sent to me by Dr. Bousfield for nasal obstruction. Three years previously had an operation on nose (? adenoids and turbinectomy), without much relief.

Mouth-breather at night, with dry throat, and coughing in the morning. Nose slewed over to the right. No respiration through left side, owing to large deviation and spur, entirely obstructing any view of turbinals.

January 18th, 1906.—Operation. Submucous injection of cocaine, which did not act well, and caused distressing palpitation. No puncture. One stitch; vaseline plugs in left side only. Duration of operation one hour.

January 19th, 1906.—Plugs removed and not renewed.

January 30th, 1906.—Free nasal respiration, and patient much pleased with improved straightness of nose.

March 12th, 1906.—Writes, "quite free from morning cough and dryness in throat. First time for four or five years he has not his usual 'relaxed throat' at this season."

Case 24.—Mr. F. M—, aged 18, a midshipman in the Royal Navy, was referred to me by Dr. Bruce Porter, for nasal obstruction. Two years ago was kicked on the nose

at football, and afterwards found that the left nostril was becoming increasingly obstructed. A short time ago an attempt had been made to straighten the septum under chloroform, but without any benefit.

A large deviation of the septum could be seen, without the aid of a speculum, projecting into the left nostril and entirely obstructing any view of the turbinals. Cannot walk or sleep without mouth-breathing.

January 26th, 1906.—Operation. Submucous injection of cocaine did not act well, causing local bleeding and palpitation. After removal of deviated cartilage and ethmoid, a long, bony spur had to be followed far back to where it was imbedded in inferior turbinal. No perforation. One stitch; vaseline plugs.

February 3rd, 1906.—Patient rejoins his ship—*i.e.* eight days after operation. Free nasal respiration; now sleeps with mouth closed.

CASE 25.—Major C—, aged 35, was brought to me by Dr. Alfred Clarke for nasal obstruction, causing "severe colds," and associated with hay-fever in summer. There was a large convexity in the left nostril, ending below in a spur, and concealing from view the inferior turbinal. In the posterior choana on that side some pus was seen. Transillumination showed both maxillary antra to be clear.

February 1st, 1906.—Operation under superficial application of cocaine and adrenalin. No perforation. Two stitches. Vaseline plugs in left and one in right.

The operation was followed by some neuralgia round the left eye, with much discharge and crusting in the left nostril. This was difficult to explain at first, as the wound healed by first intention, and the septum was smooth and plumb in the middle line, allowing of free nasal respiration. The pus was then traced to the left ethmoid and frontal sinus, and doubtless much of the patient's catarrh and "severe colds" had been due to this latent empyema in these cavities, which could only escape backwards Now there is a free discharge forwards, no pus runs into.

the post-nasal space, and the sinusitis is improving under treatment.[1]

CASE 26.—Miss A. A—, aged 18, complained of deafness in left ear and obstruction of the nose. Mouth-breather; snores at night. The right nostril was completely obstructed by deviation and spur. Moderate amount of adenoids.

November 24th, 1905.—Adenoids removed.

March 5th, 1906.—Operation under cocaine. No perforation. Two stitches. Plugs on each side for twenty-four hours.

March 16th, 1906.—Free nasal respiration.

CASE 27.—H. H—, male, aged 22, was thrown off bicycle four years ago, and was picked up unconscious, with bleeding from nose and ears. Since then his nose has become more and more blocked, and now he always sleeps with mouth open. Sense of smell not so good. Nose broadened and dented. Septum sigmoid, with a high, sharp projection of cartilage in left nostril, deviation to right, with prominent maxillary spine and large bony spur. Complains of some difficulty in speech; "when he cannot get breath, he cannot get certain words out, especially when two 'g's' come together."

March 8th, 1906.—Operation. Application of cocaine and adrenalin acted well; no pain. Puncture over sharp angle in left and spur in right. Bony spur very thick. One stitch. Carefully plugged each side to avoid perforation. Duration, one hour.

March 16th, 1906.—No perforation. Free nasal respiration.

April 3rd, 1906.—No difficulty with speech, which has lost its nasal tone. Sleeps with mouth closed.

CASE 28.—Mr. A. C—, aged 29. Blow on nose at age of ten. Mouth-breather day and night. Very little respiration through right, owing to a large, high, and irregular

[1] June 19th, 1906.—Patient quite free of nasal suppuration.

deviation obstructing all view of turbinals. Below, it ends in a bony spur. The free end of the quadrilateral cartilage projects into the left nostril. The nose is twisted to the left, and the bulge of the deviation pushes out the right side of the nose externally. Patient is anxious for relief, as he has been getting deaf for seven months.

March 15th, 1906.—Operation under cocaine. The projecting quadrilateral cartilage had to be operated on from the left side, and a second incision was made on the right (convex) side so as to deal with the deviation. This flap was punctured. The bony spur was very thick. One stitch. Plugs both sides; part removed in twenty-four hours and the rest at the end of forty-eight hours. Duration, fifty-five minutes.

March 27th, 1906.—No perforation. Septum perpendicular in middle line. Free air-way. Nose much straighter. No longer a mouth-breather. Hears better.

Case 29.—Mr. J. H—, aged 23, complained of headaches and obstruction in the nose. After two years' service in the Army, he had been discharged from it two years ago because of his headaches. Says he has to use great force to clear his nose, and that this makes his headaches worse.

No cause other than the nasal obstruction could be found to explain his frontal headaches.

Free end of the quadrilateral cartilage projected into left vestibule. Septum sigmoid, so that both nasal chambers were obstructed.

March 15th, 1906.—Operation under local application of cocaine. Septum removed from free end of quadrilateral cartilage. One puncture in right flap; none in left, large maxillary nasal spine chiselled. One stitch. Plugs. Duration, one hour. (The operation was carried out by my Clinical Assistant, Dr. R. Lee.)

March 23rd.—No perforation. Clear air-way.[1]

[1] June 22nd, 1906—Free air-way. Since the operation has had no headaches.

CASE 30.—Mr. W. H—, aged 22, mouth-breather at night, and difficulty of breathing through right side of nose for five or six years. Free end of quadrilateral cartilage in left vestibule; large deviation of septum into right side, occluding all view of turbinals, and preventing least trace of inspiration.

March 19th, 1906.—Operation under local application of cocaine. Incision over free end of cartilage in left vestibule. Second incision in front of convexity in right side. Nasal spine chiselled. One stitch through left wound. Plugs. Duration, one hour.

March 30th, 1906.—Septum quite plumb in the middle line, and free respiration through each nostril. Sleeps with mouth closed.

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DISCUSSION.

Dr. SCANES SPICER.—The idea of submucous resection of the septum for the relief of these troublesome cases dated back to Chassaignac in 1851 and was quoted by Morell Mackenzie in his second volume of "Diseases of Nose and Throat" in 1880. The operation was revived by Macdonald about 1890, and a paper read by him at the Glasgow meeting of the British Medical Association. Since that time the speaker had frequently adopted it, using the usual instruments of nasal surgery, with small, curved, blunt-pointed scissors, knives, and separators. The class of case was that in which the quadrangular cartilage was dislocated or bent, with or without thickening, into the vestibule of the nose, and causing an ugly deforming projection, with more or less obstruction of the breathway—more especially in young unmarried women to whom the disfigurement was important. The procedure was always awkward and tedious, partly owing to the difficulty of detaching the muco-perichondrium from the cartilage without special instruments, partly from the bleeding, which sufficed to interfere with a perfect view of the site, partly from the cramped space available, and partly from illumination difficulties. He used general anæsthesia, had a skilled anæsthetist and a good handy assistant, and had without exception got satisfactory results in such cases as above indicated. The great advance in the newer operation was that with the advantages of the very small specially shaped knives, raspatories, chisels, and other instruments of Freer of Chicago and Killian of Freiburg, and with the help of adrenalin, there was much more space available, better illumination, and all the manipulations were facilitated. The armamentarium and technique of Killian and Freer were quite different from each other, and had been evolved independently. He much preferred Freer's as being smaller, more delicate, and therefore more easily applied. In both a commencement was made anteriorly by removing the obstructing and deforming cartilage in the vestibule or limen, where the passage was narrowest; if that did not suffice, they were able by a bloodless procedure to work away backward and remove all cartilage and bone that might be either obstructing the passage or causing abnormal intra-nasal contacts or pressures. Further, this was done without leaving any extensive raw surfaces to bridge across to outer wall of nose, or to show prolonged suppuration and granulation ending in scar-tissue, perhaps to worry the patient by dryness-tickling or scabbing. Hence there was a saving of a large amount of tedious after-treatment inseparable from sawing, spokeshave, incision, and straightening operations; recovery was quicker, removal of obstruction more perfect. In fact, when carried out perfectly and in its pure form it was, for septal cases,

the best operation in nasal surgery. Nevertheless it was of limited applicability in hospital practice, on account of the extreme tediousness of the operation. Often when the bony septum had to be attacked it demanded an hour's hard work, and he had heard that some rhinologists took over two hours, a great contrast to the time necessitated for sawing out a spur and following up with incision, straightening, and splinting, a matter of great importance in a lesion so commonly presenting itself. This disadvantage must be borne in mind in practice. A further point was the question of general *versus* local anæsthesia. The speaker long ago came to the conclusion that the subjects of chronic nasal disorders were unusually unfit to bear pain well, and that it was better policy to tackle their trouble thoroughly under general anæsthesia given by an expert, and that so a much higher average of good results was obtained. That view applied to this operation. He was well aware that the tendency of the day was to use the unproved methods of local anæsthetisation, and he was always ready to adopt this if he thought the patient could stand it. It was not a question really of pain after a good cocaine-adrenalin or eucaine-adrenalin anæsthetisation, but of panic which so often in his experience arrested the progress of the operation and led to its postponement or to a hurried improvisation of general anæsthesia or to the reversion to older and cruder, but steadier methods of finishing off the case. Under the influence of Freer's, Killian's, and Smurthwaite's recent results, the speaker had again within the last year commenced the operation under the aforesaid local anæsthetisation several times, but the patient broke down and the procedure had to be terminated otherwise as indicated. Why should the patient be subjected to this mental distress and success jeopardised just to avoid general anæsthesia? He was open to conviction but was not yet convinced.

Dr. DUNDAS GRANT considered himself indebted to Dr. StClair Thomson for having brought before the London Laryngological Society some excellent cases of this operation, but he felt that they were both entirely indebted to Professor Killian, of Freiburg, for having perfected the operation, and, in point of fact, what Dr. StClair Thomson had described was precisely Killian's operation. Dr. Grant had practised it with considerable zeal for nearly two years, and like other operators, had found that his later results were great improvements upon the earlier ones, but that some of the earlier cases, with the artistic result of which he himself had been disappointed, had, however, given quite a disproportional amount of satisfaction to the patients. He entirely agreed with Zarniko, who had stated with regard to this operation that "every rhinologist *must* master it"; in this success demanded not only industry but "an almost ignominious love of details." Each operator

elaborated his own modifications, and Dr. Grant thought a judicious electicism might very reasonably be exercised; for instance, in regard to the incision he habitually made use of Killian's, as described by Dr. StClair Thomson, but in case of a vertical deflection he considered it preferable to make Freer's L-shaped cut, the long limb running vertically down the ridge of the projection, and the horizontal one from the base of this forwards, so that a triangular flap of muco-perichondrium was turned forwards. This incision made it possible to detach the muco-perichondrium from the septum behind the vertical ridge with much less risk of perforating it. The nervous part of the operation was the cutting through the cartilage, but Dr. Grant used a knife which he strongly recommended to beginners; it was practically a blunt-tipped tenotome, of which the cutting blade was only a quarter of an inch in length, and the sharp edge was confined to the corner, which was gently rounded off; by holding the knife obliquely the edge cut through the cartilage, and then by raising the handle the blunt tip was used as a probe and elevator; by alternately cutting and probing, the cautious operator could very easily tell when he had got through the cartilage. For the primary incision he preferred, however, a sharp-pointed knife, by means of which he could feel the creaking as soon as the cartilage was reached. Dr. StClair Thomson had described the typical and fairly simple cases, but the most difficult were those in which there was a considerable projection at the base of the septum. In such cases the detachment of the muco-periosteum from above downwards was accompanied by great risk of tearing, and it was therefore necessary to detach this from below upwards. To facilitate this proceeding the incision had then to be continued across the floor of the cavity so that the muco-periosteum covering this floor could be lifted up. He exhibited a powerful forceps for cutting downwards, devised by Dr. Robert H. Woods, of Dublin, which he had used that very day with every satisfaction. With regard to anæsthetics, he had performed a large number under local anæsthesia and also a large number under a general anæsthetic. The former was undoubtedly easier for the operator, and the patient, as a rule, complained of nothing except the jarring when the chisel was hammered through the basal crest. He had, therefore, in some cases, done the earlier part of the operation under local anæsthesia, and the chiselling under general anæsthesia by means of chloride of ethyl, and found this extremely satisfactory. He congratulated Dr. StClair Thomson and the Society on the clear and interesting exposition of this valuable operation.

Dr. LEONARD WILLIAMS said that as a beneficiary from the operation under Dr. StClair Thomson's skilful hands, his experiences might contribute something to the elucidation of the points raised. He had not had a general anæsthetic, and

although the operation was long and could by no stretch of the imagination be described as enjoyable, yet it was no worse to bear than a prolonged sitting in a dentist's chair. Every now and again, especially when he got to work upon the bony portions, the operator had made him wish that a general anæsthetic had been used, but, speaking generally, he could say that cocaine and adrenalin fulfilled all the anæsthetic requirements of the operation. The most unpleasant period seemed to him to be the forty-eight hours after the operation, when, with both nostrils plugged, he was hawking mucus in large quantities. This might have been due either to the irritation of the plugs or the reaction from the cocaine and adrenalin. The ultimate results of the operation were most satisfactory. Not only did he enjoy complete freedom of nasal respiration, but he was told by his friends that his personal appearance was much improved, a consideration which weighed with men more than was generally admitted. He was also conscious of the fact that he was less irritable than formerly and much more capable of sustained mental effort. In his case, at any rate, the operation had been a brilliant success.

Dr. StClair Thomson, in reply, said that most of the criticisms had already been met in his paper. Time had prevented him from reading them, but they would be published in full. He agreed with Dr. Spicer that the three quarters of an hour to an hour required for the operation was an objection in hospital practice. But he would rather devote this time to curing the patient radically than have his clinic crowded with their frequent visits for repeated small treatments. It certainly was the best operation in the majority of cases of nasal obstruction, as it spared the turbinals and left the mucous membranes intact. No doubt in time further improvements would develop, chiefly in the way of improving the anæsthesia.

A PAPER

ON

THE VALUE OF A SERUM (DOYEN'S) IN CASES OF MALIGNANT DISEASE

BY

ALEXANDER PAINE, M.D., B.S.LOND.

AND

DAVID J. MORGAN, M.A., M.D.CANTAB.

(COMMUNICATED BY STEPHEN PAGET).

Received December 7th, 1905—Read March 27th, 1906

WE desire to express our thanks to the Council of this Society for the privilege of bringing this paper before you.

At the request of the authorities of the Cancer Hospital we have made an inquiry into the treatment of cancer by Dr. Doyen's serum, and further, investigated the presence of the *Micrococcus neoformans* in malignant and simple growths. The result of this inquiry forms the basis of our paper this evening.

Our intention is to give a clinical account of cases treated in this manner at the Cancer Hospital, illustrated by lantern slides (very kindly prepared for us by Dr. English), followed by the results of a pathological investigation on the *Micrococcus neoformans*.

We think it advisable to preface our paper with a brief *résumé* of Dr. Doyen's work on the subject.

In 1886 Dr. Doyen sent a preliminary note to the Academy of Science at Paris recording his observations in malignant and other growths of small, spherical, mobile bodies, which he regarded as micro-organisms.

In 1901 he made a communication to the Academy of Medicine in Paris, and in the following year to the Surgical Congress at Berlin, corroborating these observations and stating further that he had isolated a micro-organism from simple and malignant growths which, when inoculated into animals, gave rise to neoplastic formations, and this organism he named the *Micrococcus neoformans*. In his opinion all these growths were the result of an infection of the body with this organism, comparable to the infective processes of tuberculosis and actinomycosis.

Early in 1904 he made a second communication to the Academy of Sciences in Paris announcing the preparation of anticancerous vaccines by attenuating and exalting the virulence of this organism. He had also, by means of its toxines, prepared an antitoxic serum from the horse. With these preventive and therapeutic remedies, combined with surgical operation, he had treated 126 cases of malignant and simple growths, and of these he regarded 21 as cured. Since this date he has published in his book on the 'Étiologie et Traitement du Cancer' an account of 116 additional cases, 42 of which he records as cured.

In the early part of the past year Dr. Doyen kindly supplied the hospital with a quantity of vaccine and serum, with which we have treated some nine cases of malignant disease. Most of the cases were seen by Dr. Doyen himself, who regarded them as suitable for the treatment.

The treatment consisted of the injection of 10 c.c. of the serum or vaccine deep into the muscles of the buttock, with strict aseptic precautions, at stated intervals.

We wish to state that as we were desirous of ascertaining the therapeutic value of these remedies all the cases were treated by them alone without surgical interference. We mention this because in many of Dr. Doyen's cases the two methods of treatment were combined.

I. Clinical Investigation.

C. C—, aged 54, road-mender, admitted March 17th, 1905, for recurrent epithelioma in the neck.

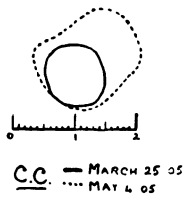
In July, 1903, he had a growth (said to have been "cancer") removed from the centre of the back of the neck.

Fig. 1.

March 25th, 1905. C. C—. May 4th, 1905.

In July, 1904, two recurrent nodules of growth appeared on either side of the back of the neck close to the middle line, and quite near to the spot wherefrom the growth was

Fig. 2.



removed in July, 1903. The patient was advised to come up to the Cancer Hospital.

This he did on September 2nd, 1904. His general health was then good, and he looked healthy. There was a healed scar in the middle line at the back of the neck. Above

and on either side of this was a rounded raised ulcer with hard edges, the base being flat, with unhealthy granulations. There was a slight discharge from both ulcers. The ulcers were apparently fixed to underlying glands which were movable on the deeper tissues. No other enlarged glands could be felt anywhere. The growth was removed on September 20th, 1904, and microscopically shown to be a definite epithelioma. Two subsequent local recurrences of the growth were removed in December of the same year and in January, 1905.

On March 17th, 1905, the patient was again admitted for a recurrent growth at the back of the neck, which was painful and increasing in size. On examination, close to the right side of the occiput was a recurrent nodule of growth, which was firm, hard, and red, adherent to the skin, which was not ulcerated, and deeper tissues. The growth was circular in shape, and had a diameter of one inch. No glands could be felt anywhere. The patient was then given injections with Dr. Doyen's serum. During his stay in the hospital he received fifteen injections, from March 27th to May 8th, his general health remained good, and he increased 4 lb. in weight. After the injections he experienced a feeling of increased tension in the growth, which steadily increased to twice the size, when it was considered advisable to stop the injections.

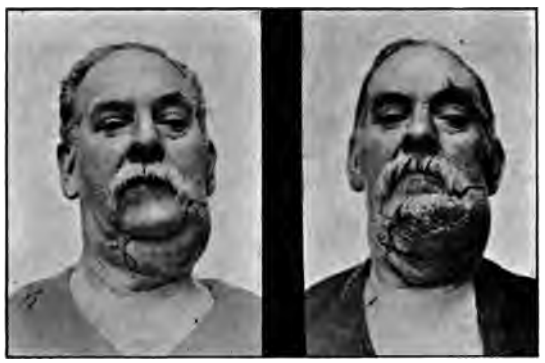
E. T—, aged 70, engineer, was admitted March 23rd, 1905, for recurrent epithelioma in lower jaw and glands (secondary to lower lip).

In July, 1903, the patient was operated on at St. Thomas's Hospital for "epithelioma of the lower lip," when the growth was removed. Since December, 1904, he had had a swelling under the left side of the lower jaw, which had steadily increased in size. He complained of pain in the growth and earache. He had not lost flesh, his appetite was good, and he slept fairly well. There was slight dysphagia. The voice was normal.

The patient was a big, stout man, whose general health

was good. There was a slight scar on the left side of the lower lip, the result of previous operation. Occupying the

FIG. 3.



March 25th, 1905. E. T—. May 17th, 1905.

whole of the left submaxillary and submental regions as far as the angle of the jaw, and extending as low as the

FIG. 4.

March 25th, 1905. E. T—. May 17th, 1905.

thyroid cartilage was a large, very hard mass of growth the size of an orange, firmly fixed to the lower jaw and skin. There was no fluctuation and no tenderness, and

the skin over the tumour was reddened. The right neck and jaw were apparently normal.

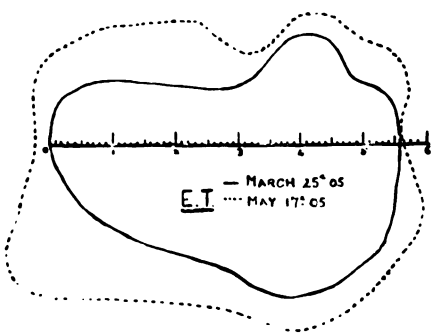
Whilst in hospital he received twelve injections between

FIG. 5.

March 25th, 1905. E. T—. May 17th, 1905.

March 27th and April 22nd, during which time his general health became much impaired and he gradually lost weight. The growth increased in size, softened, and

FIG. 6.



broke down, leaving a cavity which discharged thin, sanious fluid, and as this was followed by fever and general malaise, the injections were discontinued. The

disease ran its usual course, and the patient died on June 2nd.

M. E. D—, aged 63, was admitted in April, 1904, for recurrent carcinoma of left breast.

In 1895 the late Sir William Banks operated on the patient for carcinoma of the left breast. Four years later (1899) this recurred and was allowed to remain for five years without treatment, when she came to the hospital in April, 1904.

On admission there was a scar below the nipple of the left breast. The breast, nipple, and scar were all bound down in a large, hard mass of growth, absolutely fixed to the skin and deeper parts. Just above and external to the nipple was a small ulcer with hard edges, but with no granulations on the base. Some thickening was felt towards the axilla but no definite axillary glands. The veins over the left shoulder were dilated. No enlarged glands could be felt above the clavicle. X-ray treatment was given while in hospital with no apparent result, and she was discharged on June 10th, 1904. She was re-admitted on January 20th, 1905. Her general health was then poor. Examination at this time showed that in the scar of the amputation wound of the left breast was a small, stony, hard mass fixed to the chest wall. The surrounding skin was marked by radiating fissures. A mass of glands could now be felt in the left axilla.

The patient received five injections from March 29th to April 10th. Her general condition remained unimpaired until the last injection, which was followed by a severe constitutional disturbance characterised by depression, high fever, the temperature rising to 103·2° F., loss of appetite, dry brown tongue, and joint pains, an erythematous rash appearing over the lower part of the chest, abdomen, and both knees; heart failure and pulmonary congestion supervened, but under stimulants the cardiac condition improved, and at the end of a week the temperature returned to normal, leaving the patient very feeble.

She had lost eight pounds in weight. No change was observed in the local condition of the breast, and the injections were discontinued.

A. S—, aged 61, road-labourer. Was admitted May 1st, 1905, for epithelioma of left lower lip and cheek.

Five years ago (1900) the skin of the lower lip on the left side became broken and sore (which the patient attributes to the irritation caused by smoking a clay pipe). A wart formed at this spot, which was removed in July, 1902, at the London Hospital. A further operation was performed in October, 1902, for recurrence. In September, 1904, he was again at the London Hospital, when his teeth were removed, but nothing was done to the growth. Since November, 1904, he has attended this hospital as an out-patient.

His condition on admission as an in-patient was as follows: On the left lower lip, occupying practically its whole length, and spreading to the left angle of the mouth, and the skin down to the lower border of the jaw, and invading the margin of the gums to a little beyond the mid-line, was a ragged, raised, ulcerated mass of growth with hard edges. Its size was about 2 inches by 2 inches. No enlarged glands could be felt. His general health was good.

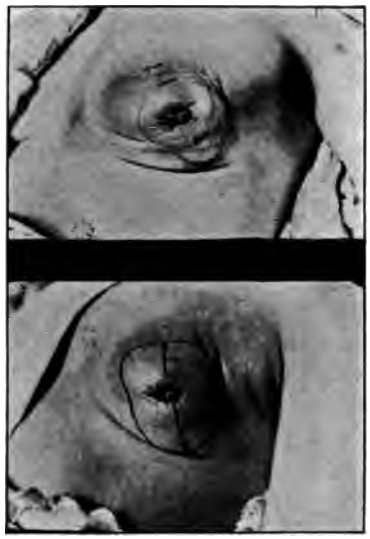
The patient received sixteen injections from May 2nd to June 19th, his general health improved, and he gained five pounds in weight, but as the growth steadily increased in size the injections were discontinued.

H. M—, aged 48. Was admitted March 31st, 1905, for carcinoma of the left breast.

Two years ago the patient had a miscarriage. After this (in August, 1903) she noticed a small hard lump in the left breast, which was not painful. In December, 1903, she went to the Samaritan Hospital, where she was told that she had "cancer" of the breast. Nothing was apparently done then. In February, 1904, she went to the Middlesex Hospital. Operation was refused there owing

to the fact that she suffered from bronchitis and emphysema, and it was thought that she was not in a fit condition

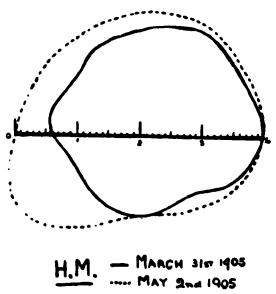
FIG. 7.
H. M—. March 31st, 1905.



May 2nd, 1905.

to withstand the anæsthetic. Since June, 1904, she has had X-ray treatment at the Cancer Hospital.

FIG. 8.



On admission, the left breast contained a large hard mass of growth the size of a Tangerine orange, which was

not painful, and which was adherent to the skin and to the pectoral muscle, though there was free lateral movement. The nipple was retracted and some enlarged glands could be felt in the left axilla, but none in the supraclavicular fossa. The right breast and axilla were normal. There was no swelling of the arm. Examination of chest showed that the patient was the subject of chronic bronchitis and emphysema.

She received eight injections from March 31st to June 8th, during which time she lost two pounds in weight, and suffered very much pain; this was so severe as to keep the patient from obtaining sleep. The pain was situated in the tumour, radiating to the shoulder and down the arms to the elbow and finger joints.

A localised erythematous rash appeared on the buttock after the third injection. At the patient's request the injections were discontinued, and this was followed by a cessation of the pain. The tumour had increased in size.

At a later date the breast was amputated by Mr. Charles Ryall and shown to be a definite scirrhus.

H. S—, aged 65, railway clerk, was admitted on April 12th, 1905, for epithelioma of the left tonsil, with secondary glands in left neck.

About three years ago (in 1902) a lump was first noticed on the left side of the neck. As the tumour grew larger, and he had severe pains at the top of the head of a gripping nature, he went to the Throat Hospital in the Gray's Inn Road in December, 1904, and was there told that nothing could be done. He went next day to St. Mary's Hospital, and was there told that he had an inoperable cancer. He went to Dr. Doyen, at Paris, early in January, 1905, and was in his hospital for just over a month. During this time he had nine injections of serum, and said he felt much better; the pains in the head had disappeared, and he thought the lump was smaller. He returned to London in the early part of February and came up to the Cancer Hospital on April 12th, 1905, as the lump was then getting larger and the pains in the head had returned.

On admission, his general health was good. On the left side of the neck was a large egg-shaped tumour, situated

FIG. 9.

April 15th, 1905. H. S—. June 13th, 1905.

below the lobule of the ear. Its long diameter measured nearly four inches over the surface, and commenced at a

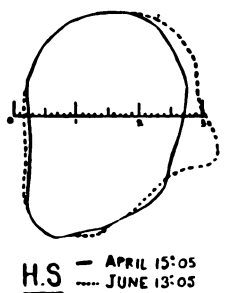
FIG. 10.

April 15th, 1905. H. S—. June 13th, 1905.

point one inch below the tip of the left mastoid process, extending downwards and forwards, following the course of the sternomastoid muscle. Anteriorly, it reached to the

angle of the jaw, and extended backwards for a length of nearly three inches. The tumour itself was firm and hard, firmly incorporated with the left sternomastoid muscle, and fixed to the deeper structures of the neck. Its surface appeared lobulated, consisting of a larger upper mass and a smaller lower one; the skin over it was freely movable and perfectly normal. This growth in the neck was continuous with an epitheliomatous mass on the left tonsil—the latter appearing as a growth with raised, hard, ragged edges, having an ulcerated surface and hard base. This extended downwards, laterally and slightly anteriorly to a point on a level with the middle of the epiglottis. His voice was husky.

FIG. 11.



The patient received seventeen injections from April 14th to June 7th. During this time his general health remained fairly good, though he lost colour. The pain at the back of the neck, which radiated over the top of the head, gradually remitted, and he expressed himself free from pain after the fourth injection. At the same time the lower end of the tumour in the neck appeared softer. After the eighth injection the pain returned with much severity, and he suffered from depression.

Immediately after the last injection, the patient, in his own words, "experienced a feeling of suffocation and great difficulty in getting his breath; there was a feeling of swimming in the head, as if the blood was rushing to the

brain. He then became confused in his mind, and felt as though he were dying."

His face became suffused, his features swollen, and his eyes injected. The expression was one of anxiety. This was accompanied by dyspnœa, followed by cyanosis of the face, breathing being shallow, laboured, and quick. The pulse became very rapid and feeble, and there was marked vaso-motor dilatation of the vessels of the skin all over the body and extremities, with general profuse sweating.

Examination of the chest showed that the breath-sounds were laboured and accompanied by a peculiar inspiratory stridor. This condition was followed by shivering, with coldness of the extremities. Cardiac stimulants were given, and the collapse treated in the usual way.

After an hour the pulse, which had become almost imperceptible, gradually improved, and the dyspnœa and cyanosis passed off, leaving the patient very weak. The skin remained injected and the features swollen for some hours. The patient slept well in the night, and in the morning his temperature was subnormal. His pulse, which had reached 100 after the injection, had also become subnormal. There was absence of dyspnœa, and the general injection of the skin had passed away, leaving the patient weaker. The injections were discontinued, and though externally the growth did not appear to have increased very much in size, an examination of the throat showed that the growth on the tonsil had extended downwards and forwards.

M. M—, aged 55, nurse, was admitted May 22nd, 1905, for carcinoma of the left breast.

Two years ago she first noticed a movable lump near the left axilla. This gradually became bigger, and for the last year the breast had progressively increased in size. The whole breast seemed to increase uniformly, and she had never noticed any tumour in the breast substance. The skin over the breast had become blue for the last three months.

On admission the whole of the left breast was uniformly enlarged, hard and firm, the whole organ being unduly prominent and firmly fixed to the deeper structures. The skin over it was of a bluish colour, and fixed in all parts over the breast; it was infiltrated everywhere over the tumour with growth, and was very much thickened. The nipple was slightly retracted. Enlarged glands were felt in the anterior border of the left side and in the left axilla.

She received four injections from June 5th to June 13th. After the second injection the pain in the breast became very severe, and increased in severity after the third. After this injection a local erythema appeared on the buttock, the skin over which became very brawny. After the fourth injection the pain in the breast became intense, and extended to the shoulder and down the arm. The latter was much swollen and covered on its extensor surface with an acute erythema. After this date no further injections were given in the hospital.

F. C. U—, aged 58, housekeeper, was admitted May 26th, 1905, for an epitheliomatous mass in the neck.

In December, 1904, he first noticed a small lump behind and below the lobule of the right ear. It grew rapidly and was operated on by Mr. Rawling at St. Bartholomew's Hospital at the end of March, 1905. He remained there for three weeks and from his own account it is doubtful if the tumour was removed or not. The growth continued to grow very rapidly.

On admission there was a large oval-shaped tumour in the right side of the neck, extending from the lobule of the ear above to within two and a half inches of the clavicle. In front it reached the anterior margin of the sternomastoid and posteriorly the anterior border of the trapezius. The surface was covered by thick, bluish, very congested skin, and the upper part traversed by a curved linear scar. There were three protuberances, over which the skin was very thin, and fluctuation could be felt. The whole mass

was fixed to the deep structures. No growth was discovered in the mouth, tongue, or pharynx. No other

FIG. 12.

F. C. U—.—May 26th, 1905.

tumours found. There was no dysphagia and speech was not affected. The patient had pricking, throbbing pain

FIG. 13.

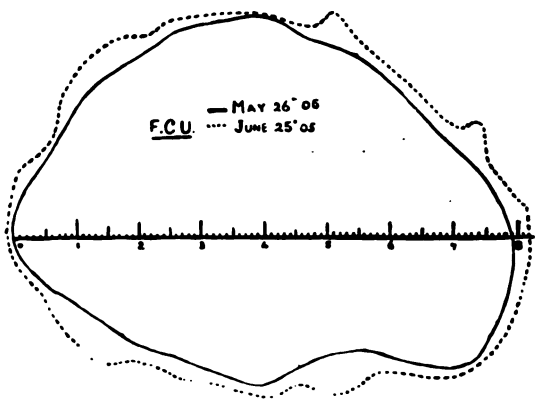
May 26th, 1905. F. C. U—. June 25th, 1905.

in the growth, especially at night. No pain in ear or in temporal region. No deafness in right ear.

The patient received eight injections from May 30th to June 19th.

Beyond a slight febrile reaction and an appearance of a local erythema on the buttock there was no change noted in the patient's condition until immediately after the last injection was given, when he experienced sensations similar to those recorded in the case of H. S—. The onset of the attack commenced with a feeling of suffocation, accompanied by a rush of blood to the head, and followed by temporary loss of consciousness. He also felt pain in the back. There was temporary cessation of

FIG. 14.



breathing, suffusion of the face, which became very red, injection of the conjunctivæ, and swelling of the features. The lips and hands became cyanosed, and the body and extremities cold. When respiration again commenced it was laboured, the breath sounds over the sides of the chest being peculiar; expiration was prolonged and followed by stridulous inspiration, with an occasional loud rhonchus. The pulse at this period was faint, fairly regular, and of medium tension—88 per minute. After a few minutes the pulse rose to 120, and this was followed by a rigor—the lips remaining cyanosed and the features swollen. There was profuse sweating of the face but not of the body. The

feet became somewhat œdematous. The collapse was treated in the usual way. During this period the temperature in the axilla rose to 104° F.; subsequently it fell to below 97°. The patient slept in the night, and next day expressed himself as feeling much better, but the eyes, cheeks, and lips were œdematous and pale, and there was slight œdema of the feet. Respiration and pulse were normal. The urine passed in the night was examined, but nothing abnormal was found.

Since June 19th, 1905, no further injections have been given. The growth subsequently ulcerated through in several places, leaving sinuses with large fungating orifices.

The patient died on August 27th, 1905.

H. M—; aged 52, housewife, was admitted May 27th, 1905, for carcinoma of the cervix uteri.

The history on admission was as follows: The patient is a married woman and has had eight children, the last fifteen years ago. Menstruation ceased ten years ago. She first noticed pain, sharp and smarting in character, in January, 1905. This is constantly present and has become more severe lately. There is no aching in the back. A vaginal discharge was noticed two months ago, becoming blood-stained one month ago. The discharge was not foul. There has been no increased frequency of micturition and the bowels are normal. She has been losing weight recently.

Abdominal examination was negative. No iliac glands were palpable. *Per vaginam* the left side of the cervix uteri was found to be occupied by a hard, friable mass which readily bled on touching, and involved about two thirds of the circumference of the external os. The whole uterus was slightly fixed on the left side.

This patient had six injections, but beyond the appearance of local erythema at the site of inoculation after the third injection, there was little to record in this case, for she refused further treatment, complaining of pain and insomnia, which she attributed to the injections.

Summary of the Cases.

Name.	Disease.	Condition.	No. of injections	Constitutional reaction.	Local change in growth.	General health.	Remarks.
Charles C—	Recurrent epithelioma of neck	Operable	15	*Nil*	Increase	Unimpaired	General health remained very good. Gained 4 lb. in weight whilst under treatment. Increased tension in growth followed the injections.
Edward T—	Epithelioma of lower jaw, secondary to lip	Inoperable	12	*Nil*	Increase	Impaired	No relief of pain. Disease ran its usual course. Death.
Hannah McC—	Scirrhus of left breast	Operable	8	Marked increase of pain	Increase	Impaired	Lost 2 lb. in weight. Local erythematous rash over site of inoculation. Marked increase of pain in breast. General aching pains in joints.
Mary Elizabeth D—	Atrophic scirrhus of left breast	Operable	5	Cardiac failure	*Nil*	Impaired	Severe constitutional disturbance accompanied by a morbilliform rash on front of body. High fever, general aching pains in joints and all over the body, together with cardiac failure, followed the last injection.
Henry S—	Epithelioma of left tonsil	Inoperable	17	Cardiac failure and collapse	Increase	Impaired	Temporary relief of pains in head. Severe constitutional disturbance followed immediately on last injection, characterised by cardiac failure and vaso-motor disturbance.
Alfred S—	Recurrent epithelioma of lower lip	Inoperable	16	*Nil*	Increase	Unimpaired	General health remained very good. Gained 5 lb. in weight during stay in hospital.
Frederick U—	Epithelioma of neck	Inoperable	8	Cardiac failure and collapse	Increase	Impaired	Temporary relief of pains in the growth, and freer lateral movement of head. Severe constitutional disturbance followed immediately on the last injection, characterised by cardiac failure and vaso-motor disturbance.
Mary M—	Carcinoma of left breast	Inoperable	4	Marked increase of pain	Increase	Unimpaired	Local pain and tenderness in buttock with injection, and brawny swelling of skin over site of inoculation. Increased pain in the breast and erythematous rash on arms.
Hannah M—	Epithelioma of cervix uteri	Inoperable	6	*Nil*	*Nil*	Unimpaired	The patient refused to continue the treatment, complaining of pain and insomnia, which she attributed to the injections.

Comment on the Cases.

The cases treated will be considered under the following headings:

(1) Those in which the injections had no influence on the course of the disease.

(2) Those in which the injections were followed by severe pain.

(3) Those in which the injections were followed by severe constitutional disturbance.

(1) *Those in which the injections had no influence on the course of the disease.*—These are four in number. One of the cases, Edward T—, has since died. A second, Charles C—, has undergone three subsequent operations for removal of recurrences of the growth in the neck. A third, Alfred S—, is now attending the hospital as an out-patient. A fourth, Hannah M—, refused to continue the treatment.

(2) *Those in which the injections were followed by severe pain.*—These were cases in which the patients were suffering from carcinoma of the breast, viz. Hannah M— and Mary M—. In the former case the pain, which was extremely severe, was located around the growth, radiating from the breast to the back, shoulders, and down the arms. Sleep had often to be procured by morphia. The pain finally became so severe that the patient refused to continue the injections. In the latter case the pain was very severe in the breast and down the arm.

(3) *Those in which the injections were followed by severe constitutional disturbances.*—These cases were characterised by cardiac failure. In one, Mary D—, this developed gradually, and was accompanied by high fever, depression, pain, and other symptoms of constitutional disturbance. In the others, Henry S— and Frederick U—, the onset was sudden, occurring immediately after the injection, and was accompanied by widespread vaso-motor disturbance and collapse.

In the case of Mary D—, the symptoms were those of a profound toxæmia, viz. continuous high temperature, headache, dry, furred tongue with loss of appetite, general aching pains throughout the body and especially in the joints, a morbilliform rash on the trunk, and local œdema over the joints, anæmia, feeble circulation, and great prostration. When the injections were withheld she made a slow and imperfect recovery, so far as her general health was concerned. This severe reaction was not accompanied by any amelioration of the condition of the breast or improvement in the general health. Two or three weeks after the last injection she developed pain down the spine and subsequently paraplegia. In this connection it is interesting to record that Mr. Charles Ryall had under his care at that time two cases of carcinoma of the breast complicated by paraplegia, and these have not been treated with serum. We mention this, because it might be wrongfully inferred that this paralytic condition was due directly to the injection.

In the other two cases, Henry S— and Frederick U—, the failure of the heart's action came on suddenly and was accompanied by severe dyspnœa, which first suggested pulmonary embolism, but examination of the chest did not confirm this.

The immediate onset and widespread distribution of the symptoms may have been due to some obscure reflex action, or might be explained by assuming that (1) the action was reflex, or (2) that possibly the injection had been made into a vessel—*i. e.* directly into the circulation. If the latter were the case, the symptoms might be explained by the serum in the one case (Henry S—), and the vaccine in the other (Frederick U—), acting either directly on the central nervous symptom, or by producing active congestion of the tumour, causing direct pressure on the great vessels and nerves of the neck, for both these patients were suffering from large tumours in the neck surrounding the large vessels and nerves. In the case of Frederick U—, who has since died, at the autopsy it was

found that these structures were closely incorporated in the growth at the level of the bifurcation of the common carotid.

The symptoms in the two cases were not exactly the same; they resembled one another in the sudden onset of the cardiac failure, but differed in the extent and distribution of the vaso-motor disturbance, being general in the case of Henry S—, but localised to the head and neck in the case of Frederick U—. This may be explained by the fact that a serum was used in the former case and a vaccine in the latter, or by the difference in the anatomical relations of the two growths.

A number of rabbits were injected intravenously at the Brown Institution with both the serum and vaccine, but although large doses were given, no ill-effects were produced; but the possibility of a difference in susceptibility to toxins between man and animals has to be borne in mind. In the light of the very valuable and most recent work of Professor Wright on 'Opsonins' a further explanation of the collapse in these cases offers itself, viz. that the inoculations might have been given to the patients during a negative phase.

Owing to the severe constitutional disturbances which followed the last injections in the three cases above mentioned, coupled with the fact that in none of the cases treated by injections was there any improvement, it was decided to suspend the treatment.

II. Pathological Investigation.

The lines upon which this investigation has been conducted are those which Dr. Doyen has set forth in his book on the 'Êtiologie et Traitement du Cancer.' We have used his methods of technique and supplemented them by others of our own. It may here be stated that the principles of the methods adopted by Dr. Doyen are those in general use in pathological research, and differ from them only in a few minor details of technique. The cases selected for

examination were all characteristic examples of simple and malignant growths, diagnosed clinically as such by the surgeons of the hospital, the diagnosis being confirmed by subsequent microscopic examination. A large number of the cases selected for investigation were mammary growths, both primary and recurrent, together with their secondary deposits in the lymphatic nodes. We chose these tumours for preference, regarding them as being less liable to infection with saprophytic organisms than those connected with mucous membranes, where the moist surface favours the excoriation of epithelium and hence the invasion of bacteria.

We have examined the acute and rapidly growing tumours as well as the more chronic and slower growing varieties, and in every case the examination of the tumour was carried out immediately after its removal from the body. In all we have investigated forty-four cases.

The microscopical examination of a very large number of simple and malignant tumours in films and sections prepared from the growth has shown us that the presence of micro-organisms in these pathological structures is by no means constant. In a large number of growths we have failed to demonstrate the presence of any organisms. In cases in which we have succeeded in detecting them the micro-organisms have been of various kinds, and were members of the coccal and bacillary groups of bacteria. No one particular organism has been found to be constantly present.

In those cases in which we have failed to demonstrate the presence of any micro-organism in films or sections cultures taken from the same growths have generally proved to be sterile.

Our attention has been specially directed to the study of those tumours in which the members of the coccal group were present. We have endeavoured to ascertain:

(1) The nature of the organism when present.

(2) The extent to which it was present.

(3) The relationship of the organism to the special cellular elements of the growth.

(1) Micrococci, when present in the tumour, appeared in the form of solitary and diplococci, and as these are the morphological appearances which micrococci assume in tissues when not in the state of active growth, it was consequently impossible to identify them by this method of examination with any one particular species of micrococcus.

(2) We also found that the organisms were present in very small numbers; and we did not find them in greater numbers in the more rapidly growing tumours than in the slower growing varieties.

(3) Owing to the small number of organisms present in such tumours, and the consequent difficulty of detecting them microscopically, we have reinforced their numbers by the method of incubating the tissues at the body temperature.

We did not find that the micrococci bore any special relation to the cells of the growth. Sometimes they were intra-cellular, but more often extra-cellular.

Cultivations were made from each of the forty-four tumours investigated, and the manner in which this was done was the same as that usually adopted in taking cultures from any solid organ. The surface of the tumour, which had been removed at the operation, was seared with a cautery, and with sterile knife and forceps portions were removed from the growing edge and also from the centre of the growth and immediately immersed in liquid media with the strictest aseptic precautions. The cultures thus made were incubated at the body temperature for a period of one to seven days. These were examined daily and films made from them, stained, and submitted to microscopical examination.

The liquid media we have used includes one specially advocated by Dr. Doyen for the isolation of his organism, namely "bouillon de mamelle de vache." This is a watery extract of the cow's udder in lactation, to which peptone and salt are added, and the whole rendered sterile by heat in the autoclave at 130° C. We also used ordinary peptone-

Tabulated Summary of the Cases.

No.	Name.	Nature of tumour.	Ulcerated or not.	History.	Organisms present.	Presence or absence of the *Micrococcus neoformans.*
1	Charles C—	Recurrent epithelioma of neck	Yes	3 mos.	Polymorphic micrococcus	Present.
2	John W—, P.M.	Epithelioma of neck secondary to tongue	Yes	12 mos.	Solitary micrococci, streptococci, diplococci, short bacilli	Absent.
3	Thos. Webster H—	Epithelioma of tongue	Yes	12 mos.	Streptococci	Absent.
4	Ada R—	Fibro-adenoma of breast	No	3–4 yrs.	*Streptococcus longus*	Absent.
5	Alice C—	Carcinoma of breast and axillary glands	No	6 weeks	None	Absent.
6	Elizabeth H—	Sarcoma of breast and axillary glands	No	4 mos.	Polymorphic micrococcus obtained from the gland	Present.
7	Emily D—	Mastitis	No	None	—	Absent.
8	John T—	Epithelioma of jaw (recurrent) secondary to lip	No	3 mos.	None	Absent.
9	Jane G—	Recurrent carcinoma of axillary glands secondary to breast	No	4 mos.	Streptococci	Absent.
10	Sarah W—	Carcinoma of breast	Yes	2 yrs.	Streptococci	Absent.
11	Agnes R—	Myxoma of parotid	No	—	Polymorphic micrococcus	Present.
12	James K—	Epithelioma of lip	Yes	4 mos.	Streptococci	Absent.
13	A. A —	Carcinoma left breast	No	—	None	Absent.
14	Mary D—	Carcinoma right breast and axillary glands	No	7 weeks	None	Absent.
15	Charles C—	Recurrent epithelioma of neck	No	3 mos.	Polymorphic micrococci, short bacilli	Present.
16	Abraham M—	Epithelioma of lip	No	3 mos.	Micrococci	Absent.
17	Annie T—	Recurrent carcinoma of breast and axillary glands	No	4 mos.	Polymorphic micrococci, streptococci in growth, polymorphic micrococci in gland	Present.
18	Charlotte R—	Recurrent carcinoma of breast	No	4 mos.	Polymorphic micrococcus	Present.

19	Martha V—	Paget's disease of right breast	Yes	4 yrs.	None	Absent.
20	Elizabeth L—	Carcinoma of breast	No	9 mos.	Polymorphic micrococcus	Present.
21	Margaret K—	Recurrent carcinoma of axillary glands secondary to breast	No	2 yrs.	None	Absent.
22	Jessie McK—, P.M.	Lymphadenoma of left neck	No	—	Streptococci	Absent.
23	Elizabeth H—	Carcinoma of breast	No	4 mos.	None	Absent.
24	Bridget O'F—	Carcinoma of breast	Yes	12 mos.	None	Absent.
25	Susannah C—	Carcinoma of breast	No	2 years	None	Absent.
26	Elizabeth W—	Sarcoma of breast	No	1 mo.	Micrococci, small bacilli	Absent.
27	Elizabeth H—	Recurrent carcinoma of supra-clavicular glands secondary to breast	No	4 mos.	Staphylococcus, polymorphic cocci, small bacilli	Present.
28	Charles C—	Recurrent epithelioma neck	No	4 mos.	Polymorphic cocci, small bacilli	Present.
29	Mary Ann W—	Melanotic sarcoma of breast, axillary glands, and abdominal wall	No	1 year, 7 mos., 6 mos. respect-ively	Breast: polymorphic bacilli; glands: polymorphic bacilli, polymorphic micrococci; abdominal wall: large and small micrococci	Present (only in axillary glands).
30	Fanny W—	Granuloma of liver	No	18 mos.	None	Absent.
31	Hannah McC—	Carcinoma of breast and axillary glands	No	19 mos.	Polymorphic bacilli, polymorphic micrococci, staphylococci	Present (in growth only).
32	Sarah C—	Fungating carcinoma of breast; enlarged glands, axilla, etc.	Yes	12 mos.	Streptococci, bacilli	Absent.
33	Elizabeth W—	Sarcoma of breast (recurrent) and axillary glands	No	3 weeks	Streptococci, bacilli in growth	Absent.
34	Ellen W—	Carcinoma of breast	No	2 weeks	Micrococci, small bacilli	Absent.
35	B. B—	Carcinoma of breast and axillary glands	No	—	None	Absent.
36	Jane D—	Carcinoma of breast	No	2 weeks	None	Absent.
37	Walter R—	Lymphadenoma of left neck	No	18 mos.	Streptococci	Absent.

Tabulated Summary of the Cases—continued.

No.	Name.	Nature of tumour.	Ulcerated or not.	History.	Organisms present.	Presence or absence of the *Micrococcus neoformans*.
38	Caroline P—	Recurrent epithelioma of glands in groin, secondary to foot	No	1 mo.	Streptococci	Absent.
39	Alexander L—	Chronic adenitis of inguinal glands	No	8 mos.	None	Absent.
40	Louisa R—	Carcinoma of breast and axillary glands	No	2 years	Streptococci in gland only	Absent.
41	Mary Ann B—	Carcinoma of breast (in lactation) and axillary glands	No	2 mos.	Diplococci in growth resembling the pneumococcus	Absent.
42	Louisa J—	Carcinoma of breast and axillary glands	No	2 years	None	Absent.
43	Elizabeth K—	Carcinoma of breast and axillary glands	No	1 mo.	Polymorphic cocci in growth and gland	Present.
44	Elizabeth B—	Fibro-adenoma of breast	No	10 mos.	Small bacilli	Absent.
45	Elizabeth B—	Recurrent carcinoma of infra-clavicular glands (secondary to breast)	No	11 mos.	None	Absent.
46	Elizabeth C—	Carcinoma of breast and axillary glands	No	5 mos.	Bacilli (in growth), polymorphic cocci (in gland)	Present (in gland only).
47	Charles C—	Recurrent epithelioma of neck	No	4 mos.	None	Absent.
48	Susannah C—	Carcinoma of breast and axillary glands	No	2 mos.	Micrococci (in growth), bacilli (in gland)	Absent.
49	Sarah F—	Lipoma of axilla	No	3 years	None	Absent.

bouillon, and similar media to which glycerine (4 per cent.) and glucose (2 per cent.) have been added in the usual way. Sub-cultures from the liquid media were made on solid media such as agar-agar, gelatine, and potato, in order to study the characters of the growth of the organisms on various media, and also for subsequent use for experimental purposes of inoculation.

In this manner we have examined 44 cases, viz.:

Epitheliomata	7
Carcinoma of breast	25
Sarcomata	3
Lymphadenoma	2
Fibro-adenoma	2
Myxoma	1
Lipoma	1
Inflammatory tumours	3
Total	44

The organism named by Dr. Doyen the *Micrococcus neoformans* was present in 11 of the 44 cases—*i. e. in 25 per cent. of all the cases examined.*

The *Micrococcus neoformans* was present in

One of the 7 cases of epithelioma,

Seven of the 25 cases of carcinoma of the breast,

Two of the 3 cases of sarcoma,

The case of myxoma,

None of the 8 cases of other tumours.

Of these 11 cases in which the *Micrococcus neoformans* was present, it appeared in pure culture in 8 cases, and in the remaining 3 it was present with other organisms.

In cultures which are sterile Dr. Doyen states that the *Micrococcus neoformans* can be demonstrated in the sediment at the bottom of the liquid cultures.

Of the 16 of our cases which gave sterile cultures the sediment at the bottom of the tubes was carefully examined, but in no single instance were we able to identify an organism with the *Micrococcus neoformans.*

Of other organisms which were found to be present in

the tumours we examined, we draw attention to the fact that a streptococcus was found in 13 out of the 44 cases, as compared with 11 in which the *Micrococcus neoformans* was present.

A study of the *Micrococcus neoformans* shows that it is a polymorphic coccus measuring from less than 0·5 to rather more than 1 μ in diameter. It possesses an outer envelope which does not stain easily, but has no definite capsule. It is usually associated in pairs, and when growing in liquid media appears in short chains. Occasionally one of the elements dividing in a direction parallel to the long axis produces a bifurcation of the chain. The organism stains well with the ordinary aniline dyes, and is not decolourised by Gram's method. It grows readily on ordinary media. On agar-agar it forms a raised, white, moist, shiny, and viscid growth, which can be easily detached from the medium. On gelatine the growth is similar, and is accompanied by slow liquefaction of the medium, and as the organism is preferably an aerobe stab cultures in gelatine are characterised by cupping of the superficial portion of the stab. In bouillon the growth appears as a general cloudiness of the medium, which gradually clarifies by sedimentation of the growth to the sides and bottom of the tube. The serum of patients suffering from malignant disease showed no *specific* agglutinative reaction with the organism.

(3) With a view to ascertaining the pathogenic action of the *Micrococcus neoformans* on animals, a series of experiments have been conducted at the Brown Institution.

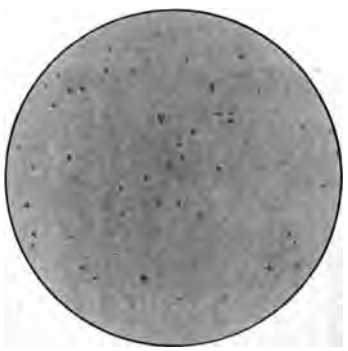
The animals used were rats and mice. The method of inoculation was intra-peritoneal, as used by Dr. Doyen in his researches. In all 200 animals were inoculated, viz. 110 mice and 90 rats.

The organisms used in these cases were obtained from four different tumours, viz.:

Carcinoma of the breast,
Carcinoma of the neck,
Carcinoma of the ovary, and
Melanotic sarcoma.

The organisms in the two latter cases had been isolated by Dr. Doyen, who very kindly supplied us with sub-cultures. Many of these animals died from natural causes, others as

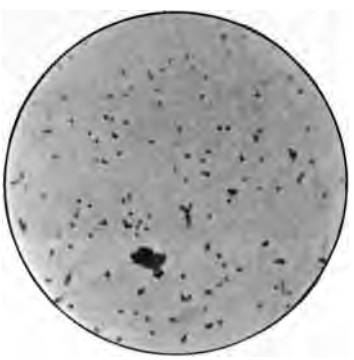
FIG. 15.



Micrococcus neoformans. × 800. Twenty-four hour agar culture.

the result of the inoculation, and of those which survived half the number were killed at the end of three months and the remaining half at the end of six months. In none

FIG. 16.



Micrococcus neoformans. × 800. Four days' agar culture.

of the animals did we find any evidence of simple or malignant tumours as a result of inoculation.

In the animals which died from natural causes we found

large tape-worm cysts in the liver, and in a few cases pneumonia.

In those animals which died as the result of the inoculation, the cause of death was found to be either peritonitis or broncho-pneumonia.

FIG. 17.

Micrococcus neoformans.
Stroke culture (agar-agar). Stab culture (gelatine).

In the animals which survived and were killed at three and six months, nothing abnormal was found beyond worm cyst in the liver in a small percentage.

It will thus be seen that the experimental results we have obtained by the inoculation of the *Micrococcus neo-*

formans into rats and mice have in every case been of the inflammatory character, analogous to those we should expect to result from the inoculation of these animals with organisms of the same class. In no single instance have we met with tumours, either simple or malignant, in the animals we have inoculated.

Most of the microscopical preparations obtained from Dr. Doyen's own animal experiments, and which we had the privilege of examining in his laboratory during our visits to his clinique at Paris, appeared to us to be of an inflammatory nature. Some of them, however, bore, microscopically, a superficial resemblance to carcinomatous and sarcomatous formations; these were localised and very small, and were unaccompanied by secondary deposits in the lymphatic nodes, or generalisation in the organs; nor were they accompanied by wasting or the other clinical attributes of malignant disease. The animals were killed by him at fixed intervals of three, six, and nine months. A few of the microscopical preparations resembled, in their structure, simple growths, such as adenoma, lipoma, and chondroma.

It is known that rats and mice, in common with the rest of the animal kingdom, are liable to tumour formations. That mice are subject to cancer, analogous to cancer in man, and that it may arise spontaneously, is now an established fact.

In no single instance has Dr. Doyen to our knowledge produced cancer in mice or rats.

The fact that malignant growths can arise spontaneously in these animals makes it highly probable that simple growths might have a similar origin. If such is the case, those tumours which Dr. Doyen has met with in the large number of mice and rats he has inoculated may have existed prior to the inoculation. He, himself, however, attributes their formation to the action of the *Micrococcus neoformans* with which the animals were inoculated, in that he found the organism present in the growths at the time he killed the animals, some months after inoculation. It is well known

that micrococci can exist for long periods in the tissues of the body as parasites, and if an animal possessing a tumour were inoculated with such an organism we think it is highly probable that it would settle in the growth, for in man a large variety of bacteria are often found to be present in tumours, and appear in cultures taken from such growths, whilst they are absent in the neighbouring healthy tissues.

The presence of organisms in tumours admits of two explanations. Firstly, in tumours arising from the deeper layers of the epithelium in the skin and mucous membranes, where organisms are constantly present, it is quite conceivable that the bacteria grow *pari passu* with the tumour and accompany it throughout its life-history, being carried in its secondary deposits to the lymphatic glands and to the metastases. A polymorpho-coccus differing from the *Micrococcus neoformans* only in its manner of growth on gelatine and potato is found in the skin, and Dr. Doyen himself has discovered the *Micrococcus neoformans* in the secretion of a breast which was not the seat of a tumour.

Secondly, in those tumours which do not arise in connection with the skin and mucous membranes it is probable the organisms reach them through the lymphatics; in this connection the occurrence of the streptococcus in pure culture in two of our cases of lymphadenoma of the neck is interesting when we consider how prevalent this class of organism is in the mucous membrane of the throat. The streptococcus obtained from these two cases inoculated beneath the skin of rabbits was not followed by any neoplastic changes in the nearest lymphatic glands.

In conclusion, we would say that the organism which Dr. Doyen has named the *Micrococcus neoformans* is, in common with other micrococci, often present in malignant tumours, but, in our opinion, it is not present in sufficient numbers or with reasonable constancy to be regarded as the etiological factor in the evolution of these growths. Moreover, in our hands, the inoculation of animals with this organism was not followed by the formation of neoplasms but by the expression of an inflammatory reaction.

DISCUSSION.

Mr. E. SETON PATTISON said that he had had two cases under his care which had been treated by Doyen's serum, in both of which improvement had taken place, but the result had not been permanent. The first case was that of a man, aged 68, who had been a great smoker and had suffered from leukoplakia of the tongue for several years. In 1904 he developed extensive epithelioma of the tongue, both sides being involved. The floor of the mouth was not implicated, and there were no enlarged glands. The breath was offensive, blood-stained mucus dribbled from the mouth, and the patient was emaciated. Pain was very severe and radiated in all three divisions of the fifth nerve. This patient was treated by Doyen's serum in Paris. After four injections the pain was much less and the general condition improved. After one month's treatment the patient gained flesh, was able to take food well, and the pain had almost gone. About this time small brown sloughs came away from the growth, and in March, 1905, a large slough came away, which caused bleeding from the lingual artery. As this could not be controlled, both arteries had to be tied. The tongue became pinkish-white in colour and the growth smaller. The improved condition was not long maintained, for the patient developed patches of growth on the gums, and died in December. The second case was that of a woman, aged 48, who four years previously had had extirpation of the uterus for malignant disease. A tumour developed in the abdomen, which on exploration was found to be malignant. The patient suffered greatly from constipation and from attacks of pain in the abdomen, and vomiting. Injections of serum were now given, and during two months the patient had twenty-four injections. She gained weight and improved greatly, and her constipation was relieved after, as she said, "something had given way inside." She returned home greatly improved, but died shortly afterwards. In another case of malignant disease of the breast, after injections of serum the growth seemed to be retarded, but, except for relief of pain, the patient was not otherwise improved. In another case of recurrent cancer of the breast pain was relieved by the injections, but the growth was not arrested.

Mr. CHARLES RYALL said that all Dr. Doyen's cases in Paris acknowledged some improvement in regard to pain. This was far greater in Paris, and naturally so where the patients went to receive injections which were supposed to cure the disease, than at the Cancer Hospital where the patients knew they were receiving injections of serum which were being tried experi-

mentally. There seemed to be considerable risk in the method; the symptoms produced by an over-dose of the serum appeared to be very similar to those produced by an over-dose of Coley's fluid. He referred to the case of a malignant tumour of the breast, which had been treated with serum, and in which subsequently the growth was removed; this he considered a most suitable case for investigating the efficacy of the serum, but it failed to produce a favourable result.

Mr. J. HOWELL EVANS said that periods of exacerbation and amelioration almost always occurred in the course of any malignant growth, and if the injections of serum were administered during a period of amelioration the improvement was apt to be attributed to the serum. It was most important to bear this in mind when considering the case. Moreover, this fact should never be lost sight of in the consideration of any new remedy. Pain, again, varied considerably, and the effect of emotion was often very marked. A word of encouragement would frequently improve the physical condition of a patient in a very striking manner.

Mr. PATTISON pointed out that the improvement in his case had taken place before the arteries were tied.

Dr. PAINE, in reply, said there might be a dual infection in cancer, and in such case it would be difficult to say how much influence on extraneous organisms any special treatment might have.

SEQUEL TO A CASE OF SUBCLAVIAN ANEURYSM

REPORTED IN THE 'TRANSACTIONS,' 1897*

BY

H. H. CLUTTON, M.C.

SURGEON AND LECTURER ON SURGERY, ST. THOMAS'S HOSPITAL.

In reporting the final result of this case I may just recall the main features of the disease and its treatment.

In May, 1895, a man of fifty-four years of age was found to have an aneurysm in the third part of his right subclavian artery. In March, 1896, an animal ligature was applied at the junction of the first and second part of the subclavian artery. This operation failed to cure the aneurysm, and in June of the same year the first part of the subclavian was again ligatured with silk, between the vertebral and thyroid axis. At the same time the thyroid axis, internal mammary, and superior intercostal arteries were also ligatured. In no case were the coats of the arteries ruptured. As the pulsation had not entirely ceased at the end of a week the first part of the axillary artery was ligatured in the same way. The pulsation then entirely ceased, and never returned, and in the course of two months there was no swelling to be felt above the clavicle.

* Vol. lxxx, p. 371.

The patient returned to work as a cooper, and remained perfectly well till June, 1903.

He died in August, 1903, seven years after the treatment described above and without any return of the aneurysm. His own doctor was away at the time so that an imperfect *post-mortem examination* was made; this showed, however, that the subclavian aneurysm was cured, but it did not show the collateral circulation or the condition of the aorta.

The cause of death was not ascertained.

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The Indices to the annual volumes are made on the same principle as, and are in continuation of, the General Index to the first fifty-three volumes of the 'Transactions.' They are inserted in the Library copy, where the entire Index to the current date may always be consulted.

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