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Groves, C. S., F.R.S., Kennington Green, S.E.
Groves, H. S., Guy's Hospital.
Growse, W., B.A., Dudley House, Kenilworth.
Gruggen, W., 67, Durban Road, Watford.
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Habershon, S. H., M.D., 88, Harley Street, Cavendish Sq., W.
Haine, C. F., Guy's Hospital.

Hall, F. W., M.D., M.S., 18, College Street, Hyde Park, Sydney, New South Wales.
Hall, Staff-Surgeon R. W. B., R.N., 4, St. Andrew's Road, Southsea.
Halstead, D. V., Guy's Hospital.
Halstead, O., Guy's Hospital.
Hammond, J. A. B., M.B., Carlyon, Hope Road, Shanklin, Isle of Wight.
Hampton, F. A., Guy's Hospital.
Hanafy, M. Z., Guy's Hospital.
Hance, J. B., Guy's Hospital.
Hancock, A. C., Guy's Hospital.
Hanreck, S., Guy's Hospital.
Hardenberg, E. F. H., M.B., Duffield House, Upton Road, Watford.
Hare, Lieut.-Colonel E. C., I.M.S., c/o King, Hamilton & Co., Calcutta.
Harkness, A. H., Guy's Hospital.
Harper, C. H. L., Guy's Hospital.
Harries, T. D., Grosvenor House, Aberystwith.
Harrington, F. J., Guy's Hospital.
Harris, E. B., St. Dunstan's, Muswell Hill, N.
Harris, L. P., Guy's Hospital.
Harris, R., M.B., 7, Queen's Road, Southport.
Harrison, S. S. B., Guy's Hospital.
Harsant, J. G., M.D., The Hive, Exeter Road, Bournemouth.
Harsant, W. H., Tower House, Clifton Road, Clifton, Bristol.
Hart, E. R., Guy's Hospital.
Harvey, J. S. S., M.D., 1, Astwood Road, Cromwell Road, South Kensington, S.W.
Hassard, W. A., Guy's Hospital.
Hearnden, W. R. G., Guy's Hospital.
Heath, T. L., Guy's Hospital.
Heatherley, F., M.B., B.S., Endellion, Rock Ferry, Birkenhead, Cheshire.
Heaton, R., Guy's Hospital.
Heaton, T. B., Guy's Hospital.
Henderson, H. J., M.B., B.S., The Red House, Amersham, Bucks.
Henderson, T. Eric, Guy's Hospital.
Henry, M. G., Guy's Hospital.
Hertz, A. F., M.A., M.D., B.Ch., 1, Weymouth Street, W.
Hetley, Henry, M.D., Beaufort House, Church Road, Norwood, S.E.
Hewetson, Major H., R.A.M.C., Navaho, The Grove, Church End, Finchley.
Hibbert, W. L., The Hospital, Loughborough, Leicester.

Hickman, H. V., M.B., The Hollies, Wanstead, N.E.
Hicks, H. T., 56, Friar Gate, Derby.
Hicks, R. G., 126, High Street, Ramsgate.
Higgens, C., 52, Brook Street, W.
Hilbers, H., 49, Montpelier Road, Brighton.
Hills, A. Phillips, Carlton House, Prince of Wales Road, Battersea Park, S.W.
Hinchliff, C. J., 211, Selhurst Road, South Norwood.
Hind, G. R., Guy's Hospital.
Hind, Wheelton, M.D., Roxeth House, Stoke-on-Trent.
Hirsch, V. R., Guy's Hospital.
Hoby, H. J., Guy's Hospital.
Hogarth, B. W., M.D., B.S., 11, Erving Terrace, Morecambe.
Hogben, H. F. T., Guy's Hospital.
Holden, G. Walter, M.D., The Agnes Memorial Sanatorium, corner Sixth and Hyde Park Avenues, Denver, Colorado, U.S.A.
Hole, Surgeon K. H., R.N., M.B., H.M.S. *Russell,* Mediterranean Station.
Holloway, S. F., Holmwood, Bedford Park, W.
Holman, F. K., M.D., Galeston, Eton Avenue, South Hampstead, N.W.
Holman, H. J., 1, Hardwick Road, Eastbourne.
Holmes, R. A., Guy's Hospital.
Holmes, T. E., M.A., M.D., B.C., Portland Lodge, Knighton, Leicester.
Hood, Donald W. C., C.V.O., M.D., 43, Green Street, Park Lane, W.
Hopkins, C. L., B.A., M.B., B.C., City Asylum, York.
Hopkins, H. L., Guy's Hospital.
Hopson, M. Fred., Guy's Hospital.
Hopson, Montagu F., 30, Thurlow Road, Rosslyn Hill, Hampstead, N.W.
Horsley, H., 81, London Road, Croydon.
Horsley, L., Guy's Hospital.
Housden, C. H., Guy's Hospital.
Howard, J. A., M.D., 40, Harold Road, Upper Norwood, S.E.
Howard, R., M.A., M.D., B.Ch., Devon House, Buckhurst Hill, Essex
Howard, Wilfred, New Buckenham, Norfolk.
Howe, G. H., Guy's Hospital.
Howe, J. D., 94, Stephenson Terrace, Deepdale Road, Preston.
Howell, J., M.B., B.S., 7, Imperial Square, Cheltenham.
Howell, J. B., 86, North Side, Wandsworth Common, S.W.
Howell, T. A. I., 59, Upper Richmond Road, Putney, S.W.
Howse, Sir Henry, M.S., The Tower House, Cudham, Sevenoaks.
Huckett, E. S., Guy's Hospital.

Hudson, A. B., Vine House, Cobham, Surrey.
Hughes, E. C., M.A., M.B., M.C., 26, St. Thomas's Street, S.E.
Hugill, George F., M.D., 197, High Road, Balham, S.W.
Hull Medical Society, c/o R. C. Annandale, Queen Street (Bookseller and Stationer), Hull.
Hunôt, F. C., Guy's Hospital.
Huntley, E., M.B., B.S., Friar Street, Sudbury, Suffolk.
Hutchinson, F. E., 80, Swanston Street, Melbourne, Victoria.
Hyde, W. S., Guy's Hospital.

Ingram, P. C. P., M.B., B.S., Royal Societies Club, 63, St. James's Street, S.W.
Iredell, C. E., M.D., 1, Weymouth Street, Portland Place, W.
Irvine, L. C. D., Guy's Hospital.
Isaacs, B., Guy's Hospital.

Jackson, P. J., 56, Tierney Road, Streatham Hill, S.W.
Jackson, T. L., B.A., M.B., B.C., Holly House, Cheadle, Cheshire.
Jacobson, W. H. A., M.A., M.Ch., Lordine Court, Ewhurst, Hawkhurst, Sussex.
Jalland, W. H., D.L., J.P., St. Leonard's House, York.
Janmahomed, H. I., M.D., B.S., F.R.C.S., The Bower, Pedder Road, Bombay.
Jap-Ah-Chit, Guy's Hospital.
Jarvie, J. M., Guy's Hospital.
Jaynes, V. A., 157, Jamaica Road, S.E.
Jephcott, C., M.A., M.B., B.C., 12, Upper Northgate Street, Chester.
Jepson, A. C., Guy's Hospital.
Jimenez, R., San José, Costa Rica, Central America.
John, D. W., Guy's Hospital.
Johnson, E. E., Guy's Hospital.
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Joly, J. M., Guy's Hospital.
Jones, B., M.D., Avenue Gate, Clifton Drive, Lytham, Lancashire.
Jones, E. Lawrence, Guy's Hospital.
Jones, F. Felix, Llanfyllin, near Oswestry.
Jones, G. B. H., Guy's Hospital.
Jones, G. H. West, Southgate, Eckington, Derbyshire.
Jones, J. Gaymer, Guy's Hospital.
Jones, J. P., Guy's Hospital.
Jones, Robert, 11, Nelson Street, Liverpool.
Jones, R. O. H., Guy's Hospital.

Jones, T. L., Guy's Hospital.
Jones, W. Makeig, M.D., Beaumont, Torquay.
Judson, T. R., 44, Mill Lane, West Derby, Liverpool.

Keates, Captain H. C., M.D., B.S., I.M.S., Petersfield, Hants.
Keer, K. J. T., Guy's Hospital.
Keith, S., Guy's Hospital.
Kelsey, Fleet Surgeon A. E., R.N., Parkgate, Reigate, Surrey.
Kemp, G. L., M.D., Worksop, Notts.
Kemp, J. W., Guy's Hospital.
Kendall, G., Battle, Sussex.
Kendall, N. E., Guy's Hospital.
Kennaway, E. L., D.M., B.Ch., Guy's Hospital.
Kennedy, R. S., Guy's Hospital.
Ker, Hugh Richard, Tintern, 2, Balham Hill, S.W.
Kidd, W. A., M.D., B.S., 12, Montpelier Row, Blackheath, S.E.
Kilroe, W., Guy's Hospital.
King, G. W., Guy's Hospital.
King, R. M., Guy's Hospital.
Knaggs, R. Lawford, M.A., M.D., M.C., 27, Park Square, Leeds.
Knott, F. A., Guy's Hospital.
Kyle, J., Guy's Hospital.
Kynaston, A. E. F., Poplar and Stepney Sick Asylum, Devons Road, Bromley-by-Bow, E.

Laborda, F. E. R., Guy's Hospital.
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Lacey, G. E. Warner, Guy's Hospital.
Lacey, W. S., Guy's Hospital.
Lakeman, W. S., Guy's Hospital.
Lamb, W. H., M.B., 23, Palace Court, Bayswater Hill, W.
Lancaster, H. F., M.D., 154, Westbourne Terrace, W.
Lancet, The, 423, Strand, W.C.
Landon, E. E. B., Elderfield Gardens, Kidderminster.
Lane, W. Arbuthnot, M.S., 21, Cavendish Square, W.
Langdale, H. M., Ulverston House, Uckfield, Sussex.
Langdon, W. M., Guy's Hospital.
Langley, L. S., Guy's Hospital.
Lansdale, W., M.D., Sunnydene, Grove Park, Lee, S.E.
Lansdale, W. M., Guy's Hospital.
Lansdown, R. G. P., M.D., B.S., 39, Oakfield Road, Clifton, Bristol.
Larkin, F. G., Grove Park, Lee, Kent.
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Lauder, J. L., Guy's Hospital.
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Lidderdale, F. J., M.D., B.C., 4, London Street, Folkestone.
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Lindsay, W. J., M.A., M.D., B.C., 84, Herne Hill, S.E.
Lipscomb, E. H., M.B., St. Alban's, Herts.
Lister, T. D., M.D., B.S., 50, Brook Street, W.
Llarena, E. F., Guy's Hospital.
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Long, G. S. B., Guy's Hospital.
Loud, F., Albion House, Lewes.
Lucas, H., Huntingdon.
Lucas, R. Clement, B.S., F.R.C.S., 50, Wimpole Street, W.
Lucas, R. H., Guy's Hospital.
Luce, R. H., B.A., M.B., B.C., 42, Friargate, Derby.
Luna, V. A., Guy's Hospital.

Macalister, G. H. K., B.A., M.D., B.C., Torrisdale, Camb.
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May, W. N., M.D., B.S., The White House, Sonning, Berks.
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Merriman, R. W., M.A., B.Sc., 244, Victoria Park Road, South Hackney, N.E.
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Meyer, Lieut.-Col. C. H. L., M.D., I.M.S., The Ridge, Malabar Hill, Bombay.
Meyrick-Jones, H. M., M.D., B.S., Overbury, Charlton Kings, Cheltenham.

Michael, C. E., M.A., M.B., B.C., Trelawne, Crystal Palace Park Road, S.E.
Millbank-Smith, H. J. M., Worthing Lodge, Worthing.
Miller, A. A., M.D., B.S., 46, Westminster Palace Gardens, S.W.
Miller, G. S., Guy's Hospital.
Miller, R. S., Guy's Hospital.
Millett H., Guy's Hospital.
Milligan, R. A., J.P., M.D., Ardmae, Northampton.
Mills, C., P.O. Box 112, Kroonstadt, O.R.C., South Africa.
Milton, L., Guy's Hospital.
Milton, W. T., M.D., M.S., Southernhay, Westmount Road, Eltham, Kent.
Minett, E. P., M.D., Georgetown, British Guiana.
Minns, A. N., Guy's Hospital.
Moberly, A. V., Guy's Hospital.
Moffatt, H. A., B.A., 118, New Church Street, Cape Town, South Africa.
Mollison, W. M., M.A., M.C., M.B., The College, Guy's Hospital
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Montgomery, L. T., Guy's Hospital.
Moore, A. G. H., Guy's Hospital.
Moore, A. M., 359, High Street, Lewisham, S.E.
Moore, G. K., Guy's Hospital.
Moore, J. York, Guy's Hospital.
Moore, Julius, M.D., Silverton, Enfield.
Moore, L. W., Guy's Hospital.
Moore, W. H., 18, Church Street, Kidderminster.
Morgan, E. C. de M., Guy's Hospital.
Morgan, J., J.P., Mount Hazel, Pontrhyd-y-Groes, R.S.O., Aberystwith.
Morgan, O. G., Guy's Hospital.
Morgan, T., The Colony, Llandovery, Carmarthenshire, S. Wales
Morice, C. G. F., M.D., Greymouth, New Zealand.
Morrell, F. H., Guy's Hospital.
Morris, Arnold, B.A., Clarendon Lodge, Clarendon Avenue, Leamington.
Morris, W. R., Guy's Hospital.
Morrish, D. B., Guy's Hospital.
Moss, E., M.D., B.S., 6, King Street, Wrexham.
Mothersole, R. D., M.D., M.S., 128, St. George's Road, Bolton.
Mugford, S. A., 103, Park Street, Grosvenor Square, W.
Muir-Smith, L., Guy's Hospital.
Mullins, R. C., M.A., M.B., B.Ch., West Hill, Grahamstown, Cape Colony, South Africa.
Munden, C., Ilminster, Somerset.
Munden, M. M., Ilminster, Somerset.

Munro, H. A., M.A., M.B., B.Ch., Lulworth, Rushey Green, Catford.
Muriel, G. B., B.A., M.B., B.C., 109, Scotch Street, Whitehaven
Murphy, Sir Shirley, 9, Bentinck Terrace, Regent's Park, N.W.
Muspratt, C. D., M.D., B.S., Tantallon, Madeira Road, Bournemouth.
Mutch, N., Guy's Hospital.
Mutch, R. S., M.D., 29, Lancaster Gate, Hyde Park, W.

Naish, G., Beechcroft, Anstey Road, Alton, Hants.
Neal, F. J., Guy's Hospital.
Neale, B. G., Two Pools, Iron Acton, Gloucestershire
Neale, C. D., Guy's Hospital.
Neely, G., Guy's Hospital.
Neely, H. B., Guy's Hospital.
Neft, R., 95, Station Road, Llanelly, Carmarthen.
Nelson, M. K., Rockside Hydro, Matlock.
Newland-Pedley, F., 22, Willow Road, Hampstead, N.W.
Newman, F. C., Guy's Hospital.
Newnham, W. H. C., M.B., 3, Lansdown Place, Victoria Square, Clifton, Bristol.
Nicholls, E. C., Guy's Hospital.
Nicholls, W. H., Guy's Hospital.
Nicholson, J. W., Red Hall, Gainsborough.
Nicholson, T. M., M.A., 293, Roundhay Road, Leeds.
Ninnis, Roger P., Guy's Hospital.
Nolan, H., M.D., LL.D., Ministry of Interior, Cairo, Egypt.
Noordhoff, P., Librairie Internationale, Groningen, Holland.
Nootts, G., Guy's Hospital.
Norburn, A. E., M.D., Oldfield Park Lodge, Wells Road, Bath.
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Norton, E. L., The Vicarage, Wingfield, Harleston, Norfolk.

Oates, J. L., Guy's Hospital.
Oddy, A. E., 5, Duchess Street, W.
Odgers, P. N. Blake, B.A., M.B., M.Ch., 16, Castilian Street, Northampton.
Ogilvie, W. H., Guy's Hospital.
Ogle, C. J., 1, Cavendish Place, W.
O'Kane, W. J., Guy's Hospital.
Oliver, C. H., Guy's Hospital.
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Oram, R. R. W., Cremyll, Bolingbroke Grove, Wandsworth Common, S.W.

Ormond, A. W., 7, Devonshire Place, Upper Wimpole Street, W.
Osborn, A. G., M.B., Clifton House, Sheet Street, Windsor.
Ozanne, R. C., Guy's Hospital.

Pakes, A. E. H., B.Sc., Inhanguvo, Box 10, Beira, East Africa
Paliologus, A. L., Royal Colonial Institute, Northumberland Avenue, W.C.
Palmer, A. E., 103, Ashby Road, Loughborough, Leicestershire.
Palmer, A. S. Morton, M.A., M.D., B.C., 96, Marine Parade, Worthing.
Palmer, F. W. Morton, M.A., M.D., B.C., 13, Orchard Gardens, Teignmouth, South Devon.
Palmer, J. Irwin, 6, Queen Anne Street, W.
Palmer, J. S., Guy's Hospital.
Palmer, P. H. Hayes, 112a, Harley Street, W.
Pantin, C. S., M.D., B.S., 1, Albert Terrace, Douglas, Isle of Man.
Paramore, Richard, M.D., 2, Gordon Square, W.C.
Parfitt, J. B., Farleigh House, King's Road, Reading.
Park, W. C. C., 264, Hither Green Lane, S.E.
Parke, C. J., St. Kilda, Breakspears Road, Brockley, S.E.
Parker, W. G., M.B., Shirley, Hazeldene Road, Weston-super-Mare.
Parkes, H. P., Guy's Hospital.
Parmiter, B. R., Guy's Hospital.
Parry-Jones, O. G., Guy's Hospital.
Parry, R., M.B., Ty Newydd, Carnarvon.
Partridge, A. A. H., M.A., M.D., B.Ch., St. Germans, Grove Road, Sutton, Surrey.
Partridge, W. L., Guy's Hospital.
Pasmore. I. W., Guy's Hospital.
Passey, R. D., Guy's Hospital.
Patey, P. E. H., Guy's Hospital.
Paul, Frank T., 38, Rodney Street, Liverpool.
Paul, F. W., Guy's Hospital.
Payne, J. Lewin, 18, Portland Place, W.
Pearce, D. G., Guy's Hospital.
Pearce, F. J., 37, Queen Anne Street, W.
Pearmund, A. S. W., Guy's Hospital.
Pearson, M., Guy's Hospital.
Peatfield, P. J., Guy's Hospital.
Pedley, C. F., Guy's Hospital.
Pembrey, M. S., M.A., M.D., B.Ch., Guy's Hospital.
Pendlebury, J. P., Knowles House, Ormskirk.
Pendred, V., M.D., 2, Lansdown Place, Coventry.
Penfold, F. W. H., Rainham, Kent.

Penny, C. H. G., Guy's Hospital.
Perceval, J. L., Guy's Hospital.
Percival, G. H., M.B., 66, Abingdon Street, Northampton.
Pern, M., Guy's Hospital.
Perry, C. E., M.D., 1, Castle Hill Avenue, Folkestone.
Perry, Sir Cooper, M.A., M.D., Superintendent's House, Guy's Hospital.
Peters, E. A., B.A., M.D., B.C., 52, Wimpole Street, W.
Petley, C. E., Guy's Hospital.
Philipps, A. E., 50, Epple Road, Fulham, S.W.
Phillipps, W. A., M.D., 73, Ashley Gardens, S.W.
Phillips, C. J., Guy's Hospital.
Phillips, F. B. Willmer, M.A., M.D., B.Sc., 7, Harpur Place, Bedford.
Pickering, D. V., Guy's Hospital.
Pickett, L. R., Guy's Hospital.
Pigeon, H. W., M.A., M.C., 6, Albion Street, Hull.
Piggot, A. P., 26, Cloudesdale Road, Balham, S.W.
Pike, Douglas R., B.A., M.B., B.Ch., Stalmine Lodge, Stalmine, near Poulton-le-Fylde, Lancs.
Pilkington, F. W., Kencott House, Lechlade, Glos.
Pillin, H. L., 33, George Street, Hanover Square, W.
Pinching, Charles J. W., 76, New Road, Gravesend.
Pitt, G. Newton, M.A., M.D., 15, Portland Place, W.
Plummer, W. E., Wenchow, via Shanghai, China.
Pochin, C. H. G., Guy's Hospital.
Pollard, C., M.D., 23, Foregate Street, Worcester.
Pollard, G. S., Midsomer Norton, Somerset.
Poole, T. B., M.D., B.S., Laurence House, Valkyrie Road, Westcliff-on-Sea.
Poolman, A. E., B.A., 10, Weymouth Street, Portland Place, W.
Portway, R. L., Guy's Hospital.
Prall, S. L., Beechwood, 151, Maida Vale, W.
Pratt, G. A., Guy's Hospital.
Pratt, W H. A., Guy's Hospital.
Preston, G. L., Guy's Hospital.
Price, H. Parry, Guy's Hospital.
Price, John A. P., M.D., 124, Castle Street, Reading.
Price-Jones, Cecil, M.B., 68, Harley Street, W.
Pritchard, G. B., Guy's Hospital.
Pryn, Deputy Surgeon-General W. W., R.N., Royal Naval Hospital, Haslar.
Pryn, W. R., Guy's Hospital.
Punch, A. L., Guy's Hospital.
Purdom, H. N., Guy's Hospital.
Purkis, K. N., Guy's Hospital.
Puzey, Chauncy, 71, Rodney Street, Liverpool.

Pye-Smith, C. D., M.B., B.S., Wentworth House, New North Road, Huddersfield.
Pye-Smith, P. H., B.A., M.D., 48, Brook Street, W.
Pye-Smith, R. J., 450, Glossop Road, Sheffield.

Quesada, R., Guy's Hospital.

Rahman, Lieutenant M. A., I.M.S., c/o Messrs. Grindlay, Groom & Co., Bombay.
Rake, H. V., "St. Ives," Fordingbridge, Salisbury.
Ramos, Dr. Alvaro, 76, Rua de Hospicio, Rio de Janeiro, Brazil.
Ramskill, Josiah, 29, Meadow Lane, Leeds.
Randall, Philip N., M.B., Tower House, Tweedy Road, Bromley, Kent.
Ransford, L. U., Hamilton Villa, Hamlet Road, Norwood, S.E.
Ransford, T. D., 6, Queen's Square, Bath.
Ransford, W. R., Soolay Pagoda Road, Rangoon, Burma.
Ray, Edward Reynolds, 52, Brook Street, W.
Rayson, H. K., M.D., Knight's Mead, Bayville, Cape Colony.
Reckitt, C. E., Guy's Hospital.
Reeve, E. G., Guy's Hospital.
Reeves, J. K., 66, Upper Tulse Hill, S.W.
Reid, A., M.B., B.S., Kuala Lumpor, Selangor, Federated Malay States.
Reid, E., 200, St. Helen's Road, Swansea.
Reinhold, Captain C. J., I.M.S., c/o Messrs. Grindlay, Groom & Co., 54, Parliament Street, S.W.
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Richardson, J. G. D., 67, Rusthall Avenue, Bedford Park, W.
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Roberts, W. O., 10, Honor Oak Park, S.E.
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Ta'Bois, F. W., 2, Mornington Villas, Woodford Green, Essex.
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Wade, C.
Wade, J., D.Sc., Hunstanton Lodge, Downe, Kent.
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Wainewright, R. S., M.D., 7, Grand Avenue, Hove, Sussex.
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Westman, K., Guy's Hospital.
Wheeler, F. J., 95, Cambridge Road, Southport, Lancs.
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Wilson, W., M.B., C.M., 184, Goldhawk Road, Shepherd's Bush, W.
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Wright, G. A., M.B., 8a, St. John Street, Manchester.
Wright, H. H., Ospringe Road, St. John's College Park, N.W.
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THE OUTLOOK OF SUFFERERS FROM EXOPHTHALMIC GOITRE.

By

W. HALE WHITE, M.D., F.R.C.P.

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THERE is much uncertainty as to whether it is desirable to operate for exophthalmic goitre, and doing so has frequently led to the death of the patient; therefore, it seemed worth while to try to form some opinion as to the outlook for sufferers from this disease. In this paper the attempt has been made to do this by following the after-history of a large number of cases. I am much indebted to my Clinical Assistant, Dr. Jan Mahomed, for kindly writing to all the hospital patients, and to my colleagues for allowing me to refer to cases under their care. The hospital patients are those—169 in number—admitted into Guy's Hospital during the years 1888—1907 (both inclusive). I did not take those earlier than 1888, for very few who were in the hospital before 1888 can now be traced. Of the 169 cases

21 died in the hospital,
54 can be traced,

75 accounted for,

leaving 94; the letters sent to 59 of these were returned "Not known," the addresses of 5 were unintelligible, and 30 did not reply, although each was written to three times. The attempt was made in the spring of 1910 to find out what had become of every private patient suffering from exophthalmic goitre whom I had seen between 1894 and the end of 1909. In nearly every instance I was able to obtain information, and I should like to take this opportunity of thanking the many doctors who have answered my letters.

Reserving patients who have been operated upon for later consideration, my material from which to try to glean some information as to the outlook of sufferers from exophthalmic goitre who have not undergone any operation for this disease is that I have been able now (1910) to trace 49 patients (see Table A, which contains 54 cases, but 5, viz., 41, 45, 50, 52, 53, have been operated upon) who have been in Guy's Hospital during the twenty years 1888—1907 inclusive, and 53 private patients first seen between the years 1894 and 1909 inclusive (Table B of 57 private patients contains two, viz., 11 and 12, who could not be traced; they are included because they are mother and daughter and the past history showed the course of the disease; one, 53, who had one lobe of the thyroid removed, and one, 57, who died while undergoing the same operation).* Among the 49 hospital patients, 8 are now dead (Nos. 3, 5, 8, 10, 12, 14, 17, 33), and among the 53 private patients, 7 are now dead (Nos. 3, 19, 27, 33, 45, 47, 52). I submitted my figures to my friend Mr. H. C. Thiselton, and he has kindly given me an actuarial report, which is as follows:—

Group of hospital cases (Table A).

Owing to the paucity of the data it was impossible to deduce a column of the "rate of mortality" which would be in any way

* It also contains two other cases operated on, but in one, No. 54, all that was done was that the isthmus was divided to relieve dyspnœa, and the other, No. 21, had had one lobe removed seven years before, was as bad as ever when I saw her, and no operation was done for the condition for which I saw her. They are therefore included in the 53 cases.

reliable; and the only means of getting a very general idea of the mortality was to compare the actual deaths with those which would have occurred among the same body of lives if the mortality had followed that of a standard mortality table.

A comparison of the actual deaths was accordingly made with the "expected deaths" according to the "Healthy Females Experience of twenty British Offices amongst Assured Lives" (1863)—H^f.

This comparison showed that the *total* number of deaths was approximately as under:—

8 actual deaths,
5 according to the H^f Experience.

In view of the fact, however, that there were no known deaths at all over age 45, and only one death under age 30, it is quite impossible to draw any conclusions as to the comparative rates of mortality at the older and younger ages.

If we compare the mortality *between the ages* 30 *and* 45, excluding two cases in which the age at death is unknown, we find that the number of deaths was as under:—

5 actual deaths,
3 according to the H^f Experience.

Group of private cases (Table B).

In this second group a similar comparison was made, with the result that the mortality would seem to be very similar to that in the case of the first group.

The actual *total* number of deaths was as under:—

7 actual deaths,
3 according to the H^f Experience.

In this case there was only one death over age 45 and two under 30. Comparing, as before, the mortality *between ages* 30 *and* 45, and excluding one death where the age at death is unknown, the number of deaths was as under:—

3 actual deaths,
2 according to the H^f Experience.

As mentioned above, the data are so few that it would be dangerous to draw any conclusions from the facts here set out, except, perhaps, the general conclusion that the mortality experience seems to be heavier than would be expected according to a well-known standard table.

I am sorry my cases are not sufficiently numerous to give more precise results, but I hope that others will add their collections of cases to the 102 (49 from Table A+53 from Table B) here considered. The total deaths were 15, but the expected deaths according to the "Healthy Females Experience Table" should have been 8. These figures suggest that if it were possible to obtain a great many more cases we should probably be able to prove that the expected mortality of sufferers from exophthalmic goitre not operated upon who have been in a hospital and discharged, and of sufferers from it in private practice who sought a second opinion (for all the private cases were referred to me by their usual medical attendant), would be about twice as great as it should be; but it must be remembered that nearly all the patients were of such an age that the expected deaths among the healthy are few, and therefore twice the expected number is not a great number. But this suggestion must not be transferred without qualification to exophthalmic goitre generally, because all the patients here considered were ill enough either to come into a hospital or to desire a second opinion. The inclusion of all cases of exophthalmic goitre, and therefore of many slight cases, would almost certainly make the expectancy of life better than appears from my figures. But, on the other hand, during the twenty years, 1888—1907, 18 sufferers from the disease died in the hospital (Table C of fatal hospital cases contains 21, but 3 died as a result of operation on the thyroid), therefore, the total number of hospital cases (apart from those operated upon) of which we know the result up to date is 49+18=67, of whom 8+18=26 are dead. This, however, gives too serious a view of the mortality, for during the twenty years under consideration there were 94 cases not operated upon who left the hospital and cannot be traced. If the mortality among

them was the same as among the 49 who could be traced, 15 would now be dead, giving a total mortality of 26+15=41 out of 67+94=161 hospital cases. These figures indicate that the outlook is more serious among the poor than among the well-to-do, for among 53 private patients only 7 died, and I shall later suggest a cause for this difference. I placed those who died in the hospital separately from those who could be traced from it, for all those who died in the hospital, apart from those who died as a result of an operation on the thyroid, were so ill that no operation on the thyroid gland could have been performed upon them, and I wished to see what became of those who left the hospital, so as to provide figures which might in the future be of use in determining whether an operation was desirable for those who were not so ill that it was impossible to operate upon them.

The fatal cases other than those operated upon need not detain us long. We will first consider those patients who died in the hospital (Table C). It is well known that diarrhœa and, to a less extent, vomiting often accompany exophthalmic goitre, and that in many instances these symptoms subside under treatment, but one or both of these were very evident in 11 (1, 2, 3, 8, 10, 11, 12, 15, 16, 18, 19) of the 18 patients not operated on who died in the hospital during the twenty years under consideration, omitting one case in which the vomiting may have been due to cerebral softening (7). These figures indicate that it behoves us at once to put the sufferer from exophthalmic goitre to bed when vomiting or diarrhœa supervene, and to do our best to stop these symptoms. Often there is naked-eye evidence of gastro-enteritis at the post-mortem examination, and often, as was pointed out many years ago, Peyer's patches are prominent. It will be of interest in future cases to try to discover the micro-organism responsible for the gastro-enteritis, for it may then be possible to do good with a vaccine. Six cases (8, 9, 10, 11, 12, 15) became delirious and one (17) became comatose. I have no reliable figures to show how many who became delirious or comatose recover, but my impression is that the supervention of

either is of bad augury. Two cases (12 and 16) had melancholia, and one (14) had mania. In one case (4) mitral disease was present, and in one (10) endocarditis and pericarditis were present. Two (6, 10) had rheumatic fever, and one (9) attributed the onset of the disease to rheumatic fever. These cases illustrate the well-known association between rheumatic fever and exophthalmic goitre. Two (11, 14) had pneumonia, and one (15) broncho-pneumonia. One (13) apparently died of diabetic coma, a point of interest when we remember that glycosuria may be present in those who have exophthalmic goitre, but I know from observation that it may pass away and may not have returned twenty years after it was found. In only one of the 8 hospital patients who died outside the hospital was I able to find the cause of death; that patient died of pneumonia. Of the 7 private patients who died (apart from operation), one (3) succumbed to phthisis, one (27) to pleural effusion, one (52) to heart disease, one (33) to alcoholism, one (47) to diarrhœa, and two (19 and 45) to diabetes. Diarrhœa does not figure nearly so largely as among those who died in the hospital, and my impression is that it is more common among hospital than among private patients suffering from exophthalmic goitre. Probably this is due to the fact that private patients are much more likely than hospital patients to go to bed when they get diarrhœa, therefore, it rarely becomes serious with them. We have already noticed the interest of death from diabetes. Considering the frequency with which cerebral symptoms (delirium, coma, melancholia, mania) occurred among the fatal hospital cases it is strange that they are not mentioned as having been present in any of the fatal private cases.

We will now see what is to be learnt from the cases which were traced and did not die. Let us first take the hospital cases (Table A) containing 54, of which 8 (3, 5, 8, 10, 12, 14, 17, 33) died. As all we know of No. 39 is that she is still alive, she cannot be considered, and Nos. 41, 45, 50, 52, 53 were operated on. Therefore, 8+1+5=14 need not now be considered, leaving 40, which I have grouped into (*a*) those that

have done well (1, 2, 4, 6, 9, 15, 18, 19, 20, 24, 25, 27, 28, 29, 30, 31, 32, 34, 35, 37, 40, 42, 47, 48, 49, 51), twenty-six in number, (*b*) those that are moderately well or simply describe themselves as better (11, 13, 16, 21, 22, 26, 36, 38, 43, 44, 46, 54), twelve in number, and those (*c*) who are not well (7, 23), two in number.

With regard to group (*a*), a glance at the table will show that they really are very well. No. 1 has required no treatment since she left the hospital twenty-one years ago; 4 was a bad case in the hospital twenty years ago, has worked hard for eighteen years, has married, has three children, is now a widow; 6, in the hospital twenty years ago, since then worked as a district nurse, subsequently married, and has four children; 9, in the hospital sixteen years ago, feels quite well, has not had a doctor for twelve years ; 15, when in the hospital eleven years ago had had the disease ten years, after leaving the hospital, since when she had had no treatment, she married, and has six children; 18, in the hospital eight and a half years ago, is now quite well, and has been in service for five years without a single day's illness; 24 is included in this group as she is able to go to work; 25 is working as a cook; 29 does not know there is anything the matter; 32 is now quite well, and has been so since her discharge; 34 is "wonderfully better" ; 35 is perfectly well; 37 has had no return of old complaint and is married; 40, in the hospital eight and a quarter years ago, has been well ever since she left the hospital, went into service for four years, then married, has four children, and never needs a doctor "although she pays into a club" ; 47 was quite cured by an American goitre cure; 48 attributes her improvement to pregnancy. The other cases do not call for any special mention.

Turning to group (*b*), 11 is included in it as she has had several attacks of mental derangement, but she is now considerably better and in a situation; 13 says her health is fairly good, but she was able to take a situation after leaving Guy's, then she married, and has two children; 16, 21 and 23 are now much better; 26 has a little breakdown occasionally, but is much better,

on the whole; 36 is now much better; 38 has improved; 43, 44, 46 and 54 are all evidently, from the words they use, considerably better. These twelve cases have all improved, and no doubt some of them might with justice be put in group (*a*). Even the two cases which I have put in group (*c*), those not well, say that they are better. It seems, therefore, to be a fair conclusion to say that these 40 hospital cases have done well, and that judging by them exophthalmic goitre appears likely to get well even if no operation is performed, a conclusion borne out by clinical experience, for we do not often see elderly women suffering from it, and the mortality from it, which we have already discussed, is certainly not severe enough to account for this.

Now let us consider the private cases which did not die. Table B contains 57 cases, two (11 and 12) of which could not be followed after I saw them, but in both the history could be traced a long way back, so they may be included. From these 57 we must deduct 2 operated upon (53 and 57), and 7 (3, 19, 27, 33, 45, 47, 52) who died, leaving 48;* of these we know very little of No. 46, so we have 47 cases to consider. Grouping them in the same way as we did the hospital cases we have (*a*) those that have done well (4, 6, 7, 8, 9, 10, 12, 14, 15, 17, 18, 20, 21, 22, 23, 24, 25, 26, 29, 30, 31, 34, 35, 36, 39, 40, 41, 42, 44, 48, 49, 50, 51, 55, 56), thirty-five in number, (*b*) those that are moderately well or better (1, 2, 5, 11, 28, 32, 37, 43, 54), nine in number, (*c*) those that have not done well (13, 16, 38), three in number.

With regard to class (*a*), as with the hospital cases, they have done very well. No. 4, a severe case, although very nervous, has done very well, and is still improving; 6 is of great interest, for she was very ill when I saw her, but now she does her household duties and goes for walks; 7 also was very ill, but her pulse is now 80, and she is expecting her confinement daily; 8 is quite well; 9 is working as a schoolmistress; 10, 12 and 14

* In a previous footnote I have stated why Nos. 21 and 54, although operated on, are not deducted.

are quite well; 15 takes average amount of exercise and is not debarred from any social function; 17 was very ill indeed, I have never seen greater exophthalmos, that is now much less, and she can walk three miles; 18 is completely cured; 20 in seven months gained 28 lb.; 21 is of great interest, for seven years before I saw her she had had one lobe of the thyroid removed for the disease, she got better for a time, but then the disease returned, and when I saw her she had most of the symptoms of exophthalmic goitre present in an extreme degree, and the remaining lobe of the gland was enormous, but after prolonged continuous rest she got quite well, and can now walk to business and do a hard day's work; her sister had the disease severely at the time the patient underwent the operation, she was not operated on, I saw her at the same time as her sister was ill and she was well; 22, 23, 24, 25 and 26 call for no comment, they are all in good health and apparently cured; 29 is in very good health and goes to dances; 30 also says she is in very good health and busy from 7 a.m. to 10 p.m.; 31 did very well; 34 was very ill, she had a loud systolic murmur and great œdema of the legs, yet "she got practically well and went to New Zealand"; 35 does not call for comment; 36 can go for long walks; 39, a very severe case, got quite well; 40 got quite well; 41 was a very severe acute case following influenza, the thyroid became much enlarged in fourteen days, and when I saw him the restlessness and sleeplessness were so formidable and his pulse was so weak that it was thought he would die, yet within twelve months he was riding across country; 42 got quite well; 44, also a severe case following influenza, got quite well; 45 occurs in the list of those who died, but she got well of her exophthalmic goitre, and then some years later fatal diabetes appeared; 48 many years ago had exophthalmic goitre and a fibroid of the uterus, when the fibroid shrank so did the thyroid, and she got well (except for slight exophthalmos) of her exophthalmic goitre; I saw her for acute pneumonia, from which she recovered at the age of 57 without any return of the exophthalmic goitre; 49 was of interest as being a very severe

case; 50 was a severe case, and when I first saw her fourteen years ago she also had glycosuria, this disappeared in two years and has not returned since, two years after she was first seen she could walk eight miles, she has for many years been perfectly well; 51, a very severe case, the exophthalmic goitre was attributed to influenza, a loud systolic murmur was audible, he had much œdema of the legs, and he got perfectly well; 55 and 56 got quite well.

Turning to group (*b*), 1 really seems to do well as regards her exophthalmic goitre, her chief trouble is arterio-sclerosis and granular kidneys; 2 would not rest and underwent treatment irregularly, but she is somewhat better; 5 has improved somewhat, but her case is complicated by the fact that she has a mild degree of Raynaud's disease; 11 was slowly improving; 28 is well except that she is highly nervous and easily excited; 32 is better, but did not rest as advised; 37 might, as regards her exophthalmic goitre, be included in (*a*), for that is quite well, but she has become an introspective neurasthenic invalid; 43 is much better and able to work, but not well, she did not rest; 54 is better and in fair health, she was very ill, and the isthmus had to be divided to relieve dyspnœa. It will be noticed that most of this group either had some other disease besides exophthalmic goitre or else they could not rest, and that all of them have improved somewhat. With regard to group (*c*), 13 refused all treatment; 16 got better, but refused to continue treatment and then relapsed; and 38 had no special treatment.

Putting together the 40 hospital and 47 private cases we have considered, we get—

	Done well.	Moderately well or better.	Not better.
40 Hospital cases	26	12	2
47 Private cases	35	9	3
87 Total	61	21	5

Therefore, the private cases have done somewhat better than the hospital cases, but really much better than these figures show, because we have seen that the mortality is higher among the hospital than among the private cases.

In the following table the cases are grouped in three groups: those called either mild or average, those called severe, and those called very severe.

	Mild or average.	Severe.	Very severe.
Cases that have done well:			
26 Hospital...	1, 6, 9, 15, 18, 19, 20, 24, 25, 27, 28, 29, 32, 34, 35, 40, 49, 51	4, 30, 31, 37, 42, 47, 48	2
	18	7	1
35 Private ...	8, 9, 10, 12, 14, 15, 20, 23, 24, 25, 29, 30, 35, 36, 40, 42, 48, 56	4, 7, 18, 22, 26, 31, 44, 50, 51	6, 17, 21, 34, 39, 41, 49, 55
	18	9	8
Cases moderately well or better:			
12 Hospital...	11, 13, 16, 22, 36, 38, 44, 46, 54	21, 26, 43	—
	9	3	0
9 Private ...	1, 5, 11, 28, 32, 37, 38	2	54
	7	1	1
Cases that did not do well:			
2 Hospital...	7, 3,	0	0
3 Private ...	13, 38	16	0
	4	1	0

It is of interest to notice that 8 hospital and 17 private cases grouped as severe or very severe have done well. We have already seen that the mortality is higher among hospital than private cases. Therefore, these figures indicate that at any rate for those severely ill the outlook is better the better the social position.

The tables at the end of this paper state how long each patient said she had been ill. I have not attempted to draw any conclusions from this, for the patient's statement may be unreliable, and the period in the illness at which the patient comes under observation depends upon the severity of the symptoms and other factors.

We will now consider the hospital cases which have been operated upon. Five (41, 45, 50, 52 and 53) are in Table A. 41 does not say what operation was performed, but as it was done in 1905 we may safely assume that one lobe of the thyroid was removed, she says she is better; 45 had the right lobe removed six years ago, now she is fairly well and better for the operation; 50 had the right lobe and isthmus removed, she "received great benefit," but her health is now "very bad at times"; 52 had right lobe removed, and is now perfectly well; 53 had the left lobe removed, she is better, but by no means well. All these five were mild or average cases, and in all three or more years have elapsed since the operation. Three hospital cases, none of them severe cases, died as an immediate result of operation, Table C (5, 20, 21); 5 died, as have many patients after removal of part of the thyroid, from nervous symptoms and pyrexia; 20 died the day after the removal of one lobe, and 21 died on the operation table while the inferior thyroid arteries were being tied. Of the private cases, three were operated on (21, 53, 57); 54 is not included, as only the isthmus was divided. No. 21, a severe case, had the left lobe removed, was better for a time, then the right lobe enlarged enormously and she had again all the symptoms of exophthalmic goitre to an extreme degree; 53, an average case, was certainly better after removal of the right lobe, but sixteen years after the report was "Distinctly better, no exophthalmos, some tachycardia, and palpitation. Nervous symptoms much the same. Still odd mentally." 57, a severe case, died on the operating table. Altogether, my series contains 11 cases operated on—only 2 of them severe—and 4 died as a result of the operation,* one is perfectly well, the others are much better, but not completely cured. We saw that the total mortality of hospital cases not operated on might be put at 41 out of 161, and among 53 pri-

* This is about the same proportion of deaths as given by Dr. Hector Mackenzie for the patients operated on at St. Thomas's Hospital, when he spoke during the debate on the surgical treatment of exophthalmic goitre held at the meeting of the British Medical Association, London, 1910.

vate cases 7 died, giving a total number of deaths of 48 out of the 214, or 1 in 4·5, so that the operation result of 4 deaths out of 11 cases gives a higher mortality, and it must be remembered that 48 deaths among those not operated upon include many (at least 18) who were so ill that no one would have dreamt of operating on them, and that the mortality of the cases operated on is a mortality as a result of the operation, death taking place at or very shortly after operation, so that as far as my series goes it appears to show that operation is undesirable, especially as the cure ascribed to it, when death did not occur, was usually not complete; indeed, one case was a few years after as bad as ever. But in the hands of surgeons doing many operations on the thyroid the mortality has gradually been brought down to 4 per cent. (Kocher, Mayo) and rather over 70 per cent. of the patients operated on are said to be cured, and Kocher states that the mortality among his more recent operations is even less. These, however, are the most encouraging results. Krecke recently collected 188 operation cases from 5 clinics, and found the mortality to be 9 per cent. But to get the best results after operation those patients are selected who have not had the disease long, who have no lesions of other organs and have no mental symptoms. We have seen that if we exclude patients who are so ill that they die while in the hospital (and therefore are quite unsuitable for operation), and follow for some years the patients who are discharged from the hospital and those who are seen in private practice, the actual deaths among sufferers from exophthalmic goitre, ill enough to go into the hospital or seek a second opinion, are 15 as against 8 expected among healthy females, although these patients afflicted with exophthalmic goitre include severe and very severe cases, those with other diseases in addition, and those with mental symptoms. As, on the other hand, the cases selected for operation are chosen mostly from among the mild cases, and a few die as an immediate result of the operation, it hardly seems likely that operations on the thyroid can diminish greatly the deaths that might, if the patients were not operated upon, be

expected among such sufferers from exophthalmic goitre as are likely to be selected as suitable for having operations performed on their thyroid. It is, however, quite possible that operation may hasten the cure; if so, the justification for doing it will be greater among wage-earners than among others. It would be of great interest if a large series of cases that have been operated on could be traced for many years after the operation, so that we might learn more about the rapidity of the improvement, the duration of it, and the number of deaths as contrasted with those that might be expected among a similar number of healthy females. This is particularly important, for if the thyroid, which, after operation consists of one lobe, shrinks, it may be that this leads after years to a mild degree of symptoms due to insufficiency of thyroid secretion. At any rate, the cases here tabulated show that many patients, even those severely ill, recover and remain well for years without any operation; and that those who decline operation can hardly be considered unreasonable, especially in this country, where the mortality from such operations is higher than in some others. Further, we have to bear in mind that we may sometimes be in error in attributing benefit to an operation for exophthalmic goitre, for we shall see directly that some patients recover without any treatment, and so some operated upon might have done well even if no operation had been performed.

A survey of the tables at the end of this paper shows that some patients get well even under most unfavourable circumstances. For example, Case 39, Table B, a poor woman, had the disease very severely, she could not rest, but she got quite well.

After each of the following cases in Table A, the number of days' stay in the hospital is placed: No. 4 (49), No. 9 (14), No. 15 (11), No. 18 (36), No. 19 (14), No. 26 (95), No. 27 (46), No. 30 (58), No. 34 (55), No. 35 (45), No. 49 (170), No. 51 (9). None of these patients improved during their stay in the hospital, often probably because of its shortness, but many stayed a long while without improvement; yet all

of these patients ultimately got quite well or very nearly well some time after they left the hospital and are now well, although the mode of life of hospital patients outside the hospital is the reverse of that which might be expected to aid cure. Thus, No. 4 got well, married, had three children, became a widow, and is now, twenty years after her discharge, working hard. No. 15 married, had six children, and has had no treatment since she left the hospital. No. 18 has been in service five years without a single illness. Only two of these, Nos. 26 and 30 are classified as severe. From these cases we must conclude that some patients recover from exophthalmic goitre without any treatment.

The treatments used have been so various, and it is so difficult to tell the duration of each, that it is impossible to draw any certain conclusions about any of them, but from my own experience of patients that I myself have seen, and reports of others that I have read, my strong impression is that the most important treatment is absolute rest in bed for weeks or months, with freedom from anxiety. Recently a woman came into the hospital suffering from exophthalmic goitre; while in the hospital she had an attack of typhoid fever, her exophthalmic goitre continued to improve and she got quite well: most likely the rest compelled by the typhoid fever contributed to the cure of the exophthalmic goitre. Probably it is because private patients are better able to rest than hospital patients that the outlook for the latter is more serious than for the former. Next to rest comes food; no patients do well if they lose weight, and those who are already thin will not improve until by abundant food they gain weight. If they are very nervous, excitable, or sleepless, it is necessary that they should be quieted and given sleep; for this bromides often suffice, but it may be necessary to use hyoscine. If the pulse is very rapid it is probably wise to give digitalis. I have often given Moebius' serum; it appears sometimes to do good, but the cases vary so that it is difficult to adduce proof of this. The anæmia usually passes away as the patient improves. Many of the women who were cured bore

children; this does not do them any harm, and they stand confinements well. Patients who are once cured do not often relapse, hence readmissions are few (7 per cent.).

I do not claim that there is any thing new in this paper, but I collected the cases because it is only by reviewing the course of a disease apart from operation that the desirability of operating can be decided.

TABLE A.

FIFTY-FOUR HOSPITAL CASES THAT CAN BE TRACED.

All or nearly all these rested during the greater part of their stay in the hospital. The reference numbers of the hospital cases refer to a list I have of all the cases of Exophthalmic Goitre which have been in Guy's Hospital. Only those which can be traced are considered here.

1. Female, aged 41; Ref. No. 6.—Hospital 14 days. Symptoms first noticed 8 years before. Average case: Considerable palpitation. Last heard of after 21 years. Result: Improved in hospital. Now writes to say she "is much better." Has required no treatment since she left the hospital. Treatment: Guaiacum.
2. Female, aged 28; Ref. No. 7.—Hospital 26 days. Symptoms first noticed 3 years before. Bad case: Much palpitation. P. 130. Very excitable. Had chorea. Last heard of after 21 years. Result: Slightly better in hospital. Now seen at hospital where she came to report herself "much better." Treatment: Digitalis.
3. Male, aged 24; Ref. No. 12.—Hospital 18 days. Symptoms first noticed 4 months before. Moderate case. Last heard of after 20 years. Result: Slight improvement during his short stay. Only information obtainable is that he died 1909. Treatment: Galvanism.
4. Female, aged 20; Ref. No. 17.—Hospital 49 days. Symptoms first noticed 1 year before. Much thyroid enlargement. Exophthalmos and tachycardia. Pulse, 140. Last heard of after 20 years. Result: No better for stay in hospital. Seen 1910, says she is quite well, has had no special treatment. Has married, has 3 children, now a widow. Works hard, and has done so for 18 years. Treatment: Bromides and belladonna.
5. Female, aged 21; Ref. No. 19.—Hospital 31 days. Symptoms first noticed 1 year before. Severe case in all respects. Result: Died of pneumonia soon after leaving the hospital. Treatment: Galvanism.
6. Female, aged 30; Ref. No. 24.—Hospital 55 days. Symptoms first noticed 1 year before. Average case except that she was very excitable. Last heard of after 18 years. Result: Slight improvement on discharge. Rested 4 months, and was then able to work

as district nurse. Seen 1910. No palpitation nor enlarged thyroid. Has married. Had 4 children. Eyes still slightly prominent, but otherwise well, and has remained so since 6 months after leaving hospital. Treatment: Galvanism, belladonna, digitalis.

7. Female, aged 24; Ref. No. 29.—Hospital 68 days. Symptoms first noticed 1 year before. Average case. Last heard of after 17 years. Result: Says she is better in some respects, worse in others. Treatment: Bromides and belladonna.

8. Female, aged 27; Ref. No. 33.—Hospital 15 days. Symptoms first noticed 6 years before. Average case. Result: Died in 1904, cause unknown.

9. Female; Ref. No. 35.—Hospital 14 days. Symptoms first noticed 7 years before. Average case. Pulse, 136. Apical systolic murmur. Last heard of after 16¼ years. Result: Left the hospital in the same condition as on admission, but now writes: "Feels quite well, and has not had a doctor for 12 years." Treatment: Electrical, belladonna, bromides.

10. Male, aged 29; Ref. No. 42.—Hospital 13 days. Symptoms first noticed 10 weeks before. Average case. Pulse, 108. Complains of weakness; systolic apical murmur. Result: Slight improvement on discharge. Died soon after leaving hospital, cause unknown. Treatment: Digitalis and belladonna.

11. Female, aged 39; Ref. No. 44.—Hospital 63 days.—Symptoms first noticed 9 months before. Average case. Systolic murmur audible at apex. Last heard of after 15½ years. Result: Improved in hospital. Now writes: "Goitre much smaller, eyes less prominent, has had several attacks of prolonged severe mental derangement, but is now considerably better." Is now in a situation. Treatment: Thyroid, belladonna, and digitalis.

12. Female, aged 25; Ref. No. 63.—Hospital 4 days. Symptoms first noticed 1 year before. Slight case. Result: Only information obtainable is she died in 1905, cause unknown.

13. Female, aged 21; Ref. No. 67.—Hospital 33 days. Symptoms first noticed 1 year before. Mild case. Last heard of after 11½ years. Result: Symptoms including tremors have disappeared. Not improved by stay in hospital. Took a situation a year after leaving hospital; then married; 2 children. Health fairly good. Treatment: Belladonna, digitalis.

14. Female, aged 26; Ref. No. 69.—Hospital 9 days. Symptoms first noticed 1 year before. Average case. Last heard of after 11¾ years. Result: Died after leaving hospital. Cause and date unknown.

15. Female, aged 23; Ref. No. 76.—Hospital 11 days. Symptoms first noticed 10 years before. Average case. Pulse, 120. Tremors. Last heard of after 11 years. Result: No better on discharge from hospital, but improved soon after; is married; has 6 children. Has required no treatment for 11 years. Treatment: Adrenalin, arsenic, digitalis.

16. Female, aged 23; Ref. No. 79.— Hospital 45 days. Symptoms first noticed 6 months before. Average case. Loss of weight a striking feature. Last heard of after 9½ years. Result: Was not so well when she left hospital as when she came in. Is now much better. Treatment: Adrenalin, digitalis, bromide.

17. Female, aged 37; Ref. No. 82.— Hospital 97 days. Symptoms first noticed 1 year before. Severe case. Pulse, 150. Delirium and vomiting. Result: Died in 1901. Cause unknown. Treatment: Cold to neck, electricity, massage.

18. Female, aged 19; Ref. No. 85.—Hospital 36 days. Symptoms first noticed 1¼ years before. Average case: Considerable anæmia. Last heard of after 8½ years. Result: Slight improvement on discharge. She is now quite well. Has been in service 5 years without a single day's illness. Treatment: Digitalis, belladonna.

19. Female, aged 54; Ref. No. 87.—Hospital 14 days. Symptoms first noticed 6 years before. Average case: Very nervous, skin pigmented. Last heard of after 7¼ years. Result: No improvement from stay in hospital, but is now very much better. Treatment: Thymus, belladonna, digitalis.

20. Female, aged 36; Ref. No. 96.—Hospital 45 days. Symptoms first noticed 6 weeks before. Average case. Pulse, 120. Tremors: apical systolic murmur. Last heard of after 8¼ years. Result: Better on discharge. Says she is now quite well. Treatment: Belladonna, potassium iodide.

21. Female, aged 28; Ref. No. 99.—Hospital 130 days. Symptoms first noticed 6 years before. Severe case: Much palpitation; wasting; mania. Last heard of after 7 years. Result: Better on discharge. Is now much better. Treatment: Belladonna, bromides.

22. Female, aged 39; Ref. No. 100.—Hospital 24 days. Symptoms first noticed 6 months before. Mild case. Last heard of after 7 years. Result: Better on discharge. Is now better. Treatment: Digitalis, opium.

23. Female, aged 34; Ref. No. 101.—Hospital 50 days. Mild case, but had glycosuria and polyuria. Last heard of after 7½ years. Result: No improvement on discharge. Now throat not swollen: better in some respects. Palpitation better. Suffers from nerves. Complains much of dryness of mouth. Treatment: Opium, belladonna.

24. Female, aged 30; Ref. No. 104.— Hospital 5 days. Symptoms first noticed 8 years before. Mild case. Last heard of after 6 years. Result: Now writes: "About the same." But is able to go to work.

25. Male, aged 19; Ref. No. 108.—Hospital 3 days. Symptoms first noticed 6 months before. Average case. Last heard of after 5½ years. Result: Much better soon after leaving hospital, and has kept so. Has never had to give up work; is a cook. Treatment: Bromides, digitalis.

26. Female, aged 34; Ref. No. 109.—Hospital 95 days. Symptoms first noticed 7 years before. Severe case. Pulse, 140. Anæmia, wasting, pigmentation. Last heard of after 6¼ years. Result: No improvement in hospital. Now "has a little breakdown occasionally, but is much better on the whole." Treatment: Belladonna.

27. Male, aged 42; Ref. No. 112.—Hospital 46 days. Symptoms first noticed 2 months before. Mild case: Complained of weakness. Last heard of after 5¼ years. Result: No improvement in hospital. Now seen at hospital, is much better, hardly any signs of the disease left. Treatment: Adrenalin, bromides.

28. Female, aged 21; Ref. No. 113.—Hospital 80 days. Symptoms first noticed 6 years before. Average case: Some diarrhœa and vomiting. Last heard of after 5¼ years. Result: Slightly better on discharge. Now "very much better." Treatment: Adrenalin, digitalis, belladonna, opium.

29. Female, aged 28; Ref. No. 115.—Hospital 18 days. Symptoms first noticed 6 weeks before. Mild case. Last heard of after 5 years. Result: Better when discharged. Now "does not know there is anything the matter."

30. Female, aged 20; Ref. No. 116.—Hospital 58 days. Symptoms first noticed 3 months before. Severe case. Pulse, 140. Wasting, sweating. Last heard of after 5 years. Result: No improvement on discharge. Now "very much better." In a situation as lady's-maid. Treatment: Digitalis.

31. Female, aged 40; Ref. No. 117.—Hospital 18 days. Symptoms first noticed 6 weeks before. Severe case: Weakness, diarrhœa, systolic murmur, pigmentation. Last heard of after 3 years. Result: Improved in hospital. When last heard of in 1909 was "alive and well."

32. Female, aged 22; Ref. No. 119.—Hospital 29 days. Symptoms first noticed 3 months before. Mild case. Last heard of after 4 years. Result: Improved when discharged. Now "quite well," and has been so since discharged. Treatment: Bromides, digitalis, belladonna.

33. Female, aged 25; Ref. No. 120.—Hospital 47 days. Symptoms first noticed 1 year before. Average case. Result: Improved in hospital. Died since; cause and date unknown. Treatment: Aspirin.

34. Female, aged 42; Ref. No. 121.—Hospital 55 days. Symptoms first noticed 3 years before. Average case. Last heard of after 4¼ years. Result: No improvement on discharge, but now "wonderfully better." Treatment: Potassium iodide.

35. Female, aged 31; Ref. No. 122.—Hospital 45 days. Symptoms first noticed 5 weeks before. Slight case. Last heard of after 4¼ years. Result: No improvement on discharge, but now "perfectly well, never needs a doctor." Treatment: Arsenic.

36. Male, aged 18; Ref. No. 124.—Hospital 49 days. Symptoms first noticed 10 years before. Average case: Has had rheumatic fever and acute tonsillitis. Last heard of after 4 years. Result: Slight improvement on discharge. Now "much better." Treatment: Bromides, digitalis.

37. Female, aged 33; Ref. No. 125.—Hospital 41 days. Symptoms first noticed 6 months before. Severe case. Pulse, 120. Apical systolic murmur, insomnia. Last heard of after 2¾ years. Result: Improved on discharge. Since leaving hospital has been in good health. No return of old complaint. Is married. Treatment: Belladonna, opium.

38. Female, aged 13; Ref. No. 48.—Hospital 29 days. Symptoms first noticed 2 months before. Slight case, but had pneumonia and acute rheumatism. Admitted June 27th, 1905; re-admitted January 10th, 1907, for palpitation. Other symptoms slight. Has had acute rheumatism several times. Last heard of after 15 years. Result: Is now attending Out-patients. Her symptoms of exophthalmic goitre have improved. Treatment: Thymus tablets.

39. Female, aged 19; Ref. No. 127.—Hospital 27 days. Average case. Last heard of after 3 years. Result: Better on discharge. Is now alive, but we cannot learn anything about state of health.

40. Female, aged 27; Ref. No. 132.—Hospital 32 days. Symptoms first noticed 2 years before. Mild case as regards cardinal symptoms, but had much headache, vomiting, and giddiness. Last heard of after 8¼ years. Result: Better on discharge. Now writes: "Am quite well, and have been ever since I left Guy's." Went to service 4 years, and then married, 4 children. Has never needed a doctor "although she pays into a club." Treatment: Belladonna, digitalis.

41. Female, aged 32; Ref. No. 136.—Hospital 16 days. Symptoms first noticed 6 years before. Very mild case in all respects. Last heard of after 7¾ years. Result: Better on discharge from Guy's. In 1905 went to King's College Hospital; was operated on, and says she has been better since. Treatment: Rest and subsequent operation.

42. Female, aged 29; Ref. No. 137.—Hospital 30 days. Symptoms first noticed 2 years before. Severe case. Pulse, 140. Palpitation, pigmented skin, vomiting, and diarrhœa. Last heard of after 7 years. Result: Better on discharge. After that improved slowly. Now appears quite well. Treatment: Belladonna.

43. Female, aged 39; Ref. No. 138.—Hospital 131 days. Symptoms first noticed 2½ years before. Severe case. Pulse, 120. Wasting, pigmentation, vomiting, diarrhœa, sweating, systolic murmur. Last heard of after 6¾ years. Result: Better on discharge. Is now better and stronger, but has to be careful. Treatment: Belladonna, opium.

44. Female, aged 53; Ref. No. 140.—Hospital 19 days. Symptoms first noticed 2 years before. Average case, but some diarrhœa and vomiting. Last heard of after 6 years. Result: Better on discharge, and has continued to improve. Is sure rest does good. Treatment: Belladonna.

45. Female, aged 19; Ref. No. 141.—Hospital 16 days. Symptoms first noticed 4 years before. Average case. Last heard of after 6 years. Result: Writes to say health has been fairly good, and has felt better since operation. Treatment: The right lobe of thyroid was removed.

46. Female, aged 18; Ref. No. 142.—Hospital 61 days. Symptoms first noticed 6 months before. Mild case. Last heard of after 5½ years. Result: Better on discharge. Now writes that she is much better as result of homœopathic treatment. Treatment: Adrenalin, belladonna, digitalis.

47. Female, aged 34; Ref. No. 143.—Hospital 73 days. Symptoms first noticed 1 year before. Severe case: Diarrhœa, vomiting. Last heard of after 5 years. Result: Better on discharge. Quite cured by an American goitre cure. Treatment: Moebius' serum, belladonna.

48. Female, aged 25; Ref. No. 146.—Hospital 43 days. Symptoms first noticed 3 years before. Severe case: Sweating, wasting. Last heard of after 4½ years. Result: Better on discharge. Now all the symptoms have disappeared, except that there is slight enlargement of the thyroid. In 1906 married; has one child born same year. Attributes much of her improvement to her pregnancy. Treatment: Moebius' serum.

49. Female, aged 34; Ref. No. 149.—Hospital 170 days. Symptoms first noticed 1½ years before. Wasting, otherwise mild case. Last heard of after 4 years. Result: Did not improve much in hospital, but is now quite well, and began to improve when she began work four months after leaving hospital. Treatment: Moebius' serum.

50. Female, aged 53; Ref. No. 162.—Hospital 21 days. Symptoms first noticed 10 years before. Average case. Pulse, 138. Last heard of after 8 years. Result: Writes that she "received great benefit from the operation," but "my health is very bad at times." Treatment: Operation—Isthmus and right lobe of thyroid removed.

51. Female; Ref. No. 165.—Hospital 9 days. Symptoms first noticed 2½ years before. Average case. Last heard of after 3¼ years. Result: No improvement during 9 days' rest in hospital. Is now quite recovered, goitre is gone. Is married.

52. Female, aged 23; Ref. No. 168.—Hospital 47 days. Symptoms first noticed 3 months before. Average case, but had diarrhœa. Last heard of after 3 years. Result: Better on discharge. Now says "perfectly well since operation." Treatment: Operation—Right lobe of thyroid removed.

53. Female, aged 23; Ref. No. 169.—Hospital 23 days. Symptoms first noticed 9 months before. Average case. Last heard of after 3 years. Result: Better on discharge. Now says still suffers from attacks of palpitation, but they are much less. Has greater self-control. Feels cold more than before operation. Since operation has been subject to attacks of dizziness and lassitude, for the first twelve months almost daily, but they are getting less. Has been in doctor's hands since leaving hospital for a slight attack of anæmia. Treatment: Operation—Left lobe of thyroid removed.

54. Female, aged 40; Ref. No. 172.—Hospital 44 days. Symptoms first noticed 11 years before. Mild case. Last heard of after 2¾ years. Admitted for hysterectomy. Now writes: "Much better." Treatment: No special treatment for exophthalmic goitre.

TABLE B.

Fifty-seven Private Cases.

The name in brackets is that of the doctor under whose care the patient was.

1. Female, aged 40; Ref. No. 23·144 (Monier-Williams).—Average case: Slight thyroid enlargement and exophthalmos. Good weight. Much tachycardia, palpitation, and dyspnœa on exertion. Thick arteries, big heart, albumen and high tension (170). Last heard of after 5½ months. Result: Better. When in bed seems well. Eats reads, and enjoys life. This is third long rest (many months) in bed. They did much good previously. Before first seemed to be dying. Treatment: Chiefly rest in bed.

2. Female aged 24; Ref. No. 23·170 (H. A. Monro).—Bad case: Much thyroid enlargement, exophthalmos, tachycardia, and palpitation. Slight tremor. Very nervous and excited. Occasional albumen and œdema. Considerable Rigg's disease. Last heard of after 5½ months. Result: A little better. But no inference should be drawn, for would not stay in bed and took serum irregularly. Treatment: Moebius' serum.

3. Female, aged 19; Ref. No. 23·210 (E. L. Adeney).—Bad case: Complicated with severe phthisis. Last heard of after 3 months. Result: Died from phthisis 3 months after being seen.

4. Female, aged 35; Ref. No. 22·177 (A. W. Soper).—Severe case: With all the chief symptoms. Very nervous and irritable. Last heard of after 7 months. Result: Exophthalmos and thyroid much better. Almost lost extreme nervousness and irritability. Normal in mental capacity. Heart sounds better. Tachycardia still present. Occasional dyspnœa, but still improving. Treatment: Bed 7 months. extra food, Moebius' serum.

5. Female, aged 37; Ref. No. 21·258 (C. C. Gibbes).—Moderate case: Slight thyroid, tachycardia. Pulse, 120. Palpitation, slight cardiac dilatation, tremor. Very nervous. Fingers go pale and cold. No exophthalmos. Last heard of after 12 months. Result: Rest did a "lot of good." More peaceful and quiet. "Now I get about more, but do not feel well yet." Gained weight. Treatment: Bed 6 weeks. Moebius' serum did not appear to do good.

6. Female, aged 30; Ref. No. 21·338 (R. B. Duncan).—Very bad case: Big thyroid (neck round it 13½ in.), tachycardia. Pulse, 140. Palpitation, much tremor, anæmia, and weakness. No improvement up till now on any treatment. No exophthalmos. Last heard of after 11 months. Result: Very much better able to attend to household and go out for short walks, but cannot hurry. Pulse, 80—90. Neck, 11⅝ in. Treatment: Bed 6 months.

7. Female, aged 33; Ref. No. 20·20 (A. E. Tonks).—Bad case: Huge thyroid, great exophthalmos, tachycardia, dilated heart, slight tremor. Last heard of after 19 months. Result: Much better. Expecting every day to go to bed to be confined. At end of 2 months pulse 80 and exophthalmos less. Dr. Tonks thinks the rest, and not the serum, is responsible for improvement. Treatment: Bed many months, Moebius' serum.

8. Female, age not stated; Ref. No. 20·331 (A. W. Soper).—Mild case: Considerable thyroid enlargement, moderate exophthalmos, tachycardia, and tremor. Last heard of after 18 months. Result: At end of 2 months quite cured. Thyroid, pulse, eyes, normal. Stil well at end of 18 months. Treatment: Bed for 2 months.

9. Female, aged 44; Ref. No. 20·359 (E. F. Hardenberg).—Average case: Thyroid normal, much exophthalmos and tachycardia. Weak tremor, dilated heart. Last heard of after 18 months. Result: Much better. At end of 6 months after rest able to work as schoolmistress fairly well. Much stronger. Pulse normal. Exophthalmos remains and diplopia has developed. Treatment: Prolonged rest.

10. Female, aged 35; Ref. No. 20·362 (H. A. Burrowes).—Moderate case: Much exophthalmos, thyroid normal, tremors, tachycardia. Pulse, 105. Very nervous. Last heard of after 18 months. Result: Soon began to improve. Pulse, 80. Exophthalmos hardly noticeable. Irritability gone. For some time has been able to lead a normal quiet life. No tremor. Treatment: Rest every day, Moebius' serum.

11. Female, aged 21; Ref. No. 19·45 (Doctor's name missing).—Moderate case: Is slowly improving under rest. Has had some symptoms of it for 6 years.

12. Female; Ref. No. 19·45 (Doctor's name missing).—Moderate case: Mother of No. 11. Has got well with rest.

13. Female, aged 49; Ref. No. 19·124 (F. A. Brooks).—Moderate case: Tachycardia, slight thyroid enlargement, attacks of diarrhœa. Last heard of after 24 months. Result: No improvement, refuses rest and treatment.

14. Female, aged 48; Ref. No. 19·262 (F. Stephenson).—Moderate case: Much tachycardia (pulse, 120), thyroid enlargement, and tremor. Very nervous. Last heard of after 24 months. Result: Five months after much better. Pulse 90. Takes food well. Nervousness gone. Not being attended now; is well. Treatment: Rest in bed.

15. Female, aged 48; Ref. No. 19·357 (F. Evered).—Mild case: All cardinal symptoms. Last heard of after 23 months. Result: Excellent general health, takes average amount of exercise, not debarred from any social functions. Has gained weight. No symptoms of the disease except slight exophthalmos, which is lessening. Treatment: Rest in bed. This more efficacious than any other treatment.

16. Male, age not stated; Ref. No. 19·376 (J. R. Watt).—Severe case: Tachycardia (pulse, 120), loss of weight, exophthalmos, tremor, no thyroid enlargement, diarrhœa. Last heard of after 23 months. Result: After 5 weeks' rest in bed improved, exophthalmos less. Pulse fell to 96. Gave up rest, lost what he had gained, and is now as he was when first seen. Treatment: Rest in bed and Moebius' serum.

17. Female, aged 40; Ref. No. 18·24 (R. W. Rouw).—Very severe case: Extreme exophthalmos, tachycardia (pulse, 120), tremor, slight thyroid. Last heard of after 33 months. Result: Cured, except exophthalmos still evident, but much diminished. Can walk 3 miles a day. Pulse, 80—90. Thyroid normal. Rest in bed many months. Moebius' serum.

18. Male, aged 24; Ref. No. 18·146 (T. F. Woodroffe).—Severe case: Large thyroid, tachycardia (pulse, 140), cardiac dilatation, tremors. Last heard of after 32 months. Result: Completely cured. Treatment: Rest in bed and digitalis, but no improvement. When rest continued and Moebius' serum given, "wonderful improvement, pulse falling at once."

19. Male, aged 40; Ref. No. 18·413 (G. F. Hugill).—Had exophthalmic goitre for years, and diabetes for last 12 months. Result: In spite of his diabetes the exophthalmic goitre has been getting better, and now no signs of it, except eyes a little prominent. Died of diabetic coma a few days after I saw him.

20. Female, aged 35; Ref. No. 17·76 (G. Whiteley).—Moderate case: Marked exophthalmos and thyroid, tachycardia (pulse, 120), many miscarriages, dysmenorrhœa, wasted. Last heard of after $3\frac{1}{4}$ years. Result: At end of 7 months had gained 28 lbs. Pulse, 84 in morning. Much better. At end of 3 years said she was very much better. Treatment: Rest in bed 9 months.

21. Female, aged 35; Ref. No. 17·77 (M. J. Bulger).—Very severe case: Seven years ago left lobe of thyroid removed for exophthalmic goitre. Says she was better for a time, but soon got bad again. Now marked exophthalmos, tachycardia (pulse, 170). The remaining lobe has hypertrophied greatly. Too weak to stand; very thin, impulse outside nipple. Last heard of after 3½ years. Result: Slowly got better, and when heard of 3¼ years after was able to walk to business and do a hard day's work. She has a sister (whom I saw) who had the disease at the same time as patient was operated upon. This sister slowly got well, and has remained so till now (1910). A brother also has the disease. Treatment: Rest in bed 4 months after I saw her; also took arsenic.

22. Female, aged 26; Ref. No. 17·389 (R. Tilbury).—Severe case: Marked exophthalmos, thyroid enlargement, and tachycardia. Last heard of after 1½ years. Result: Very much better in all respects, and got well enough to go with her husband to South Africa. Treatment: Rest in bed 4 months.

23. Female, aged 39; Ref. No. 16·67 (J. P. Pendlebury).—Average case: Much loss of weight, and insomnia. Exophthalmos, thyroid, tachycardia moderate. Last heard of after 3¾ years. Result: Much better. Enjoys very fair health. Occasional palpitation, but only after over-exertion. Attends many social functions. Signs of exophthalmic goitre slight. Well nourished. Treatment: Rest in bed for some weeks.

24. Female, aged 15; Ref. No. 16·157 (Stanley Smith).—Average case: Considerable exophthalmos, tachycardia, and thyroid enlargement, very nervous and excitable. Some cardiac dilatation. Last heard of after 3½ years. Result: Very well, able to take her ordinary part in life. Going to be married. Pulse and thyroid normal. Eyes slight exophthalmos. Treatment: Rest in bed many months.

25. Female, aged 34; Ref. No. 16·304 (Fraser Nash).—Mild case: All the usual symptoms. Pulse, 130. Last heard of after 3½ years. Result: Improved in every way, but still feels nervous when out alone. After a few weeks' rest improvement very evident. Pulse, 96. Thyroid normal, slight exophthalmos. Treatment: Rest in bed a few weeks.

26. Female, aged 30; Ref. No. 15·145 (E. F. Heap).—Severe case: Extreme nervous symptoms, great tremor, much weeping, considerable thyroid enlargement. Pulse, 90. Last heard of after 4¼ years. Result: Well, leading active life, but easily excited, and then slight tremor visible. Gradually got quite well, and has been so for 2 years. Treatment: Rest in bed a few weeks, then very quiet life with much rest on the Riviera.

27. Female, aged 63; Ref. No. 15·279 (G. Levick).—Very severe case: Slight exophthalmos, some tremor, extreme tachycardia (150—160), trace albumen, general œdema, wasting, fluid in pleura. Result: Died 14 days after I saw her, suddenly. The pleural effusion increased rapidly, but aspiration was not allowed.

28. Female, aged 45; Ref. No. 14·128 (R. G. Hicks).—Slight case in all respects. Result: Left England after rest, but Dr. H. has heard that she is highly nervous and easily excited, but otherwise well. Treatment: Rest.

29. Female, aged 17; Ref. No. 13·132 (R. Kirkland and F. Hinds).—Average case: Large thyroid, slight exophthalmos, some tachycardia (pulse, 130), slight tremor. Last heard of after 5½ years. Result: Very good health, thyroid and eyes normal, good weight, able to go to dances. Treatment: Rest in bed some months, belladonna.

30. Female, aged 22; Ref. No. 13·260 (F. Hinds).—Average case: Large thyroid, no exophthalmos; tremor, anæmia, wasting, all present; extreme tachycardia. Last heard of after 5½ years. Result: Very good health, thyroid and eyes normal, good weight, busy from 7 a.m. to 10 p.m. Treatment: Rest in bed some months.

31. Female; Ref. No. 12·158 (Doctor's name missing).—Severe case. Large thyroid, slight exophthalmos and tremor, some tachycardia, some diarrhœa. Last heard of after 1 year. Result: "Did very well." Cannot be traced after 1 year. Treatment: Rest.

32. Female, aged 33; Ref. No. 12·208 (Newlyn Smith).—Average case: slight thyroid enlargement and exophthalmos, much tachycardia and tremor. Last heard of after 5¾ years. Result: Certainly improved upon rest, but there is every probability that this was not carried out for long. When last seen, 1907, she was much the same as in 1905. Now (1910) writes: "Getting on fairly well, leading quiet country life." Treatment: Rest for a time, also arsenic, bromide, and iron.

33. Female, aged 40; Ref. No. 11·101 (C. J. Woollett).—Moderate case: Patient drinks. Last heard of after 1 year. Result: died from alcoholism a year after I saw her.

34. Female, aged 29; Ref. No. 11·200 (T. B. Scott).—Very severe case: Exophthalmic goitre for some time. Latterly thyroid and exophthalmos much less, but loud mitral murmur has appeared. She now has great œdema of feet, relieved by Southey's tubes. Very nervous. Last heard of after 1 year. Result: Dr. Scott wrote: "She got practically well gradually, and is now at home in New Zealand." Treatment: Rest, digitalis.

35. Female, aged 39; Ref. No. 11·208 (J. F. Hossack).—Mild case in all respects. Result: Passed out of Dr. H.'s hands, but he sees her in the street, and she appears well. Treatment: No note.

36. Male, aged 46; Ref. No. 11·349 (S. Wacher).—Average case: Exophthalmos, tremor, tachycardia, slight wasting, diarrhœa. Last heard of after 6½ years. Result: Recovered to all intents and purposes. Can go for long walks. Recovery gradual. Treatment: Rest, and then a sea trip.

37. Female, aged 27; Ref. No. 11·366 (H. F. Vincent and J. S. Richards).—Mild case in all respects. Last heard of after 6½ years.

Result: Recovered completely from exophthalmic goitre, but has degenerated into complete invalid; an introspective, selfish neurasthenic. Treatment: Occasional rest, but no treatment was continued for long.

38. Female, aged 30; Ref. No. 10·52 (R. Alexander).—Mild case of exophthalmic goitre in all respects. She did not come for this, but for headaches. Last heard of after 7½ years. Result: Exophthalmic goitre no more pronounced. Treatment: None special.

39. Female, aged 23; Ref. No. 10·72 (A. Matcham).—Very severe case: Lost 3 stone last 18 months. Much thyroid enlargement, exophthalmos, and tachycardia (pulse, 130), temperature, 99·2°, tremor, frequent severe diarrhœa. Last heard of after 7½ years. Result: Got quite well, put on flesh, and remains well to present time. Dr. M. attributes her recovery to the thyroid. Treatment: Poor woman, who could not rest. Thyroid gr. v. 3 times a day for 3 months, then gr. x. 3 times a day for a year. Went into country.

40. Female, aged 19; Ref. No. 10·235 (E. R. Fothergill).—Mild case: Enlarged thyroid, no exophthalmos, tremor, tachycardia. Last heard of after 7 years. Result: Got quite well as result of rest, and has remained well. Now (1910) looks quite well in all respects. Is married, and expecting her confinement. Treatment: Rest in bed 6 weeks.

41. Male, aged 30; Ref. No. 10·378 (P. J. Lush).—Very severe case: Acute exophthalmic goitre following influenza. Thyroid has enlarged much in 14 days. Pulse, 100. Impulse nipple line. Temperature, 99°. Slight exophthalmos, great tremor, exceedingly restless, so bad it was thought he would die. Last heard of after 6¾ years. Result: Got quite well. Within 12 months was riding across country, and has remained well ever since. Treatment: Restlessness controlled by hyoscine, and was kept in bed many months.

42. Female, aged 18; Ref. No. 10·393 (S. C. Austin).—Moderate case: Tachycardia, tremor, enlarged thyroid, very slight exophthalmos. Last heard of after 5½ years. Result: Got quite well, and has remained well since. Is now married. Treatment: Poor girl; could not rest. No special treatment.

43. Female, aged 35; Ref. No. 9·32 (H. M. Stewart and G. B. Batten).—Moderate case: Tachycardia (pulse, 150—160), tremor, moderate thyroid, slight exophthalmos. Last heard of after 8½ years. Result: Much better than she was. Is able to do her work, but not well. Treatment: Could not rest. No special treatment, except that lately she has had 75 applications of X-rays over thyroid. This improved her.

44. Female, aged 27; Ref. No. 9·155 (R. H. W. Wilbe).—Severe case: Followed influenza, much wasting, tachycardia (pulse, 110), impulse outside nipple, large thyroid, moderate exophthalmos, in-

somnia. Last heard of after 3 years. Result: Got quite well. Treatment: Rest in bed, feeding. Faradism to neck (this did no good). Later on massage.

45. Female, aged 31; Ref. No. 9·265 (W. W. Wingate).—Severe case: Big thyroid, great tremor, tachycardia, some exophthalmos. Last heard of after 8 years. Result: For some months very quiet life. Greatly improved, eyes and thyroid became almost normal. In 1908 was discovered to have diabetes, from which she died in 2 months. Treatment: Rest.

46. Female, aged 25; Ref. No. 9·293 (W. A. Brailey).—Severe case: Much tremor, exophthalmos, thyroid enlargement, and tachycardia. Heart much dilated. Has had rheumatic fever. Sister of 4·57, who died. Result: Improved very much, but while the improvement was progressing I lost touch of the case. Treatment: Rest in bed. Cannot be traced for long.

47. Female, aged 27; Ref. No. 8·39 (E. L. Adeney).—Average case: Much tremor, some diarrhœa. Result: Improved for a time with rest, and died subsequently from diarrhœa. Treatment: Rest.

48. Female, aged 57; Ref. No. 8·167 (E. R. Carter).—Many years ago was under Sir S. Wilks for exophthalmic goitre. She also had a fibroid of uterus. The thyroid and fibroid shrank together. Now the only evidence of the disease is some, but not much, exophthalmos. She is thin and liable to diarrhœa. Result: I saw her for lobar pneumonia. Severe case. She completely recovered, and the pneumonia did not lead to any return of the exophthalmic goitre.

49. Female, aged 34; Ref. No. 6·190 (F. H. Hollingshead).—Very severe case: Much thyroid enlargement and tachycardia, impulse nipple line, systolic murmur, slight exophthalmos, great tremor, very thin, much diarrhœa. Last heard of after 11½ years. Result: Gained 13lb. in 2 months, and in that time got much better. Seen July 16th, 1899. Much better. Dr. H. writes March, 1910: "Much better I believe, but I have not seen her for several years." Treatment: Rest in bed 2 months.

50. Female, aged 21; Ref. No. 5·35 (C. A. Ensor).—Severe case: Exophthalmos, thyroid enlargement, tremor, tachycardia, all present. Diarrhœa, urticaria. Six months later glycosuria appeared. Irritable. Last heard of after 14 years. Result: Six months later better. Glycosuria persisted 2 years, but was not found after this time. By 1898 was "practically well," could walk 8 miles. Slight tachycardia, thyroid, exophthalmos and irritability, but by 1899 normal in all these respects. 1910, normal in every way. Pulse, 72. Thyroid normal, no tremor, no glycosuria. Eyes somewhat prominet. General health excellent. Treatment: Rest.

51. Male, aged 32; Ref. No. 5·301 (W. Howells).—Severe case: Much thyroid enlargement, exophthalmos, tachycardia, and tremor. Very nervous. Disease attributed to influenza. Much cardiac dilatation and wasting. Polyuria, no sugar or albumen. Last heard of after 5 years.

Result: Got much œdema, because the cardiac symptoms became very severe, and it was thought he would die, but by the end of three years was quite well and back at business. Treatment: Prolonged complete rest.

52. Female, aged 15; Ref. No. 4·57 (W. A. Brailey).—Severe case: Much thyroid enlargement, exophthalmos, tachycardia, and nervousness. Took food badly. In spite of all treatment the cardiac dilatation became extreme and the most troublesome feature. Last heard of after 6½ years. Result: Died October 23rd, 1900. The dilatation of the heart and the resulting symptoms were very severe, and probably the cause of death. Treatment: Prolonged rest, various drugs.

53. Female, aged 32; Ref. No. 4·97 (Kinsey-Taylor).—Average case: Very nervous. All usual symptoms present. Last heard of after 16 years. Result: Seen 6 months after operation. Feels better. Exophthalmos less, but tachycardia well marked. Cardiac dilatation unaltered, likewise nervousness. The left lobe of thyroid has grown bigger since operation. Sixteen years after operation "distinctly better. No exophthalmos. Some tachycardia and palpitation. Nervous symptoms much the same. Still odd mentally." Treatment: Right lobe of thyroid removed.

54. Female, aged 20; Ref. No. 4·185 (L. Roper).—Very severe case: Disease has lasted 5 years. Much exophthalmos, diarrhœa, tremor. Very large thyroid, neck 17 inches. Much cardiac dilatation. Gets syncopal attacks. The thyroid presses on trachea and renders breathing very difficult. Cannot lie down. The isthmus was merely a fibrous band. Last heard of after 5 years. Result: Dyspnœa much relieved by operation. Could lie down, heart less rapid. Saw her 18 months later and then, although still a severe case, she was undoubtedly better. Heard from Dr. A. Caddy (Calcutta) in 1899 that he had just seen her; he reported: "Is in fairly good health, her symptoms have much lessened." Treatment: Isthmus divided. Local anæsthetic as general considered too dangerous. Rested as much as possible, but this was not as complete as could be wished.

55. Female, aged 27; Ref. No. 4·305 (W. Weaver).—Very severe case: Much exophthalmos, insertion of recti visible, large thyroid, much tremor, tachycardia (pulse, 150). Impulse outside nipple, loud systolic murmur. Much wasting. Result: "Did well." Treatment: Rest in bed, thyroid.

56. Female, aged 29; Ref. No. 4·355 (C. F. Routh).—Average case: Enlarged thyroid, moderate exophthalmos, tachycardia (pulse, 130), cardiac dilatation, impulse outside nipple. Last heard of after 15 years. Result: Got quite well. Is still well in 1910. Treatment: 3 months' rest in bed, thymus.

57. A severe case: I was present at the operation of removing the right lobe of the thyroid. Just after this had been done, but before the wound was closed, the patient, while still under the anæsthetic, died.

TABLE C.

TWENTY-ONE CASES THAT DIED IN THE HOSPITAL.

1. Female, aged 31; Ref. No. 1.—Hospital 14 days. Symptoms, ordinary: Been ill 18 months. Exophthalmos, tachycardia, palpitation, thyroid, all considerable. Special: Much palpitation, diarrhœa, vomiting. Course: Palpitation, diarrhœa, and vomiting, all got worse. Terminal pyrexia and jaundice. Post-mortem appearances: Gastro-enteritis, broncho-pneumonia. Treatment: Rest in bed, bismuth, strophanthus.
2. Female, aged 24; Ref. No. 5.—Hospital 60 days. Symptoms, ordinary: Been ill 15 months, ordinary symptoms average. Special: Great weakness. Course: Diarrhœa and vomiting set in and progressed. Slight jaundice. Post-mortem appearances: Large thymus, gastro-enteritis. Treatment: Rest in bed, galvanism to neck, bromides, belladonna.
3. Female, aged 23; Ref. No. 9.—Hospital 2 days. Ill 6 months, ordinary symptoms considerable. Special: Very rapid pulse, much weakness and vomiting. Course: Vomiting persisted. Post-mortem appearances: Large thymus.
4. Female, aged 54; Ref. No. 10.—Hospital 13 days. Ill 6 months, ordinary symptoms average. Special: Much palpitation, mitral regurgitation. Course: The cardiac trouble became worse and was the cause of death. Post-mortem appearances: Large left ventricle. Treatment: Rest in bed, digitalis.
5. Female, aged 30; Ref. No. 38.—Hospital 9 days. Ill 12 months, ordinary symptoms considerable. Special: Patient anxious for operation because exophthalmos prevented her following her occupation as barmaid. Course: A.C.E. given, right lobe removed. Next day extremely excitable. Temperature, 103°. Death. Post-mortem appearances: Nothing to explain death. Treatment: Operation.
6. Female, aged 22; Ref. No. 52.—Hospital 4 days. Symptoms, ordinary: Symptoms of exophthalmic goitre for 7 years. Special: Came in for rheumatic fever. Pulse, 150. Course: Got rapidly worse, and died apparently from severe rheumatic fever. Post-mortem appearances: Thymus persistent, Peyer's patches prominent. Treatment: For rheumatic fever.
7. Female, aged 32; Ref. No. 23a.—Hospital 59 days. Symptoms, ordinary: Average case. Special: Much headache. Course: Headache became very severe, also much vomiting. Post-mortem appearances: Thrombosis right middle cerebral artery and consequent softening. Treatment: Rest in bed, belladonna, opium.
8. Female, aged 36; Ref. No. 53.—Hospital 19 days. Symptoms, ordinary: Severe case: Special: Apical systolic murmur; diarrhœa. Course: Diarrhœa. Delirious for 14 days before death. Post-mortem appearances: No cause for death found. Treatment: Rest in bed, belladonna, digitalis.

9. Female, aged 37; Ref. No. 62.—Hospital 7 days. Symptoms, ordinary: Been ill 9 months. Pulse, 130—150. Other ordinary symptoms average. Special: Great weakness, apical systolic murmur. Attributes onset of exophthalmic goitre to an attack of rheumatic fever. Course: Became delirious and cyanotic. Died suddenly. Post-mortem appearances: Thymus large, no endocarditis. Treatment: Rest in bed, Leiter's coils, belladonna.

10. Female, aged 26; Ref. No. 71.—Hospital 15 days. Symptoms, ordinary: Ill 2 months. Average case. Special: Admitted for rheumatic fever and pericarditis. Course: Diarrhœa supervened. Became delirious. Post-mortem appearances: Endocarditis, pericarditis.

11. Female, aged 24; Ref. No. 80.—Hospital 39 days. Symptoms, ordinary: Ill 11 months. Average case. Special: Had pneumonia with delirium. Course: Vomiting and diarrhœa supervened. Post-mortem appearances: No post-mortem.

12. Female, aged 26; Ref. No. 81.—Hospital 27 days. Symptoms, ordinary: Ill 20 months. Severe case. Special: Much dyspnœa, became melancholic. Course: Diarrhœa, delirium, and pyrexia supervened. Post-mortem appearances: Trachea compressed by thyroid. Treatment: Rest in bed, belladonna, digitalis, bromides.

13. Female, aged 41; Ref. No. 83.—Hospital 13 days. Symptoms, ordinary: Ill 8 years, ordinary symptoms slight. Special: Diabetes discovered soon after onset of exophthalmic goitre. Course: Had had both diseases 8 years; died of coma. Post-mortem appearances: Old endocarditis.

14. Female, aged 25; Ref. No. 86.—Hospital 24 days. Symptoms, ordinary: Ill 18 months, ordinary symptoms moderate. Special: Weakness, had mania and later pneumonia. Course: Died from pneumonia. Post-mortem appearances: Lobar pneumonia.

15. Female, aged 33; Ref. No. 103.—Hospital 83 days. Symptoms, ordinary: Ill 2 years, ordinary symptoms average. Special: Much wasting delirium, vomiting, and diarrhœa. Course: Died from cardiac weakness. Post-mortem appearances: Broncho-pneumonia. Treatment: Rest in bed, belladonna, digitalis.

16. Female, aged 22; Ref. No. 110.—Hospital 47 days. Symptoms, ordinary: Ill 9 months, ordinary symptoms moderate. Special: Melancholia, vomiting, and diarrhœa. Course: The vomiting and diarrhœa increased and delirium supervened. Post-mortem appearances: Thymus enlarged. Treatment: Rest in bed, belladonna, digitalis, opium.

17. Female, aged 27; Ref. No. 111.—Hospital 18 days. Symptoms, ordinary: Average. Special: None. Course: Became comatose and died. Post-mortem appearances: Report missing.

18. Female, aged 27; Ref. No. 118.—Hospital 5 days. Symptoms ordinary: Very severe. Special: Vomiting, very severe tremor. Pulse, 192. Post-mortem appearances: Nothing found to explain death.

19. Female, aged 21; Ref. No. 150.—Hospital 59 days. Symptoms ordinary: Average, but much tremor. Special: Vomiting, jaundice. Temperature, 102. Post-mortem appearances: Liver small, bile stained, acute ascending nephritis due to bacillus coli. Treatment: Belladonna, strophanthus.

20. Female, aged 19; Ref. No. 166.—Hospital 9 days. Symptoms ordinary: Average. Special: Diarrhœa. Course: Cocaine used locally, chloroform given, right lobe and isthmus excised. Died day after operation. No post-mortem. Treatment: Operation.

21. Female, aged 29; Ref. No. 167.—Hospital 30 days. Symptoms, ordinary: Average. Special: Much sweating, also diarrhœa. Course: Eucaine and adrenalin locally and chloroform, both superior thyroids tied. Later, under same anæsthetic, attempt to tie inferior thyroids. Patient died on the table. Post-mortem appearances: Enlarged thymus, fatty infiltration of heart. Treatment: Operation.

THREE CASES OF PERSISTENT MECKEL'S DIVERTICULUM.

By

PHILIP TURNER, M.S.

During the past twelve months I have had occasion to operate on three patients for troubles resulting from the persistence of a Meckel's diverticulum. Two of these patients were suffering from intestinal obstruction, while the third was a child with a fæcal umbilical fistula and a cyst beneath the abdominal wall. A persistent Meckel's diverticulum, though its presence may be entirely unsuspected, may give rise to many lesions, the most serious and important of which are acute abdominal troubles, which may be very obscure and present many difficulties, both in diagnosis and treatment. A few years ago I endeavoured from an examination of our clinical and post-mortem records, and by the consideration of museum specimens, to collect and classify all the lesions which might result from the presence of this structure. (Guy's Hospital Reports, vol. lx., p. 279.) Each of the present cases, though in many respects typical, presents some unusual features, and this, combined with the fact that they illustrate or amplify my former paper, is the reason for their publication.

Case 1 (reported by Mr. E. Billing).—Lilian C., aged 1 year and 11 months, was admitted into Miriam, under Sir Cooper

Perry, on January 14th, 1911, for vomiting and abdominal pain. Until the present trouble, the child's health had been quite good, and there were no previous illnesses. On January 10th—four days before admission—she was suddenly seized with abdominal pain while at stool. Shortly afterwards she was sick. During the next two days the pain continued, and everything taken by the mouth was vomited. There was also absolute constipation, and the abdomen became tender and rigid. On January 12th the child was given some calomel and pulv. rhei. co., but without effect. On January 14th, before admission, she had a glycerine enema without result, but after a soap enema a small amount of hard fæces was passed. There was no history of the passage of blood or mucus. A cough had been noticed for a few days.

On admission the child looked very ill. The face was pale, the eyes sunken, and the respirations were rapid and shallow. The extremities were cold and the knees drawn up. The pulse rate was 152, respirations 40, and temperature 99°. The abdomen, though distended, was neither rigid nor tender, and the child did not resent examination. There was no enlargement of liver or spleen, and no tumour was palpable. On percussion there was dulness in both flanks. A rectal examination showed nothing abnormal. The base of the left lung was dull, and numerous crackling râles were heard in this situation. The tongue and lips were dry and brown.

A diagnosis of intestinal obstruction was made, and immediate operation decided upon. The abdomen was opened by an incision 3 inches long just to the right of the umbilicus. Dilated and congested coils of small intestine at once presented. Two fingers were then introduced, and the peritoneal cavity explored for an intussusception: nothing abnormal could be felt. The transverse colon was, however, found to be empty and contracted, as was also the cæcum. Some empty contracted coils of ileum were then noticed, and on tracing these upwards to the dilated coils, a Meckel's diverticulum, springing from the free border of the gut, was found about one foot above the ileo-cæcal valve. From

its extremity, a fibrous cord extended to the mesentery. An arch was thus formed, but to the best of my belief no intestine was strangulated beneath this. It was difficult to make out the exact condition of things, as the coil from which the diverticulum projected was situated deeply in the pelvis, but most probably the diverticulum had caused a twist and kink in the ileum, and had thus produced the obstruction. It was deeply congested, and on manipulation it ruptured near its apex, allowing the escape of some yellowish fluid. The coil was then drawn outside the abdominal wound. The base of the diverticulum, which was fortunately narrow, was ligatured, and it was then removed, the stump being subsequently invaginated by a purse-string suture. The bowel which, for some distance above the obstruction, was very dark and congested, but not actually gangrenous, was washed over with saline and returned.

The child was desperately ill on admission, and during the operation the pulse became imperceptible. She also vomited fæcal fluid freely during the administration of the anæsthetic. Subsequently the patient was infused, and strychnine and pituitary extract injected, but she died eight hours later.

At the autopsy, the diverticulum was found to have been 15 inches above the ileo-cæcal valve. There was much peritonitis. Below the diverticulum the bowel was collapsed and of a dark slate colour. For a distance of 4 feet above, the intestine was distended and deeply congested, one coil being almost gangrenous.

Case 2.—James Rendall W., a healthy and robust-looking man, aged 22 years, was admitted to the Eltham Cottage Hospital on August 9th, 1911, for abdominal pain and vomiting. He gave a history of numerous previous attacks of abdominal pain. When asked the number of these and their duration, he said that he had had at least twenty in the past four years. The pain in these attacks was severe, and experienced in the region of the umbilicus. A point of great interest is, that while the pain was acute, he felt "drawn in," and found it difficult or impossible to stand upright. Many of the attacks were ac-

companied by vomiting, after which he was usually better, though on one occasion he vomited on and off all night. He was never kept in bed for more than a day, and himself ascribed the attacks to indigestion. He had seen two medical men for these attacks, one of whom diagnosed "gastric influenza" and the other "colic." The last of these attacks had occurred in June. Except for these, he had always had excellent health.

His present illness commenced with abdominal pain, which he first noticed while having breakfast on August 9th. He had been playing cricket on August 7th, but remembered no special twist or strain, and felt perfectly well afterwards and during the following day. The pain was similar in character to that experienced before, and so he went to work expecting it to pass off. After two hours, however, it became so bad, and he felt so ill, that he was unable to work. He did not vomit at all. His bowels had acted only slightly that morning, and not satisfactorily on the preceding day. He saw a doctor, who diagnosed colic, gave him some castor oil and opium, and sent him home to bed. The pain, however, got worse, and as he vomited several times in the course of the afternoon, he sent for Dr. Patterson, who, suspecting intestinal obstruction, sent him into the hospital.

I saw him with Dr. Patterson on the following morning (August 10th). He had not vomited in the fifteen hours since his admission, but his bowels had not acted, and the pain was still present and very severe, and he felt very weak and ill. On examination the abdomen was full and slightly tender, but there was no visible peristalsis, and no abnormality could be detected on palpation. A rectal examination revealed an elastic bulging in the recto-vesical pouch showing the presence of distended intestinal coils in the pelvis. The temperature was 99°, the pulse rate 90, and respirations 19. A diagnosis of intestinal obstruction was made, and either a Meckel's diverticulum or peritoneal adhesions secondary to appendicitis suggested as the cause.

The abdomen was opened by an incision about 4 inches long just to the right of the mid line between the umbilicus and the pubes. When the peritoneum was opened, several ounces of yellow serum escaped and deeply congested and dilated coils of small intestine bulged forwards into the wound. The cause of the obstruction was readily found, for on introducing the fingers a strong tense cord of about the diameter of an ordinary lead pencil could be felt traversing the peritoneal cavity. Above, it was attached to the abdominal wall just to the right of the umbilicus; below, it extended into the pelvis. The tension on the cord was remarkable, and it was impossible to trace its lower attachment until the upper end had been divided. Several coils of empty contracted ileum were then found, and on tracing these away from the cæcum the site of the obstruction and the lower attachment of the cord were soon found. This proved to be a short stumpy Meckel's diverticulum about $1\frac{1}{2}$ inches long and $1\frac{1}{2}$ inches in diameter at its base, springing from the lateral aspect of the intestine. The fibrous cord was attached to its apex. The diverticulum itself was very dark in colour, and the junction of the dilated and contracted ileum was immediately below it. The coil of intestine to which it was attached was situated deeply in the pelvis, and it could only with difficulty be drawn into the wound. I attribute this to recent peritonitis; there were no adhesions about either the coil or the diverticulum, and no signs of old peritonitis in any part of the abdomen. The cord was ligatured below, and as one could not be sure that the lumen of the diverticulum was not opened, the stump was invaginated by means of a purse-string suture. The diverticulum itself was not removed, for its attachment was so wide and the intestine below so small, that I felt that suturing under these conditions might readily lead to further obstruction. The intestines were then washed over with saline and returned, and the abdomen closed. The patient stood the operation fairly well, but his pulse rate rose to 120. His bowels acted naturally on the second day, and his recovery afterwards was uneventful.

Obstruction caused by an adherent diverticulum usually occurs in young adults, and in this respect Case 2 is typical. It is not infrequent in children, though very seldom so young as Case 1. Persistence of the diverticulum is distinctly commoner in males than females, and it produces obstruction three or four times as often in the former as in the latter. It is thus of some interest to notice the sex of this child.

A point of very great interest in the history of Case 2 is the history of numerous previous attacks of abdominal pain. A history of slight attacks of abdominal pain and constipation is obtained in some cases, but the only case I know of in any way comparable to the present patient was a man, aged 24, under Dr. Taylor in 1899, for acute intestinal obstruction also caused by a diverticulum extending from the small intestine to the umbilicus. This patient had one severe attack of colic followed by several slighter ones. The history given by the present patient suggests the possibility of diagnosing the presence of the diverticulum and removing it before it had set up any acute trouble.* At any rate the occurrence of numerous attacks of severe abdominal pain associated with vomiting, and usually requiring the patient to rest in bed for a day, would amply justify an abdominal exploration, though the appendix would most likely be suspected of causing the trouble. The fact that the present patient felt "drawn in" and unable to stand or sit upright can only be explained by the tension on the diverticulum and its cord, which would naturally be relaxed by assuming the stooping posture. I do not know of any other case in which this symptom has been recorded.

The diagnosis in each case presented points of difficulty. In Case 1 there was no difficulty in diagnosing intestinal obstruc-

* Since writing the above I have heard that this patient, when a few weeks old, underwent an operation for "patent urachus." Had this fact—of which the patient was unaware—been known, a persistent diverticulum might have been diagnosed with certainty. It is interesting to note, though the fistula must have communicated with the intestine, that, owing doubtless to the inodorous character of the thin yellow discharge, the fistula was thought to communicate with the bladder.

tion, but to the best of my belief no one suggested strangulation by a persistent diverticulum as the cause. I thought that an intussusception was the most probable explanation of the symptoms.

In Case 2 the diagnosis of obstruction was not easy. Though the abdominal pain continued, the vomiting had become less, and he had only been twenty-four hours without any action of the bowels. It may here be pointed out that when the obstruction is caused by a diverticulum attached to the umbilicus, the symptoms are usually less acute than when it is fixed to the mesentery. A rectal examination proved of great assistance in the diagnosis, for dilated coils could readily be felt bulging back the anterior wall of the rectum in the region of the recto-vesical pouch. I should like here to point out the value of a rectal examination in all cases of doubtful intestinal obstruction, with a view to the detection of dilated coils of intestine in the pelvis. This sign is, however, of less value in women than men, as the uterus is very likely to interfere with the palpation of the coils.

The situation of the diverticulum was typical. In Case 1 it was 15 inches from the ileo-cæcal valve, while in the adult it was about 2 feet. In the former it joined the free border of the gut, and in the latter was situated mid-way between the free and the mesenteric borders. In each case the diverticulum was short, but from its free extremity a fibrous cord extended in (1) to the mesentery, and in (2) to the umbilicus. The diverticulum is the remnant of the vitelline duct, while the cord is derived from the obliterated vitelline vessels. It is the fibrous band thus formed rather than the diverticulum which is the cause of the obstruction. The cord, when present, may be attached to the umbilicus, to the mesentery, or rarely to some viscus, or it may be free in the peritoneal cavity.

In the former case obstruction may be caused in one of the following ways:—

(1.) A coil of intestine may be forced beneath the shallow arch formed by the cord.

(2.) The cord may cross and obstruct the ileum at the base of the diverticulum.

(3.) By traction on or volvulus of the coil from which the diverticulum springs.

(4.) By adhesions around an old inflamed diverticulum.

When the cord is not attached it may lead to obstruction by becoming firmly knotted round an intestinal coil.

In many cases it is difficult to be sure of the exact mode in which the obstruction is produced. In Case 1 the cord formed a narrow arch through which a coil of small intestine might have readily been forced. However, no coil was seen in this situation in the course of the operation, and the appearance of the intestine at the autopsy did not suggest that this had occurred. The obstruction was almost certainly caused by the cord crossing the ileum at the base of the diverticulum, probably combined with some twisting of the mesentery. The same difficulty in ascertaining the exact mechanism of the obstruction was found in Case 2. Here, the congested and dilated coils of small intestine, which required the most careful manipulation, prevented the site of the obstruction coming into view until the tense cord had been divided, thus relieving the actual cause of the obstruction. It was then seen, however, that there was a sharp line of demarcation immediately below the diverticulum, the intestine below being pale and contracted, while that above, including the diverticulum itself, were deeply congested and dilated. Thus, there can be no doubt that in this case the obstruction was produced by the cord crossing the ileum, very probably again associated with some twisting of the gut at this fixed spot. The tenseness of the cord was probably in part due to the weight of the obstructed coil, which was also fixed in the pelvis by recent peritonitis, and also by the weight of other distended coils pressing upon the cord and the obstructed coil.

The prognosis in these cases is always very bad. In Case 1 it was realised that it was practically hopeless. In Case 2, owing to the early diagnosis and more chronic nature of the symptoms,

the outlook was more hopeful, but even here the condition of the bowel was already very bad, and any temporising would, I am convinced, have seriously jeopardised a successful result.

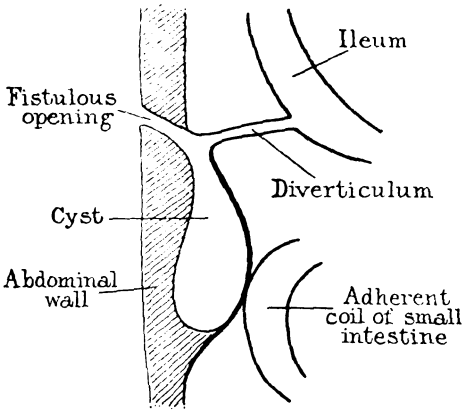
Case 3.—Daisy B., aged 3 years, was admitted on August 27th, 1910, for a fæcal fistula at the umbilicus. The discharge, which had been noticed for only three weeks, followed an attack of constipation associated with some abdominal pain.

On admission there was a small red patch of granulations at the umbilicus. In the centre of this was a sinus along which a probe could be passed in a downward direction for some inches. On pressing below the umbilicus, brown fluid with a fæcal odour, could be forced from the sinus. The child's mother, however, stated that the discharge was occasionally clear, yellow, and odourless. The abdomen was rather distended, but was not tender.

It was decided to remove the diverticulum. An oval incision was made around the umbilicus, and the peritoneal cavity opened. It was then found that the fistulous track led into a large cyst which appeared to be situated between the peritoneum and the abdominal wall, and extended downwards towards the pubes. A coil of intestine was adherent to this below, but a probe would not pass from the interior of the cyst into the gut in this situation. This portion of the intestine was freed by tearing through some recently formed adhesions. A narrow pedicle was then found forming a communication between the upper portion of the cyst and another coil of small intestine. This was ligatured close to the gut, and the stump invaginated by a purse-string suture. An attempt was made to remove the entire cyst, but though the upper part could be readily dissected away, the lower part was so adherent to the abdominal wall that it could not be separated. The upper part was accordingly removed and the peritoneal cavity closed, while the lower portion of the cyst was packed with gauze. It quickly granulated, and the child was discharged on September 22nd with a very slight amount of non-fæculent discharge.

The wound soon healed, and no further trouble was experienced. On inquiry it was found that the child died of measles in March, 1911.

The condition found at the operation is indicated in the following diagram:—



One of the most interesting points about this case was the large cyst-like cavity in the anterior abdominal wall. Occasionally the proximal extremity of the vitelline duct may atrophy, while the distal part persists, giving rise later on in life to a cyst beneath the umbilicus. Such a cyst may for a time resemble an umbilical hernia, but usually it becomes inflamed and suppurates, leading to the formation of an umbilical sinus. As in these cases the communication with the intestine is usually obliterated, the discharge is not fæcal, but consists of a clear yellow fluid resembling urine, and thus suggesting that there is a patent urachus (see footnote, page 38). It may, however, be distinguished from urine by its alkaline reaction and soapy feel, and also by the presence of albumen, and is doubtless very similar to succus entericus.

In the present case, though the diverticulum must have been congenital, the fistula did not appear until the child was nearly 3 years old. Probably the distal end of the diverticulum, though

closed, was dilated. Inflammation and suppuration must, then, have occurred in the cyst, which burst externally, while pus very possibly burrowed in the abdominal wall, giving rise to the downward extension of the cavity. The adherent intestinal coil and the close connection between the sac and the abdominal wall are strongly in favour of this sequence of events. It is interesting, too, to notice that the appearance of the fistula was preceded by constipation and some abdominal pain, probably caused by the inflammation in the sac.

In these cases the treatment is to remove the whole diverticulum, for even if the sinus closes after the use of the cautery, the patient is still in danger from the possibility of inflammatory troubles or of intestinal obstruction, as is well shown in Case 2.

NEUROLOGICAL STUDIES.

EDITED BY

ARTHUR F. HERTZ, M.A., M.D. Oxon., F.R.C.P.,

Assistant Physician, and Physician-in-Charge of the Neurological Department.

1. THE TENDO-ACHILLIS-JERK.

BY

A. F. HERTZ, M.D., AND W. JOHNSON, M.B.

THE object of this paper is to demonstrate the great importance of the tendo-Achillis-jerk in the diagnosis of organic nervous disease. It is constantly present in normal individuals, and it probably disappears before the knee-jerk in a large proportion of cases in which the latter is eventually lost.

Most surgeons confronted with a joint, the appearance of which is suggestive of Charcot's disease, would be inclined to exclude this diagnosis if the pupils reacted normally and the knee-jerks were present. Similarly in suspicious cases of gastric pain, of vesical disorders, of impotence and of numerous other conditions which may be the earliest manifestations of tabes, the presence of knee-jerks and of normal pupils is too often regarded as sufficient evidence to exclude that disease. Still more frequent pain in the legs, arms or trunk is ascribed to "rheumatism" or "neuritis" after an examination of the knee-jerks and perhaps of the pupils has convinced the observer that no more definite organic disease is present. If in all such cases the tendo-Achillis-jerks were examined instead of or in addition to the knee-jerks, many serious mistakes would be prevented, as the tendo-Achillis-jerks are frequently lost in tabes at an earlier period than the knee-jerks and while the pupils are still normal. This fact was discovered by Babinski* in 1898, but has never received the attention it deserves. It is rare to find a patient with tabes whose symptoms have not been ascribed to some apparently trivial cause for months or even years before the correct diagnosis is made. It is possible that symptoms of tabes may sometimes appear before any physical signs, but there can be no doubt that the routine examination of the tendo-Achillis-jerks would do much to assist in the early diagnosis of the disease. The importance of this from the point of view of prognosis and of treatment can hardly be over-estimated, for it is in the early stages that anti-syphilitic treatment is most likely to arrest the degenerative changes in the spinal cord.

The tendo-Achillis-jerks are of no less value in toxic peripheral neuritis, especially when this is due to alcohol or diabetes. In both alcoholic and diabetic neuritis the tendo-Achillis-jerks are lost before the knee-jerks; sometimes, indeed, the latter are at first exaggerated, and in mild cases they may not dis-

* J. Babinski: Sem. Méd., vol. xviii., p. 439, 1898, and Revue Neurologique, vol. ix., p. 482, 1901.

appear at all. The absence of the tendo-Achillis-jerk is not only important in the early diagnosis of cases, in which the prominent symptoms are due to the neuritis itself, but the sign is also of great assistance in the recognition of the alcoholic origin of heart-failure, as a latent neuritis, the only sign or symptom of which is the absence of the tendo-Achillis-jerks, is frequently present in this condition. Absence of the tendo-Achillis-jerks would also be of great value in confirming a suspicion of alcoholism in an otherwise healthy applicant for life insurance. Indeed, the investigation of the tendo-Achillis-jerks is quite as important in the examination of applicants for the public services and for life insurance as that of the urine for sugar, as diabetes is considerably less common and may be no more serious than tabes and latent peripheral neuritis.

In 1896 Babinski* demonstrated that the tendo-Achillis-jerk is sometimes lost in sciatica. Soon afterwards Biro† published statistics which showed that it was affected in more than 30 per cent. of cases. The sign is valuable as showing the neuritic origin of the condition; the absence of the jerk proves the case to be a serious one and indicates the need for prolonged treatment.

In order to obtain the tendo-Achillis-jerk the calf muscles must be relaxed. This can be accomplished most easily if the patient kneels with one knee on a cushioned chair with the foot projecting just over the edge, and with his weight supported principally on the other leg placed close to the side of the back part of the chair. His body should be erect, his knee being bent at a right angle, whilst his hands grasp the back of the chair. The proper degree of relaxation is present when squeezing the calf with the hand produces well-marked plantar-flexion of the ankle. In doubtful cases the left hand may be placed against the sole of the foot in order that a movement too small to be visible may be felt. The tendo-Achillis is sharply tapped,

* J. Babinski: Sem. Méd., vol. xvi., p. 515, 1896.

† M. Biro: Deuts. Zeitschrift f. Nervenheilkunde, vol. xi., p. 207, 1897, and vol. xix., p. 188, 1901.

preferably by means of an india-rubber tipped hammer. The jerk occurs immediately after the stroke, and must be distinguished from the slight movement which occurs from the simple pull upon the tendon when the true jerk is absent.

If a patient cannot get out of bed, the jerk can generally be obtained by tapping the tendon of the uppermost limb when the thigh and the leg are flexed and the patient is lying on one side. It is much less easily obtained than in the erect position, and the absence of the tendo-Achillis-jerk in a bed-ridden patient cannot be regarded as a certain sign of organic disease if the knee-jerk is present.

In young and healthy individuals the tendo-Achillis-jerks can always be easily obtained without even removing the boots. Edwin Bramwell* found them in all of 50 children in the medical wards of a children's hospital, in 108 healthy school children and in 80 medical students. We found them to be present on both sides in 81 out of 82 students.† In older people it is often less easy to obtain the jerks, and Bramwell failed to obtain them at a single examination of 12 out of 15 individuals over 80; 41 out of 65 between 70 and 80; 28 out of 80 between 60 and 70; 5 out of 42 between 50 and 60; and in none out of 28 between 40 and 50. On the other hand, they were found by Williamson in 100 individuals over the age of 50, who were either in good health or not suffering from any nervous disease.

(a) *Tabes.*—Out of 700 patients seen in the Neurological Out-Patient Department between 20th April, 1910, and 19th July, 1911, there were 36 cases of tabes dorsalis. The tendo-Achillis-jerk was absent in every case on both sides, except in one man, in whom it was present on the right side. His knee-jerks were

* E. Bramwell: Brain, vol. xxiv., p. 554, 1901.

† The one exception was a student who had had many illnesses as a child, possibly including a slight attack of anterior poliomyelitis. The right tendo-Achillis-jerk and knee-jerk were normal; the left tendo-Achillis-jerk was absent and the knee-jerk feeble. There was no atrophy nor muscular weakness.

present, but a history of temporary ophthalmoplegia, the presence of fixed pupils, suspicious bladder symptoms and a positive Wassermann reaction made the diagnosis of tabes extremely probable. In 8 cases, however, in which the tendo-Achillis-jerks were absent, both knee-jerks were present, and in an additional case the right knee-jerk was present, but difficult to obtain. In 2 of the 9 cases the knee-jerks were actually exaggerated; in 3 one or both were diminished and only obtainable by reinforcement.

In addition to these cases we may mention that of a man who was sent to general out-patients three years ago for attacks of severe vomiting with some pain, the attacks occurring at intervals of several weeks and lasting for a few days. A provisional diagnosis of gastritis was made, which agreed with that of the patient's own medical attendant. Six months later he was admitted, as the treatment advised had had no effect. It was now found that both tendo-Achillis-jerks, which had not been examined before, were absent, although the knee-jerks were normal, and no other signs of nervous disease were present. A diagnosis of gastric crises due to tabes was made, because of the suspicious character of the gastric symptoms and the absent tendo-Achillis-jerks. A year later the knee-jerks could only be elicited with difficulty, and the pupils were unequal and reacted sluggishly to light.

A woman, aged 35 years, was brought for mental symptoms suggestive of general paralysis of the insane. The pupils were irregular in shape; the right one reacted neither to light nor to accommodation, the left feebly to both. There was no tremor of the tongue, lips or hands, and speech and writing were unaffected. The knee-jerks were normal, but both tendo-Achillis-jerks were absent. The latter sign and the pupil changes associated with the mental symptoms justified a diagnosis of tabo-paralysis.

(b) *Toxic peripheral neuritis.*—Eleven patients, complaining of pains in the legs, were found to have lost their tendo-Achillis-jerks, although the knee-jerks were still present. The tender-

ness of the calves, in contrast with the analgesia found in tabes, showed that the pain and the lost jerks were probably a result of peripheral neuritis and not of tabes. In no case of neuritis were the tendo-Achillis-jerks present and the knee-jerks absent. Other symptoms and the history and appearance of the patients indicated that in eight cases, at least, the neuritis was probably due to alcohol. In two of these patients the combination of neuritis with loss of memory for recent events made up the picture of *Korsakow's syndrome*. In one of the remaining three cases an examination of the urine led to the discovery of diabetes, which had not previously been suspected. In two the cause of the neuritis remained doubtful.

Williamson* has pointed out that in cases of heart failure due to chronic alcoholic poisoning, the tendo-Achillis-jerks are often absent, although no other sign or symptom is present. Out of 18 well-marked cases both tendo-Achillis-jerks were lost in 16 and one lost in 2. In 11 of these cases both knee-jerks were present. On the other hand, the tendo-Achillis-jerks were present in 98 out of 100 cases of cardiac disease not due to alcoholism; in the 2 remaining cases other signs of commencing tabes were present.

The results of our own observations and of some unpublished observations of Mr. Gordon Goodhart on cases of heart failure are in complete agreement with those of Williamson. So frequent is the association of an absent tendo-Achillis-jerk with heart failure due to alcoholism that the sign may be used with a considerable degree of confidence to determine whether a case of heart failure is alcoholic in origin when other evidence is inconclusive.

This latent alcoholic neuritis is rarely present in diseases due to alcohol other than heart failure. In a large number of cases of cirrhosis of the liver and of alcoholic gastritis we have only once found the tendo-Achillis-jerk absent; in this case the knee-jerks were present.

* R. T. Williamson: *Lancet*, 1907, vol. ii., p. 1774.

The remarkable difference between the frequency of the association of latent neuritis with heart failure and with other diseases due to chronic alcoholism suggests that the former may be due to the effect of the poison on its nerve supply rather than on its muscle. This would correspond with the fact that no degeneration changes have been found in the myocardium of patients dying from heart failure due to alcohol. Mr. Goodhart tells us that his still incomplete investigations on this subject support this view. We found, moreover, that a rapid pulse is almost constantly present in patients with severe alcoholic neuritis, even in the absence of all signs of heart failure. Just as the absence of tendo-Achillis-jerks is a sign of value in the diagnosis of alcoholic heart failure, so a rapid pulse is an important diagnostic point in determining the cause of peripheral neuritis affecting the legs.

Williamson* has also shown how frequently the absence of the tendo-Achillis-jerks indicates the presence of neuritis in diabetes, even when the knee-jerks are normal. In 50 consecutive cases the tendo-Achillis-jerks were both lost in 19 cases, and one was lost in 2 cases; in only 8 of these were the knee-jerks lost, and in none were they lost while the tendo-Achillis-jerks were still present. Mr. Gordon Goodhart found both tendo-Achillis-jerks lost in 2 and one in 3 out of 6 consecutive cases; the knee-jerks were present in all. When the patient complains of cramp and tenderness of the calves, the absence of the tendo-Achillis-jerks supports the view that these symptoms are due to a definite neuritis, but the sign is often present in patients who have no pain or discomfort at all. In some of these the loss of the jerks may be due to the degenerative changes in the posterior columns of the spinal cord, which Williamson has shown may occur in diabetes.

J. D. Rolleston† has studied the condition of the tendo-Achillis-jerks in diphtheria. Though completely lost in 20 and

* R. T. Williamson: Review of Neurology and Psychiatry, vol. i., p. 667, 1903.

† J. D. Rolleston: Brain, vol. xxviii., p. 68, 1905.

sluggish in 27 out of 100 cases, they were never absent when the knee-jerks were present, although the latter were lost in 11 and sluggish in 11 cases in which the tendo-Achillis-jerks were present. Diphtheritic neuritis thus differs from alcoholic and diabetic neuritis in that the examination of the knee-jerks is more likely to give evidence of latent neuritis than that of the tendo-Achillis-jerks.

(c) *Neuritis of the Sciatic and External Popliteal Nerves.*—During the period covered by these reports we have seen three cases of sciatica at Out-Patients and two in private, in whom the tendo-Achillis-jerk was absent on the affected side, which was in each case the left. In two of these there was no wasting, and the absent tendo-Achillis-jerk was the only sign pointing conclusively to an organic cause for the pain. The absence of the tendo-Achillis-jerk in sciatica shows that the case is a severe one, and the patient should continue to be careful after all pain has disappeared until the jerk returns, although this may not be until another year or more has elapsed.

A man, aged 56 years, felt a sudden sharp pain in his right leg. This was quickly followed by weakness and anæsthesia in the distribution of the external popliteal nerve. Eight months later the pain and anæsthesia had disappeared, and motor power was almost normal, but the tendo-Achillis-jerk was still absent. The nature of the lesion was never discovered.*

(d) *Other Diseases.*—In three cases of *anterior poliomyelitis* one tendo-Achillis-jerk was absent, though the knee-jerks were unaffected; in one of these, except for very slight weakness of the dorsi-flexors of the ankle, this was the only evidence that the leg had been affected, atrophy and paralysis of the deltoid of the opposite side being the prominent symptom.

* Since the above was written we have seen a patient with typical symptoms of a gumma involving the right side of the cauda equina: the knee-jerk was slightly less brisk on the right side than the left, and the tendo-Achillis-jerk, which was normal on the left side, was absent on the right.

A woman, aged 36 years, with the *neuritic peroneal type of progressive muscular atrophy (Charcot-Marie-Tooth),* which began to develop 20 years before, had naturally no tendo-Achillis-jerks, but both knee-jerks were still present. This is what is commonly found in the disease, and is due to the fact that the vastus internus remains in good condition.

A man, aged 64 years, with typical symptoms of *paralysis agitans* had no tendo-Achillis-jerks, although both knee-jerks were present. This is the only instance among our 12 cases of paralysis agitans in which the knee-jerks or tendo-Achillis-jerks were absent, but we had previously seen two other cases in which the tendo-Achillis-jerks were absent and knee-jerks present. Possibly in these cases some lesion of the spinal cord or peripheral nerves was present.

In a case of *subacute combined degeneration of the cord,* the knee-jerks were exaggerated, but the right tendo-Achillis-jerk was feeble and the left absent.

In conclusion, we wish to record our indebtedness to Dr. R. T. Williamson, in whose wards at the Manchester Royal Infirmary the importance of the tendo-Achillis-jerk was first demonstrated to one of us seven years ago. We are also indebted to Mr. Gordon Goodhart, who has kindly allowed us to make use of the unpublished investigations which he carried out at the suggestion of one of us on the latent neuritis of diabetes and alcoholic heart failure.

2. BABINSKI'S "SECOND SIGN"—COMBINED MOVEMENT OF THE TRUNK AND PELVIS.

By

A. F. HERTZ, M.D.

With Case Reports by T. I. Bennett, G. A. Blake, E. A. Penny and B. R. Parmiter.

When a normal individual, lying down with his legs widely separated and his arms folded, tries to sit up, both legs rise from the ground to an equal extent. On now letting himself fall back sharply on to a pillow both legs again rise equally from the ground.

In a case of organic hemiplegia, as soon as the patient is strong enough to be able to sit up with little or no assistance, the paralysed leg rises higher than the healthy limb. This is not what the uninitiated would expect, and consequently in hysterical hemiplegia—in which the paralysis conforms to the lay conception of paralysis—the paralysed leg remains flat on the ground, both on sitting up and lying down, although the voluntary action of some of the muscles supposed to be paralysed is required for the purpose. This important distinction between organic and hysterical hemiplegia was first observed by Babinski, who described it as the sign of "combined movement of the trunk and pelvis." For the sake of brevity I am in the habit of referring to it as the "second Babinski sign."

My experience completely confirms Babinski's statements as to its value. I have rarely failed to obtain the combined movement of the trunk and pelvis in an organic upper neurone paralysis of one leg, whether present by itself or as part of a

hemiplegia, and I have never seen it in a case of hysterical paralysis.

As a rule, the presence or absence of the well-known Babinski sign—the extensor plantar reflex—is sufficient to distinguish between organic and hysterical hemiplegia. But occasionally no plantar reflex can be obtained, even after the foot has been soaked in hot water. Moreover in children under the age of three the reflex is normally extensor, so that the sign is of no value. Finally, in rare instances, a flexor plantar reflex is found in cases in which the history, the gait and the presence of an exaggerated knee-jerk and ankle-clonus render a diagnosis of organic paralysis extremely probable. It is in these three conditions that Babinski's second sign may be of great assistance.

In the following cases the diagnosis of an organic upper neurone paralysis received valuable confirmation from Babinski's second sign, when the plantar reflex had failed to give the required information.

1. *Case of Birth Hemiplegia.* Reported by G. A. Blake.

Caroline C., aged 17 months, was a full term twin, the other being still-born. The labour was difficult and prolonged, but no instruments were used. The left arm and leg appear to have always been weak, but all movements can be performed, no muscle being completely paralysed. She is still unable to walk, and supports most of her weight on her right leg when she stands. She generally keeps the left arm flexed at the elbow, and the fingers clenched, but opens them when told to do so.

The knee-jerks and tendo-Achillis-jerks are distinctly more active on the left than the right side, but there is no ankle clonus. There is no muscular atrophy, and the history and general appearance of the limbs point to a diagnosis of organic hemiplegia, due to some lesion of the right side of the brain produced at birth. The plantar reflex is extensor on both sides, as is normally the case in infants. The abdominal reflex is not less brisk on the left than the right side.

Although the symptoms suggested an organic upper neurone lesion, and the increased knee-jerk supported this diagnosis, the conclusive evidence which an extensor plantar reflex might have afforded in an older patient was wanting. The presence of a well-marked "Babinski's second sign" was therefore of considerable importance. The child was easily persuaded to sit up with her legs widely apart, and regarded being pushed back again as part of a game.

2. *Case of Hemiplegia following Typhoid Fever.* Reported by E. A. Penny.

Theobald J., aged 31 years, an army pensioner, attended the hospital on December 7th, 1910. He had typhoid fever in 1902 in South Africa; about the end of the second week of his illness he woke one morning to find that the left side of his face and his left arm and left leg were paralysed. The paralysis diminished for a time, but after some months no further improvement occurred. There was decided weakness of the lower facial muscles on the left side; the arm muscles were weak, but well developed, and the jerks on the left side increased; the left leg was weak, and both knee- and ankle-jerks were markedly increased, true ankle clonus being obtained. The gait was characteristic of an organic hemiplegia. The evidence was, so far, strongly in favour of the case being one of organic hemiplegia, due probably to cerebral softening following thrombosis occurring during typhoid fever. It was therefore expected that the plantar reflex would be extensor on the left side. This, however, was not the case, for the reflex was as definitely flexor on the left as on the right foot. "Babinski's sign" being absent, the organic nature of the hemiplegia became less certain. The patient, lying flat upon his back with his arms folded over his chest and his legs separated from each other, was told to try and rise to the sitting posture without making use of his arms. At each attempt to do so, both legs rose from the floor, but the paralysed leg always rose higher than its fellow. Exactly the same thing happened when the patient fell back from the sitting to the dorsal position. "Babinski's second sign" being positive, there could be no further doubt about the organic nature of the hemiplegia.

3. *Case of Hemiplegia of doubtful origin.* Reported by T. I. Bennett.

Middleton L., aged 31 years, became suddenly hemiplegic while at work. He fell down, but did not lose consciousness. For ten days his left arm and leg and the left side of his face were almost completely paralysed. He then gradually improved. When first seen—three weeks after the onset—the left arm was still very weak, but the left side of the face was only slightly affected, and the patient could walk well. though the left leg was inclined to drag. The left knee-jerk was exaggerated, there was no ankle-clonus and the plantar reflex was flexor. Babinski's second sign was, however, very well marked.

The Wassermann reaction was negative, his heart was healthy, and there was no albuminuria. No cause for the attack could be discovered.

4. *Case of Cerebral Hæmorrhage.*

Mr. H., a patient of Dr. Randell of Beckenham, was perfectly well until the 11th November, 1911, when he suddenly had a sensation of pins and needles and felt weak in his right leg whilst he was playing billiards.

A few minutes later the sensation spread to his right hand, and he found that delicate movements such as writing could not be efficiently performed. He was also occasionally unable to find the correct word when talking. The weakness and numbness rapidly diminished, and on the 14th the numbness had almost disappeared. The right leg was held somewhat stiffly, but was not obviously weak, and the grip of the right hand was quite powerful, although there was still some difficulty in performing delicate movements accurately.

On examination a trace of albumen was found in the urine, and the blood-pressure was 218 mm., although the heart was not obviously hypertrophied. The wrist-jerks could not be obtained on either side, the knee-jerk was very slightly brisker on the right side than on the left, and ankle clonus was absent. The plantar reflex was quite definitely flexor on both sides; the abdominal reflexes were normal.

In spite of the history, which pointed very strongly to the occurrence of a small cerebral hæmorrhage as a result of the high blood-pressure associated with granular kidney, no definite physical signs of organic hemiplegia were present, and the flexor plantar reflex might have been regarded as evidence that the condition was functional. However, "Babinski's second sign" was extremely well marked, particularly when the patient raised himself from lying down to the sitting position.

5. *Case of Hemiplegia from Cerebral Hæmorrhage.* Reported by B. R. Parmiter.

Albert D., aged 54 years, a hop porter, had rheumatic fever twenty years ago. Fourteen days ago he caught a chill, and two days later he noticed weakness of his left arm and left leg, and he had some difficulty of articulation. All these signs have since improved, and the gait is now quite normal. Pupils are equal and react to light and accommodation; in winking the left orbicularis is weaker than the right and is more easily pulled open when voluntarily contracted. His leg muscles are weaker on the left side. The knee-jerks are both brisk, and the left tendo-Achillis-jerk is the stronger. The plantar reflex is flexor on both sides. Sensation is normal. Babinski's second sign, however, was very well marked, and showed that the weakness of the left leg was due to an organic upper neurone lesion. The patient's blood-pressure is 205 mm. Hg, and his arteries are bad. His urine has sp. gr. 1008 and contains a small quantity of albumen. The hemiplegia is, therefore, probably due to cerebral hæmorrhage, the result of granular kidney.

3. SALVARSAN IN THE TREATMENT OF SYPHILITIC DISEASE OF THE CENTRAL NERVOUS SYSTEM.

By

G. H. HUNT, M.A., M.B., B.Ch.

Case 1.—*Juvenile Tabes.*

Ellen M., aged 15 years, was admitted in November, 1910, under Mr. Ormond. She had been suffering from headache and defective sight for the last nine months; she had also some difficulty in beginning the act of micturition. On admission the eyes did not react to light nor to accommodation; there was well-marked optic atrophy on both sides, and vision in both eyes was less than 6/60. The knee-jerks and tendo-Achillis-jerks were absent; the plantar reflex was flexor. Sensation was normal. Lymphocytes were found in the cerebro-spinal fluid. The Wassermann reaction was positive.

There were nodes on both tibiæ, but no other signs of congenital syphilis, and nothing suggestive of it in the mother's personal history, although her blood gave a partial Wassermann reaction. Salvarsan was injected intramuscularly. After the injection the headaches completely ceased and there was no further difficulty with micturition.

The eyesight, however, did not improve. The patient was re-admitted in July, and whilst in hospital suddenly developed an organic hemiplegia involving the face, arm and leg on the left side. This was treated with mercury and iodide, and rapidly improved. The patient was examined again on August 30th; all trace of the hemiplegia had disappeared. The condition of the eyes and reflexes was unchanged. The Wassermann reaction was still positive.

Case 2.—*Syphilitic Paralysis of Sixth Nerve.*

Henry H., aged 28 years, was admitted in December, 1910, under Dr. Shaw from the Neurological Out-Patient Department. He complained of diplopia when looking to the left. The symptoms started about six months before admission. On admission there was partial paralysis of the left external rectus muscle. The plantar reflex was extensor on both sides; the knee-jerks were brisk, but otherwise the reflexes were normal. The cerebro-spinal fluid was examined before and after injecting salvarsan and was normal on each occasion. The patient had had syphilis eight years previously, and the Wassermann reaction was positive. Salvarsan 0·6 gm. was injected intramuscularly, and the patient was also

treated with mercury and iodide for six months. He was examined again in July, 1911, but the condition of the eyes showed no improvement, and the plantar reflexes remained extensor. The Wassermann reaction was still positive.

Case 3.—*Gumma of Cauda Equina.*

Richard C., aged 40 years, was admitted in January, 1911, under Dr. Shaw from the Neurological Out-Patient Department. For three months he had suffered from pain and weakness in both legs; the muscles of the right calf were first affected, then those of the right thigh; later on the muscles of the left thigh became weak, and finally those of the left calf. The patient had had syphilis nine years previously, but was only treated for seven weeks.

On admission the muscles of both legs were very weak, flabby and somewhat wasted. The knee-jerks and tendo-Achillis-jerks were absent on both sides. The plantar reflex was flexor. There were some rather indefinitely limited patches of anæsthesia on both legs, and some tenderness over the sacrum. The Wassermann reaction was positive.

Salvarsan 0·6 gm. was injected intramuscularly. After the injection the pains ceased at once, but during the next three weeks there was only a very slight improvement in muscular power. Mercury and iodide were accordingly prescribed, and labile cathodal galvanism was applied to both legs. Under this treatment the patient gradually improved, and when seen in July he was able to walk without the aid of a stick. The left knee-jerk had returned, but the other deep reflexes were still absent. He had had no return of the pain. The Wassermann reaction was still positive.

Case 4.—*Disseminated Sclerosis, possibly syphilitic.*

Edwin S., aged 27 years, was admitted under Dr. Shaw in December, 1910. The patient complained of difficulty in walking in a straight line, tremor of the hands, deafness, headache, difficulty in speaking and occasional incontinence of urine. The symptoms started about nine months before admission. He denied having had syphilis, but the Wassermann reaction was positive.

On admission the patient could walk without assistance, but the gait was spastic. The knee-jerks were exaggerated, and the plantar reflex was extensor on both sides. There was some loss of power and an intention tremor in the right hand and forearm. The abdominal reflexes were absent. There was well-marked nystagmus ; the optic discs were normal. The speech was hesitating and slightly staccato. Sensation was normal. A few lymphocytes were found in the cerebro-spinal fluid.

Although the symptoms were suggestive of disseminated sclerosis, which was the accepted diagnosis during the two months he attended the Neurological Out-Patient Department before admission, the presence of a positive Wassermann reaction and of lymphocytes in the cerebro-spinal fluid made a syphilitic origin of the disease probable.

The patient showed some slight improvement under mercury and iodide, but it was doubtful whether this was due to general treatment or to the medicine, and therefore the change did not assist in settling the diagnosis. He was re-admitted towards the end of February, 1911, and salvarsan 0·6 gm. was injected intravenously. This did not cause any further improvement, and when he was seen in July, 1911, his condition was unaltered. The Wassermann reaction was still positive.

Case 5.—*Syphilitic Spinal Meningitis.*

Robert R., aged 35 years, was admitted in February, 1911, under Dr. Shaw from the Neurological Out-Patient Department. He complained of attacks of acute pain in the lower part of the thorax and upper part of the abdomen. The symptoms started about two months before admission. The patient had had syphilis seven years previously, and received treatment for about a year.

On admission there was marked tenderness over the seventh and eighth dorsal spines, and a zone of hyperæsthesia on the skin supplied by the corresponding spinal segments. Cutaneous sensation was otherwise normal; deep sensation was impaired in the muscles of the calf, and testicular sensation was much diminished. Both recti abdominis muscles were weak, but there was no loss of power in the legs. The knee-jerks were present, and the plantar reflex was extensor on both sides. A considerable number of lymphocytes were found in the cerebro-spinal fluid, and the Wassermann reaction was positive.

Salvarsan 0·6 gm. was injected intravenously, but no improvement resulted. Three weeks later mercury and iodide were prescribed, but as there was no change after a month, salvarsan 0·6 gm. was again injected intravenously, again no improvement followed, and the patient was accordingly given intramuscular injections of perchloride of mercury. After five weeks of this last treatment the pain completely disappeared and the recti became stronger, but the extensor plantar reflex remained unaltered. The Wassermann reaction was still positive.

Case 6.—*Syphilitic Spinal Softening.*

Charles M., aged 53 years, was admitted in April, 1911, under Dr. Shaw. For the last nine years the patient had suffered from weakness of the legs. He had syphilis 31 years ago, but was only treated for a short time.

On admission the gait was spastic, and the patient was only able to walk with great difficulty. The knee-jerks and tendo-Achillis-jerks were exaggerated; both plantar reflexes were extensor; ankle clonus was present on the right side. The Wassermann reaction was positive. The patient had been treated with mercury and iodide for four months in the Neurological Out-Patient Department without any improvement. Salvarsan 0·6 gm. was injected intravenously. A very marked improvement followed. When seen in August the patient was able to walk almost as well as a normal person, and the Wassermann reaction was negative.

Case 7.—*Syphilitic Basal Meningitis.*

Sarah A., aged 52 years, was admitted in May, 1911, under Dr. Shaw. For some years the patient had suffered from headache and noises in the left ear. Three years ago she developed facial paralysis. There was no history of syphilis.

On admission the left side of the face was completely paralysed; the left half of the tongue was greatly atrophied; the adductors of the left vocal cord were paralysed, and there was considerable weakness of the left sterno-mastoid. There was nerve deafness on the left side. There was no optic neuritis. The Wassermann reaction was positive. As mercury and iodide had been given for two and a half months in the Neurological Out-Patient Department without result, salvarsan 0·5 gm. was injected intramuscularly. There was no immediate result, but when the patient was seen again at the end of August she stated that the headaches and noises in the ear were much less troublesome since the injection. There was a distinct increase in power in the sterno-mastoid muscle, but otherwise the paralysis showed no improvement. The Wassermann reaction was negative.

Case 8.—*Syphilitic Meningitis.*

The patient, a man aged 26 years, was admitted in August, 1911, under Dr. Hertz. Three days before admission he was seized with severe headache which continued without intermission. During this period he vomited about six times. There was a small patch of anæsthesia on the outer side of the right foot, but otherwise nothing abnormal was detected in the nervous system, and the optic discs were normal. The vascular, respiratory and alimentary systems were healthy. A condition of atrophic rhinitis was present, but there was no evidence of disease in the accessory nasal sinuses. The patient denied syphilis, but the Wassermann reaction was positive.

Salvarsan 0·4 gm. was injected intravenously. The injection was followed by a rigor and vomiting, and the temperature was raised for some hours. On the next day the pyrexia had disappeared, and the headache was much better. On the third day the patient's general condition was very satisfactory, and the headache had completely gone.

Comments.

The results of treating cases of syphilitic paralysis with salvarsan are not very encouraging. In Case 6, it is true, the patient derived very striking benefit. When he came into hospital he had so much difficulty in walking that he was completely incapacitated for work. The injection of salvarsan accomplished an almost complete cure in a few weeks. This was the more remarkable in view of the fact that the symptoms

had first appeared nine years previous to his admission, and it was hardly to be expected that much improvement would take place in a case where the process of degeneration had gone on for so long. A very slight improvement was noticed in Cases 1 (bladder), 3 (sternomastoid), and 7 (leg muscles), but in none of the other cases was the paralysis at all affected.

It has already been shown that salvarsan seems to be of greater service in treating the pain associated with syphilitic disease of the central nervous system than in treating paralysis,* and the results in these cases are in harmony with this observation. In only one case (5) did it fail to relieve pain; in three cases (1, 7, 8) severe headaches were either completely cured or much relieved, and in Case 3 the pains in the legs completely disappeared after the injection. Case 8 is particularly striking in this respect.

With regard to the relative merits of mercury and iodide and salvarsan, the results are conflicting. The most striking contrast is found in Cases 5 and 6. In Case 5, two injections of salvarsan were given without the smallest benefit, whereas the pains completely disappeared under the influence of intramuscular injections of mercury. This case also illustrates the fact that mercury given in this way may yield better results than when taken by the mouth. In Case 6, on the other hand, the salvarsan treatment was more successful. The patient had taken mercury and iodide for at least four months without any obvious relief, but he rapidly improved after the injection of salvarsan. In Cases 3 and 7 the difference was not very striking ; in the former, mercury seems to have given better results, in the latter, salvarsan. In Cases 2 and 4 neither drug was of any service.

It is important to remember that the majority of cases of syphilis of the central nervous system do very well under the influence of mercury and iodides. In a large proportion of cases seen in the Neurological Out-Patient Department improvement was so rapid and so complete that it was not considered necessary to inject salvarsan.

*Bresler : *Salvarsan bei Syphilitischen Nervenkrankheiten*, Halle, 1911.

In view of the doubts that have been cast upon the value of the Wassermann reaction, it is of interest to notice that in all cases the reaction was positive. In spite of treatment with mercury and salvarsan the reaction only became negative in two cases (6 and 7), which were also those in which the improvement was most marked. This is in accordance with the observation of Willige,* who found that the reaction became negative in cases which showed the most progress. In future it may be advisable to repeat the injections in the hope that the reaction may become negative.

There were no very serious ill effects from the administration of salvarsan. In only one of the cases (8) in which the intravenous method of injection was used was there any marked immediate disturbance. In the other three cases there was a slight rise of temperature and pulse rate accompanied by sensations of general discomfort and pain; on one occasion morphia had to be injected to relieve the pain. After intramuscular injection the local reaction was always rather painful, and on two occasions went on to abscess formation; the wounds resulting from the opening of these took some weeks to heal. In one case there was considerable constitutional disturbance after an intramuscular injection. The intravenous method is certainly to be preferred, as being much less painful and more rapidly efficacious. In Case 1 an organic hemiplegia lasting a few days developed six months after the injection. This completely disappeared under mercury and iodide, and was probably a syphilitic manifestation and not a result of poisoning by salvarsan.

My thanks are due to Dr. Shaw, Mr. Ormond and Dr. Hertz for permission to publish these cases.

Addendum.

Among the cases of syphilitic disease of the nervous system treated with salvarsan since the above report was written one is of such special interest that a short account of it is added.

*Quoted by Bresler, loc. cit.

Spastic Diplegia from Bilateral Syphilitic Cerebral Endarteritis.—George M., aged 24 years. was admitted under Dr. Hertz at the end of August, 1911. Two years previously he had noticed some stiffness in the right arm and leg; he recovered completely after being given medicine for six weeks. A week before admission he came to the Neurological Out-Patient Department for spastic paresis of the right leg, which had developed during the previous two or three weeks. The knee-jerk was increased and the plantar reflex was extensor; the other limbs were unaffected, and there were no other signs of disease. The paresis was believed to be due to syphilitic cerebral endarteritis, and Pot. Iod. gr. xxv and Liq. Hydrarg. Perchlor. 1 dr. were given three times a day for a week. In spite of this no improvement occurred, and during the week the other leg and both arms became affected.

On admission the patient could not walk without the aid of a stick. The knee-jerks and tendo-Achillis-jerks were exaggerated, the plantar reflex was extensor on the right and unobtainable on the left; a week before it had been definitely flexor. Ankle clonus was present on the left side and patellar clonus on the right. The grip of the right hand was rather weaker than that of the left, but both sides were obviously weaker than normal. Syphilis was denied, but the Wassermann reaction was positive.

Salvarsan 0·5 gm. was injected intravenously, and two days later there was a distinct increase in power in the right hand; a few days later the patient was able to walk without assistance. The same amount of salvarsan was again injected intravenously after a fortnight.

When seen at the end of September he had no difficulty in walking, except that the right leg was still dragged a little, and both arms had regained their normal strength. The plantar reflex was still extensor on both sides. The Wassermann reaction was now negative.

The main interest in this case lies in its bearing on the question of the relative efficacy of mercury and salvarsan. In the course of a single week a spastic monoplegia developed into a diplegia, although during this period the patient was taking mercury and iodide. Then salvarsan was injected and the paralysis of the left leg and arms rapidly disappeared, and that of the right leg was greatly improved. It will also be noticed that in this case, as in the two others in which the improvement was most pronounced, the Wassermann reaction became negative.

4. A STUDY OF THE ÆTIOLOGY AND SYMPTOMS IN SEVENTEEN CASES OF TABES.

BY

H. W. BARBER, B.C.

I HAVE compiled from various authoritative sources a list of the ætiological factors possibly concerned in the causation of tabes together with the chief symptoms of the disease, and I propose in the following paper to consider these with reference to seventeen cases which I have had the opportunity of examining. With one exception these cases were under the care of Dr. Hertz as Out-Patients, and I have to thank him not only for allowing me to make my investigations, but also for valuable help and advice in preparing this paper.

A.—ÆTIOLOGY OF TABES.

1. *Venereal Disease.* (a) *Syphilis.*—The view that syphilis is an essential factor in the production of tabes is held by many authorities, and an enormous mass of evidence in its favour has been put forward by various observers. Whether tabes ever occurs without previous syphilis can hardly be absolutely proven, but it must be remembered that a patient—especially among the lower classes—may deny the disease in all good faith, because his attack has been slight enough to pass unrecognised. Indeed, it seems likely that these mild attacks of syphilis—possibly because they are treated inefficiently or not at all—are more commonly followed by parasyphilitic affections than those in which the symptoms are severe.

Of my own cases nine gave a definite history of the disease. Of the remainder two admitted gonorrhœa, but denied syphilis, although they both gave a positive Wassermann reaction; one

gave a history of a soft sore; four denied venereal disease of any kind; and in the remaining case—a woman who had married twice—there was a history of sterility following the birth of one child, but no history of miscarriages.

Of the four patients who denied venereal disease, one gave a positive Wassermann reaction on two occasions; one had had no children by two wives, and gave a positive Wassermann reaction; one gave a negative Wassermann reaction on three occasions, but in his groin was the scar of an inguinal abscess, and he had no children, his wife having miscarried on three occasions. The remaining patient strenuously denied all venereal infection—in fact he stated he had never had connection before his marriage—and his family history was without suspicion; unfortunately I did not have the opportunity of performing Wassermann's test on him.

It is now well known that the blood serum and cerebro-spinal fluid of tabetics generally give a positive reaction to Wassermann's test. In twelve of my cases the blood serum was tested, and eleven positive reactions were obtained; in two of these the cerebro-spinal fluid was also examined with positive results.

Interval between the attack of Syphilis and onset of Tabetic Symptoms.—The interval could be determined in eight of my cases: in five of these it was between 9 and 14 years; in the remaining three it was 24, 34 and 38 years respectively.

(b) *Gonorrhœa.*—More than one authority has suggested that gonorrhœa may play an important part in the ætiology of tabes. Of my cases ten admitted infection, but it seems to me that it is extremely unlikely that the disease is a factor of any importance.

Granting that a syphilitic soil is essential, it is probable that there are certain secondary factors which predispose to the development of tabes. Many have been suggested, but the most important appear to be physical and mental stress of any kind, injury, alcoholism, sexual excess and exposure to debilitating atmospheric conditions.

2. *Physical Stress.*—In the large majority of tabetics the legs are affected either alone or before the arms, and a history of

excessive standing is often volunteered by tabetic patients. Thus of my cases thirteen gave such a history. In those cases in which the arms are first or chiefly involved it is usually found that the patient's occupation has thrown a greater strain on his upper than on his lower extremities; thus, in two of my cases the symptoms were marked in the arms: one was a carpenter, the other a clerk.

3. *Mental Stress and Worry.*—A history of worry is more commonly obtained in cases of general paralysis or tabo-paralysis than in ordinary tabes, but of my cases five gave an unsolicited story of family and other troubles which they considered were partially responsible for their disease.

4. *Injury.*—Some observers have described cases of so-called traumatic tabes, but, although a history of injury preceding the onset of tabetic symptoms is not uncommon, it is very doubtful whether trauma is ever anything but a contributory cause of the affection. Two of my patients attributed the onset of their symptoms to injury. In both cases the association was rather striking, but one of them had suffered from lightning pains for some time before his accident, although the latter was almost immediately followed by difficulty in micturition and marked ataxy.

5. *Alcoholism and Sexual Excess.*—Tabetics and general paralytics have often been heavy drinkers, and many of them admit sexual excess, but it must be remembered that alcoholic and sexual intemperance are often early symptoms of general paralysis, and that the early stages of tabes may be associated with increased sexual appetite. Probably also severe attacks of lightning pains may drive a man to seek relief in drinking bouts. At the same time the pernicious influence of alcoholism and sexual excess on the nervous system is undoubted, and they may rightly be regarded as exciting causes in the production of parasyphilitic affections. Of my cases six gave a history of alcoholism, and six—not the same patients—of sexual excess.

6. *Exposure to Cold or Wet.*—This has been suggested as a rare primary cause of a few undoubted cases of tabes, but

such a view is probably erroneous. That it may aggravate the disease when already present is well shown by one of my cases, who for two years had had lightning pains with little or no ataxy. One day, however, he had a long and weary tramp in the rain over ploughed fields, and on the following morning he was almost unable to rise from his bed, much less to walk. When, after a few days' rest, he was capable of getting about again, his ataxy was so great that he could not walk without a support on either side of him. His ataxy eventually diminished in an extraordinary way under the influence of Fraenkel's exercises.

It may thus, I think, be safely concluded that syphilis is the essential factor in the development of tabes, but that, in the presence of syphilis, debilitating influences acting on the central nervous system predispose to the disease.

B.—Age of Onset.

Of my cases, the age of onset in four was between 30 and 40, in five between 40 and 45, in two between 45 and 50; in one it was only 23, and in another it was 61.

C.—Mode of Onset.

1. *Lightning pains* are usually the first symptoms noticed by the patient. Twelve of my cases dated the beginning of their trouble to the appearance of these pains.

2. *Diplopia.*—In two of may cases this was the first symptom. Diplopia, however, due to ocular paralysis of specific origin, often occurs without the subsequent supervention of tabes, so that it is not necessarily a symptom of a parasyphilitic affection. One of my cases had diplopia seven years before the onset of the lightning pains, and it is probable that the latter was the first symptom of his tabes.

3. *Failing vision* marked the onset in my case of optic tabes; this was followed a year later by lightning pains.

4. *Difficulty in micturition, with occasional incontinence,* was the first symptom in one of my cases; lightning pains supervened a year later.

5. In a case of amyotrophic tabes *weakness in the hands with paræsthesiæ* was the first complaint.

D.—The Symptoms of Tabes.

1. *Ocular Symptoms* (a) *Pupils.*—The pupil changes in tabes are usually marked and of considerable importance in diagnosis. Irregularity of outline and of size, and eccentricity of position are common and characteristic features, but I am convinced that a true Argyll-Robertson pupil, *i.e.*, complete absence of response to light with normal response to accommodation, is rarer than is usually supposed. In testing the response to light great care must be taken to ensure that any contraction that occurs is not due to accommodation. In all of my cases, without exception, the pupil outline on one or both sides was irregular; in eleven the two pupils were unequal in size. In *only three* was there a true Argyll-Robertson pupil, but in the remainder the reaction to light was sluggish, though distinct. In twelve the reaction to accommodation was brisk, in three very sluggish; in one there was complete inactivity both to light and accommodation; and in the remaining patient the right pupil reacted sluggishly to accommodation and the left to neither.

In addition to the above features myosis is often very marked. This was so in eight of my patients, and in another one pupil was very small and the other widely dilated.

(b) *Diplopia.*—Six of my patients gave a history of diplopia, and in every case it occurred early in the course of the disease. The external rectus muscle is most frequently affected, but in two of my cases, in which the paralysis was present at the time of examination, the internal rectus was at fault.

(c) *Ptosis.*—In only one of my patients was there ptosis at the time of examination; it was unilateral, and was accompanied by complete paralysis of the corresponding internal rectus and

paresis of the other muscles supplied by the third nerve. The ptosis and diplopia had been present for five years.

(d) *Optic Atrophy.*—In only one of my cases, the majority of whom were examined by experienced oculists, was there optic atrophy. This patient was an example of so-called optic tabes. Failing vision was his first symptom, and this was followed one year later by typical attacks of lightning pains. On examination it was found that with the right eye his vision was 6/24, but with the left was less than 6/60; both discs showed optic atrophy, more especially the right. The patient had no trace of ataxy, and did not exhibit Romberg's sign. His knee-jerks were absent.

2. *Sensory Symptoms.*—These may be divided into subjective and objective. The chief subjective ones are lightning pains, girdle pains and various paræsthesiæ. The objective sensory disturbances in tabes are numerous and very tedious to investigate.

(a) *Lightning Pains.*—This is an extremely important and very distressing symptom of the disease, but it is one that is oftentimes misinterpreted. Several of my patients informed me that they had been thought to suffer from "rheumatism" or "neuritis" or sciatica." The importance of the symptom is due to its constancy and its early appearance. It was present in all my cases. In fifteen the legs were affected first, and in six alone. The arms and the thorax are the next commonest regions to be involved.

The characteristics of the lightning pains vary somewhat in different cases. Thus they may be felt to be deep or superficial or both. In nine of my cases they were deep, in two superficial, in five both kinds were present, and in one—a patient with severe thoracic pains—they were felt "between the skin and the ribs." In some of my cases the attacks of pain lasted for only a few minutes, in some for several hours; in four patients they were followed by superficial tenderness. Fatigue, cold, and in some cases the warmth of bed were predisposing causes.

(b) *Paræsthesia and Girdle Sensations.*—With two exceptions some form of paræsthesia was present in all my cases, and three patients complained of a definite girdle sensation.

In most cases there was numbness, tingling and coldness of the feet; two patients said they felt as though they were walking on cotton-wool, another on snow, and another on springs.

In five cases there were numbness and tingling in the hands, and in two of these the paræsthesia was confined to the little and ring fingers. I have never met with facial paræsthesia (Hutchinson's mask).

(c) *Objective Sensory Disturbance.* (i.) *Anæsthesia; hyperæsthesia.*—Areas of complete or partial anæsthesia of the skin can almost always be found in tabetics, if systematically sought for. The commonest situations for anæsthetic patches are the feet, the legs, the inner side of the arms, the genitals and the thorax. The frequency of relative anæsthesia of the ulnar side of the forearm is particularly noticeable. It was present in nine of my cases. In some cases patches of hyperæsthesia are present, due presumably to irritation prior to destruction of the root fibres. I have found that the soles of the feet are often extremely hyperæsthetic, and this is accompanied by a much exaggerated plantar reflex. This was so in seven of my cases, but in two of these a second examination after an interval of some months showed that anæsthesia and loss of the plantar reflex had intervened. One of my cases had a complete zone of hyperæsthesia round the trunk, corresponding to the sensory distribution of the sixth and seventh dorsal nerve roots; this hyperæsthesia was accompanied by frequent "girdle sensations."

I have neither met with *allocheiria,* in which a touch or prick on one side of the body is referred to the other side, nor *polyæsthesia,* in which a single touch or prick may be felt in several situations at once.

(ii.) *Analgesia* is, to my mind, a very important symptom. I have found that the commonest situation for analgesia is the ulnar border of the forearm. It was present in nine of my cases.

The sensation produced by compressing the calf muscles, which is often so markedly increased in peripheral neuritis, is usually diminished in tabes. This was so in eleven of my cases.

(iii.) *Biernacki's Sign.*—I have been greatly impressed by the importance of Biernacki's sign, as it was present in 15 out of 16 of my cases. It is tested by pressing the ulnar nerve firmly against the internal condyle of the humerus. In normal people an extremely unpleasant sensation is thus produced, which may be accompanied by a tingling feeling along the inner side of the forearm. Biernacki's sign is positive when the procedure causes no discomfort.

(iv.) *Egger's Test.*—A vibrating tuning-fork pressed firmly on the bones of a tabetic often produces no sensation of its vibration. This sign was present in five out of nine of my patients. The bones of the leg and the lower end of the spinal column in my limited experience most frequently yield the sign, but in the case of optic tabes the third, fourth and fifth ribs were the only bones affected, and the overlying skin was the only area of tactile anæsthesia and analgesia that could be discovered.

(v.) *Insensibility of the Testicles to pressure* was present in 9 out of 13 patients, and was usually associated with diminished sexual desire or with absolute impotence.

3. *Visceral Disturbances.* (a) *Bladder.*—Inquiry into the history of my 17 tabetics elicited some story of bladder trouble in 15. Such symptoms often occur quite early, and in fact may be the first to be noticed by the patient, but it is often only temporary. Difficulty in beginning the act of micturition, imperfect control with occasional incontinence, and inability to empty the bladder completely are the most usual symptoms. Incontinence came on quite suddenly in two of my cases, but more or less complete control was subsequently regained.

My most interesting case was that of a man who never had any desire either to micturate or defæcate; but he was quite able to perform both acts, and this he did at regular intervals.

(b) *Rectum.*—Constipation is very common among tabetics, but two of my cases had a peculiar kind of "morning diarrhœa"

accompanied by tenesmus, and presumably of the nature of a *rectal crisis*. At the suggestion of Dr. Hertz, he and I have carried out a series of investigations on the rectal muscle-sense in tabetics, comparisons being made with that of normal persons. A preliminary account of our results appeared in Dr. Hertz's Goulstonian Lectures, but we hope to publish them more fully at another time; suffice it to say that in nearly every case of tabes a higher pressure was necessary to produce the call to defæcation than in normal persons, and that, whereas in normal persons the sensation only remained for a few seconds, in tabetics it remained much longer—sometimes for several minutes —after the stimulus had ceased to be in operation.

(c) *Crises.*—Curiously enough in only one of my cases could I obtain a history of *gastric crises*. My patient was no exception to the rule that gastric crises are accompanied by complete or partial anæsthesia in the mid-dorsal region, and often by " girdle sensations," for he had a most marked band of trunk anæsthesia, and was frequently seized with a girdle sensation quite apart from his gastric crises.

Bladder crises are very rare, but one of my patients gave a history very suggestive of them. Two years before examination he used at times to be seized with violent pain in the bladder region; the desire to micturate was intense, but he was unable to do so.

Laryngeal crises are said to occur next in frequency to those of the stomach. In only one of my patients could I obtain a history of them. In his case they consisted of a sense of constriction in the throat, accompanied by cough and considerable dyspnœa.

4. *Locomotor Disturbances.*—One of the most characteristic features of tabes is the impairment of muscle-sense, and this would seem to be the chief cause of the ataxy, the muscular hypotonus, and the loss of the tendon responses. Closely allied to muscle-sense is joint sensibility, which is also usually affected in tabes, and is no doubt partly responsible for the ataxy. Seven

out of 13 of my patients were unable to state the position of their toe-joints after the latter had been moved in different directions.

Romberg's Sign, "Rombergism" and Ataxy.—Romberg's sign, like the Argyll-Robertson pupil, has become one of the classical signs of tabes. Like the ataxy, it is dependent on impairment of muscle and joint sensibility, the patient, when robbed of the guidance of vision, being unable to maintain his equilibrium. Not every tabetic exhibits Romberg's sign in the strict sense of the term; but it will usually be found that those who do not are more unsteady when standing on one leg than normal people, and that they are quite unable to keep their balance on one leg with closed eyes. There are thus numerous degrees of "Rombergism" which are of considerable importance in the early diagnosis of tabes.

In the same way ataxy may not be noticeable in a tabetic patient when he is allowed to walk in the ordinary fashion, but it can usually be elicited when he is told to walk with his eyes closed or fixed on the ceiling. A very delicate test of ataxy is walking along a straight line in "toe-to-heel" fashion; thus, in three of my patients Romberg's sign was absent, and they were able to walk without obvious ataxy with their eyes closed, but they were absolutely unable to keep their balance when walking "toe-to-heel."

Among my cases only the patient with optic tabes had no sign whatever of Rombergism or ataxy; three had very marked ataxy and Rombergism; four had marked Rombergism without much ataxy, but all these cases had formerly been very ataxic, one having improved enormously by means of Fraenkel's exercises since he first attended Out-Patients two years before; the rest had both symptoms in a slight or moderate degree.

5. *Superficial Reflexes.*—The epigastric and abdominal reflexes are usually present, but if the area of skin stimulated is anæsthetic, the reflex is absent. Thus in one of my patients the epigastric reflex was absent, the abdominal present; the absence

of the former was associated with an area of tactile anæsthesia in the upper part of the abdomen. The cremasteric reflex is of importance, because its absence is usually correlated with loss of testicular sensation and diminished sexual desire or actual impotence. In five out of fifteen of my patients both cremasteric reflexes were absent, and both testicles were devoid of sensation; in five both testicles were sensitive and both reflexes present; in one an insensitive left testicle was associated with an absent reflex on the left side ; in three the reflexes were present although the testicular sensation was absent; and in one the reflex was absent and the sensation present. Unfortunately only five patients were interrogated with regard to their sexual desire; of these four had neither testicular sensation nor cremasteric reflex, and the remaining one, although without the former, had retained the latter.

The Plantar Reflex.—In my experience, loss of the plantar reflex is always associated with complete or partial plantar anæsthesia; in other cases there is hyperæsthesia associated with an exaggerated reflex. Out of fourteen of my cases, the former condition was found in four; in seven there was hyperæsthesia with increased reflexes; and in three sensation and reflex appeared normal. In all cases the response was flexor.

6. *Tendon Phenomena.*—To my mind the presence or absence of the arm-jerks is often so difficult to determine in normal individuals that it is of little use testing them in tabetics. The relative importance of the tendo-Achillis-jerk and knee-jerk is fully discussed in another paper in this series. In five of my cases the knee-jerk was present; of these three had no tendo-Achillis-jerk on either side, in one it was present on the right side, and in one on both sides. The latter case was one of cervical tabes; his lightning pains began and were most severe in his arms. When I saw him they had just begun to affect his legs. In the remaining twelve cases both knee-jerks and tendo-Achillis-jerks were absent.

7. *Hypotonus.*—This is often a very characteristic feature. It is usually most marked in the legs, but may affect other parts,

e.g., the arms and the abdominal wall. It was well marked in ten of my patients.

8. ***Trophic and Vasomotor Symptoms.***—Perforating ulcers were present in three of my cases. One patient had four—one under the ball of each big toe, one under the left little toe, and one under the right heel. They were very resistant to treatment, and caused the patient considerable pain. Another patient had had three ulcers which had healed; when I saw him there was one under the fifth metatarsal bone, and two more under the first and second toes. The metatarsal ulcer was associated with fracture of the underlying bone. This was demonstrated by means of an X-ray photograph, and later by an operation performed by Mr. Rowlands; after excision of the bone the ulcer healed.

Other trophic symptoms were not present in my patients with perhaps one exception—a patient who complained that for about six months before examination his teeth had been falling out for no apparent reason.

I have noticed vasomotor disturbances in none of my cases.

5. UNILATERAL MUSCULO-SPIRAL PARALYSIS—"SATURDAY NIGHT PARALYSIS."

By

A. F. HERTZ, M.D.

THIRTEEN patients came to the Department on account of unilateral musculo-spiral paralysis. The onset was gradual in one case which will be presently referred to, and in another it was due to pressure by a crutch. In the remaining eleven cases the patients had found an arm paralysed on waking. The majority had fallen asleep in chairs, only three having been to bed. The right arm was affected in five men and three women, and the left arm in three men and no women. Four of the patients were between 20 and 30 years old, four between 30 and 40, two between 50 and 60, and one, a woman, was 68.

In six out of the eleven cases the paralysis was first noticed late on Saturday evening or on waking on Sunday morning. In three cases the day of onset was not remembered, the paralysis having been present for three or more weeks when the patients were first seen. In only two cases was there a clear history that the paralysis had begun on other days—in one, a total abstainer, on a Tuesday, in the other on a Thursday; both patients had fallen asleep with one arm over the back of a chair.

The paralysis, which results from the pressure on the musculo-spiral nerve when a drunken individual falls asleep with his arm over the back of a chair, has long been recognised. The present series of cases is reported, as it shows how much more frequent this cause of unilateral musculo-spiral paralysis is than any other. When a sober individual falls asleep with his arm over the back of a chair or in bed with his arm in such a position that the nerve is compressed, the discomfort caused is almost

invariably sufficient to awake him before any great damage is done. Consequently nothing more than a temporary sensation of tingling and sometimes a slight degree of weakness, lasting for a few minutes, result. It is so exceptional for well-marked paralysis to occur that a total abstainer, such as our Tuesday patient, runs considerable risk of being suspected of having for once indulged in excess of alcohol. When a drunken individual falls asleep under similar circumstances, his central nervous system is temporarily so greatly depressed that discomfort sufficient to awaken a sober man has no effect upon him, with the result that he continues to sleep until the effects of the alcohol have worn off, by which time the nerve is sufficiently damaged to result in a more or less severe degree of paralysis.

Unilateral paralysis in the distribution of a peripheral nerve must be due to some local cause; bilateral paralysis is generally due to a toxin circulating in the blood. The only local cause of musculo-spiral paralysis of any importance in addition to those already discussed is fracture of the humerus. When these causes can be excluded, and particularly if the onset of the paralysis is gradual, as in the one case of this kind in our series, the possibility of a toxic origin must be considered. On testing the arm which the patient himself considered unaffected, it was found that there was distinct weakness in extension of the wrist. A toxic origin was therefore considered probable, and further investigation showed that the patient was suffering from chronic lead poisoning.

6. MIRROR-WRITING.

By

T. I. BENNETT.

May Whitworth, aged 13 years, was sent to Dr. Hertz's Nervous Out-Patients on February 22nd on account of partial paralysis of the legs.

There was a history of difficult labour, though the child was born at full-term. At the age of three months she had fits, and has always been partially paralysed since then; she could not sit up until she was six years old. She has been able to walk a little, but latterly this has become more difficult, and she complains of pain in the pelvis on standing unsupported.

On examination no abnormality was found in the eyes or in the facial or ocular muscles. The arm muscles were well-developed, but there was some slight loss of power in them, rather more marked on the right side; the arm-jerks were easily obtained, but were not definitely exaggerated. The leg muscles were weak, but not wasted; the knee-jerks were exaggerated on both sides, and the tendo-Achillis-jerks were easily obtained. The plantar reflex was extensor on both sides, but ankle clonus was not obtained. Sensation was unaffected. There was complete control over both rectum and bladder. There was no sign of any abnormality about the spine. The patient could not walk alone, but with a little assistance she walked with a typically spastic gait.

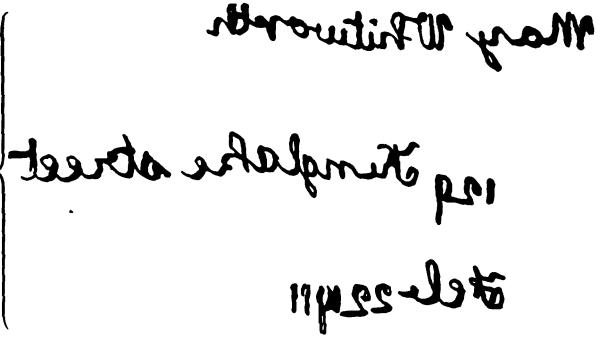
The patient is a perfectly intelligent child. When left to herself she writes with the left hand a mirror-image of ordinary writing; she can write with the right hand, but not nearly so quickly or well; she can also, when told to do so, write with the left hand in the ordinary way, though with much more difficulty.

The case must be regarded as double hemiplegia rather than as paraplegia, as the arms are definitely affected, though not markedly so. The cerebral diplegia was probably caused by symmetrical foci of inflammation or possibly of hæmorrhage, occurring when the child had the fits when she was three months old.

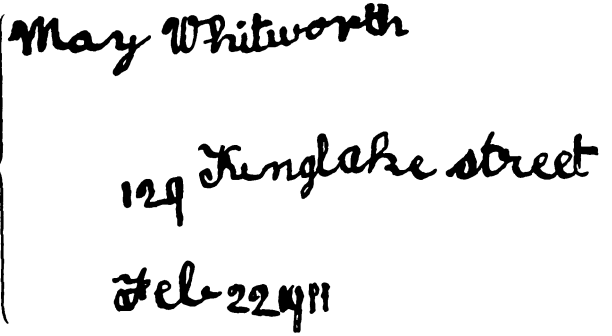
A certain percentage of normal persons when told to write with the left hand produce mirror-writing; but in persons suffering from cerebral disease, and especially in hemiplegics, the percentage is much higher.

It is recorded that Leonardo da Vinci left a manuscript written in this way, and it seems probable that this is accounted for by the fact that he was paralysed in his right hand during his last years.

LEFT HAND MIRROR-WRITING



REFLECTION OF THE ABOVE EXAMPLE OF MIRROR-WRITING



RIGHT HAND

LEFT HAND FORWARD-WRITING

If mirror-writing be carefully examined it will be seen that not all the movements producing the writing are reversed; the movements in the vertical axis are the same and it is only those in the horizontal axis that are reversed; the movements which produce the right to left writing with the left hand are the same as those which produce the left to right writing with the right hand, the same muscles being called into action in each case.

There is evidence that movements of the hands are partially represented in the cortex of both sides, and it seems probable that if the left side of the brain has been educated to control the movements of writing, this side will considerably influence the right cortical cells when the act of writing is afterwards performed by the left hand. The influence of the left cerebral cortex on the right will be felt to an even more marked degree when the pyramidal fibres are in some way cut off from the anterior cornual cells.

It will be noticed that, on holding the mirror-writing up to a looking-glass, the image exactly resembles the ordinary writing in character; it would immediately be recognised as written by the same person. This is strong evidence in favour of the movements being controlled by the same centres that produce ordinary writing.

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7. NOTE ON CASE OF "CEREBRAL CYST IN A MAN WITH AN ABNORMALLY SITUATED ROLANDI FISSURE SUCCESSFULLY REMOVED BY OPERATION."

Reported in the Guy's Hospital Reports, vol. lxii., p. 33, 1908,

By

A. F. HERTZ, M.D., and R. P. ROWLANDS, M.S.

In the report of this case it was stated that the patient had written on the anniversary of the operation to say that he had had no more fits, and had never felt so well. A year later, however, the fits returned, and the patient died in convulsions. There was no post-mortem examination.

THE ASPECT OF LEUKÆMIA FROM THE BONE MARROW.

By

CECIL PRICE JONES, M.B.

(Gordon Laboratory, Guy's Hospital).

Much difficulty is still felt in the interpretation of the different conditions observed in the blood which are known generally under the term "leukæmia." It appears that this confusion is partly one of nomenclature, partly also of technique from the effects produced by a variety of staining methods, but it is due chiefly, I think, to an imperfect understanding of the cytology of the bone marrow and of the genetic relations of the blood cells met with on hæmatological examination.

I propose, therefore, before discussing the hæmatology of leukæmia, to give some account of the histology and genetic relations of the cells found in the healthy bone marrow and circulating blood.

In a previous paper in these Reports (i.), and again more fully in the Journal of Pathology and Bacteriology (ii.), I have described a phylogenetic scheme founded on a study of the transitional forms which may be observed connecting one cell type with another, and although not claiming that this scheme is absolute or final, I have endeavoured by experimental methods to establish it as a useful one for practical purposes (iii.).

The Cytology of the Bone Marrow.

The cells of the marrow are included in two main groups: (A) those which are derived from large primitive cells and produce white cells; (B) those which are derived from small primitive cells and produce red cells.

Both these groups of primitive cells are considered to be derived from the nuclei of the giant cells; it is also probable that the larger variety is developed from the smaller by simple increase in size, but not, however, inversely, since I have never observed division occurring in the large primitive cells.

(A) The White Cell Group.

This group includes (1) *large primitive cells,* and (2) *large primitive lymphocytes (myeloblasts)** and their derivatives

The *large primitive cell* appears as a pale-blue† homogeneous disc or nucleus, having no recognisable cytoplasm, or differentiation of cell wall; it is inclined to be oval in shape, and measures 9 μ to 12 μ in long diameter; it has two, sometimes more, deeply stained nucleoli; this cell is the parent of the myeloblast.

The myeloblast.—This is the most important cell we have to consider. In its completely developed form it consists of a large pale-blue nucleus, resembling a large primitive cell, surrounded by a deeply blue-stained homogeneous margin; the size of the cell varies from 10 μ to 20 μ in diameter. The deep blue margin is of very varying width; in the typical cell it measures one-sixth to one-eighth of the entire cell diameter, being often developed more on one side than on the other. In some cells it is only represented by a fine dark blue ring, and in others it is only manifest at one side as a barely perceptible line. These transitional forms constitute the histological evidence that

* In previous papers I have used the term "large primitive lymphocyte," but I consider the word "myeloblast" is better, and I propose to use it in the present account.

† Jenner's stain was used for staining both films of marrow and blood films.

the large primitive lymphocyte is derived from the large primitive cell by this latter acquiring a differentiated periphery.

Note on the Constitution of a Cell.—Before detailing the developmental modifications which occur in the large primitive lymphocyte in the production of its derivatives, it will be useful to consider the changes, especially in staining reaction, which take place in the different constituents of the cell, when passing from a young or more primitive form to one more evolved and mature. These staining characters have been exhaustively studied by Pappenheim (iv.). Expressed briefly, his results show that the constituents of a cell are to be regarded as *cytoplasm*, composed of *spongioplasm* and *paraplasm*, and *nucleus*, composed of *chromatin* and *parachromatin*..

Spongioplasm is indifferent cyto-reticular ground substance; in young and more primitive forms it is relatively abundant and stains strongly basophil; in older or more evolved cells it stains only faintly basophil, and is diminished in amount, or even absent.

Paraplasm is the specific functional plasma parenchyma; in young and more primitive forms it is very scanty and stains faintly basophil; in more mature and more evolved cells it is relatively abundant and stains oxyphil.

Chromatin is nuclear function-material, and stains amphophil or basophil.

Parachromatin is apparently analogous to spongioplasm, but stains like paraplasm; in young and immature nuclei it is basophil, and when the paraplasm has become oxyphil, the parachromatin also become oxyphil.

Developmental Modifications of Myeloblasts.

These cells are polypotential, that is to say, they have the properties (1) of multiplying by division to product the same type of *myeloblast*, and by various modifications in the peripheral

margin, and in the nucleus, of giving rise, under healthy conditions, to (2) the *lymphoid* and (3) *leucoid* series of cells found in the bone marrow and in the blood, and (4) to *metrocytes* under certain abnormal conditions.

I would lay stress on the probability that the various developmental modifications occur only after a certain variable number of generations from the parent myeloblast.

The formation of lymphocytes.—The earliest change towards the formation of a *lymphocyte* from a *myeloblast* is a reduction by division of the size of the cells, and a diminution in the width of the peripheral margin. This has assumed a compact granular appearance owing to a less basophil stained condition of the paraplasm, whereby the network of the spongioplasm is made more obvious; the nucleus retains the myeloblast type. This cell is named a *lympho-myelocyte*. It develops into the *prolymphocyte* by a modification of the nucleus, which no longer appears as a homogeneous disc, but stains more deeply basophil, the chromatin elements standing out in contrast to the now less stained parachromatin. The nucleolus being of the same nature as the parachromatin is also less basophil. This *prolymphocyte* measures 10 μ to 12 μ in diameter; under normal conditions it is only found in the marrow and lymphatic tissues, and is never met with in healthy blood. This cell gives rise by division to the *small lymphocyte* of the blood.

Large Mononuclear Lymphoid Cells.—The *large mononuclear (hyaline and transitional) cells* of the blood are also *myeloblast* derivatives, but although from a study of transitional forms I am led to believe that they may arise from quite early generations of *myeloblasts*, yet I think they are more commonly derived from the *prolymphocytes*. The developmental change consists in an increase in the amount of paraplasm which distends the meshes of the relatively scanty spongioplasm. The paraplasm is very faintly stained by basophil dye, or even not at all, and the spongioplasm also appears less deeply stained; the nucleus

may retain the primitive type (when derived from *lymphomyelocytes*), or may resemble that of the *prolymphocyte*.

In the blood these cells present many and various forms. It is convenient to class them generally as large mononuclear lymphoid cells, but two chief types can be recognised, (a) those in which the nucleus is round, (b) those in which the nucleus is indented or polymorphous; in all varieties the cytoplasm contains a large amount of paraplasm, but in some there is more than in others, and causes the formation of a cell often exceeding 20 μ in long diameter.

The Formation of Leucocytes.—The earliest change towards the formation of a *leucocyte* from a *myeloblast* occurs in the deep blue peripheral margin with an alteration in the staining reaction of the paraplasm, which appears as faintly oxyphil stained spaces in the meshes of the spongioplastic reticulum; later, these spaces are seen to contain definite granules, the oxyphil staining of which is in some cases partly masked by the strongly basophil spongioplasm in which they are held; this cell is named a *promyelocyte*. In a later generation the spongioplasm has almost disappeared, whereas the paraplasm composed of fine neutrophil (oxyphil) granules is enormously increased, the nucleus, however, retains its primitive type. This cell is the *neutrophil (oxyphil) granular myelocyte*. It still possesses the power to multiply by division, and after probably a varying number of generations, gives rise to the *pro-leucocyte (metamyelocyte)*, a fine neutrophil granular cell in which the nucleus is no longer homogeneous. This nuclear change commences at the periphery by the appearance of deeply stained chromatin elements, the centre of the nucleus seeming to be thinned and less stained, the nucleolus being no longer distinguishable. This results in the formation of a cell with a ring-shaped nucleus, which very commonly becomes incurved to form a horse-shoe or half-moon form. From this cell is developed the *polymorphonuclear leucocyte* of the blood. Usually the leucocyte developed in this series is a much smaller cell

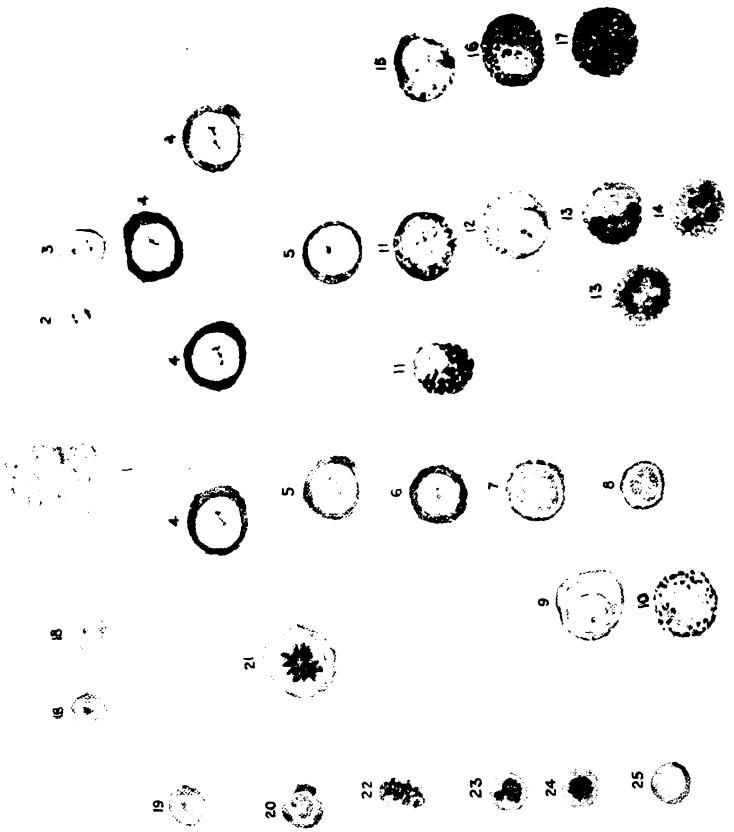
than the parent myelocyte or promyelocyte from which it has been derived, but in leukæmic blood, as will be referred to later, the leucocytes are often very large cells, and it seems possible that they have arisen from myelocytes that have passed through fewer generations to the proleucocyte type.

The Formation of Eosinophil Leucocytes.—The *coarsely granular oxyphil leucocyte* arises from a *coarsely granular myelocyte,* and this again from a promyelocyte in which the paraplasm has developed coarse oxyphil granules. The transitional forms in this series are fewer than in that of the polymorphonuclear leucocyte, and may partly account for the fewer numbers of eosinophil cells found in the blood.

The Mast Cells of the Blood.—These cells are always present in the normal blood, though in some individuals their number is very small, less than 0·1 per cent.; but, since in leukæmic blood, especially of the leucoid variety, their number is usually raised, it is necessary to give some description of their appearance and account of their probable origin.

The mast cell of the blood has about the size of a polymorphonuclear leucocyte; the nucleus is stained faintly basophil, is often indistinct and usually divided or polymorphous; the cytoplasm consists of apparently homogeneous unstained paraplasm and spongioplasm which appears as variously scattered granules. These granules, unlike those of the eosinophil and neutrophil leucocytes which are concentrated around the nucleus, are manifest chiefly at the periphery of the cell and away from the nucleus ; they are irregular in size and shape, are commonly not very numerous, and have a violet metachromatic staining. According to Pappenheim, this staining reaction is an indication of *mucin* (v.), and he regards these granules as the results of a *mucoid degeneration* of spongioplastic network. He suggests that these cells are derived from the *large mononuclear cells.* What relation these cells bear to the basophil granular myelocytes or to the mast cells found in the tissues is at present undertermined.

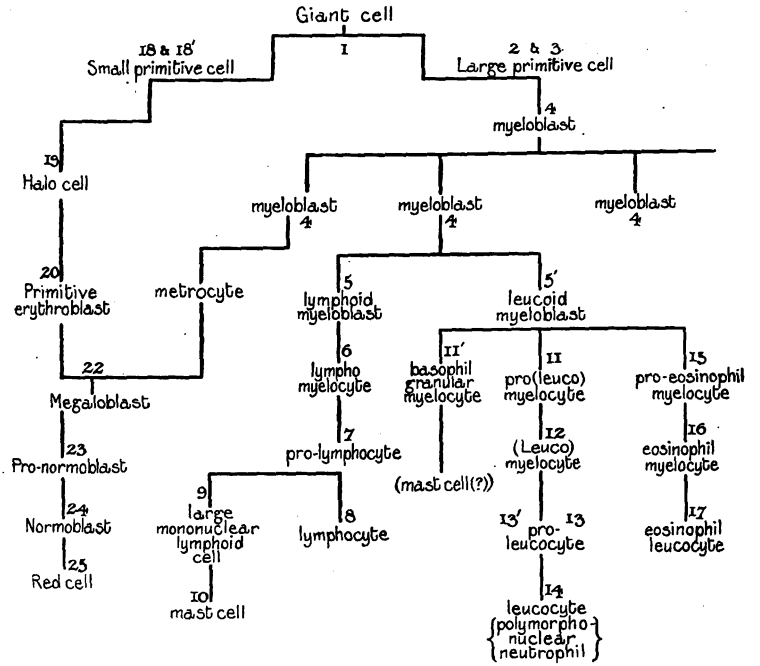
The Aspect of Leukæmia from the Bone Marrow.



Coloured Diagram of Marrow Cells.

Owing to want of space these cells have not been drawn to scale.

From the preceding account of the white cells found in the marrow and circulating blood, the following phylogenetic diagram can be constructed:—



(B) The Formation of Red Cells.

The red cells of the blood are derived from the small primitive cells by a series of generations through transitional forms, which I have described elsewhere, viz., *halo cells, primitive erythroblasts, megaloblasts,* and *normoblasts,* and further details of the morphology of these forms do not seem necessary for the purpose of this paper; but, inasmuch as *leukæmia* may be associated with the anæmic conditions known as *lymphanæmia* and *leukanæmia,* it is desirable to understand where these two otherwise distinct series A and B may become related. As was mentioned above, under normal conditions the red cell and white cell series are united in the *primitive cells,* both varieties of which are re-

garded as *giant cell* derivatives, and also the *large primitive cell* is considered as probably arising from the *smaller primitive cell;* but under certain abnormal conditions, when the demand for more red cells by the blood is urgent, the normal red cell production is assisted by the formation of *metrocytes* derived from *myeloblasts*. This results from a third modification of the nucleus and marginal ring, and is distinct from those which give rise to the cells of the lymphoid and leucoid series. The nucleus loses its primitive type and shows an arrangement of deeply basophil chromatin elements, and appears slightly contracted, being separated by a clear unstained area from the marginal cytoplasm. This appears homogeneous, showing no differentiation of spongioplasm and paraplasm, and assumes a grey tint, becoming oxyphil or polychromasoic in later generations. The *metrocyte—gigantoblast* of Muir (vi.)—thus formed is a large nucleated red cell, about 12 μ in diameter, and is regarded as the mother cell of megaloblasts. The diagram on page 89 shows the phylogenetic relation of the red cell series.

Leukæmia.

Leukæmia is a morbid condition of the blood in which there is a persistent and progressive increase in the number of white cells, which include besides those varieties normally present in the blood, a variable number, often a preponderance, of immature parent white cells derived from the bone marrow. Leukæmic blood does not always present the same histological picture, and many names have been employed to express the different types of this disease, but, although there are many transitional states, it is convenient to recognise two main varieties, viz., (1) *lymphoid*, (2) *leucoid*, depending on the particular kind of marrow cell that predominates.

Leucoid leukæmia is also known as *spleonic leukæmia*, or *spleno-medullary leukæmia*, or *myelogenous leukæmia*, but, inasmuch as all varieties of leukæmia result from some irregular action in the bone marrow, it would seem that these expressions are redundant and general, and have no special significance.

The term *lymphatic leukæmia* is often confusingly used in reference to the enlargement of lymphatic glands which sometimes occurs in these cases; and similarly, *splenic leukæmia* refers to the enlargement of the spleen. But enlargement of the lymph glands and spleen, either or both, may occur in either or both varieties of leukæmia, or either or both may show no enlargement; and enlargement of lymphatic glands and spleen are frequently met with in cases where the blood is not leukæmic, such conditions being described as *pseudo-leukæmia, splenic anæmia,* etc.

In the present account I propose to consider *lymphoid leukæmia* and *leucoid leukæmia* and the anæmias associated with them, and which are known respectively as *lymphanæmia* and *leukanæmia.*

Lymphoid Leukæmia.

The histological appearance of the blood depends on the period of the disease, that is to say, on its severity and rate of progress. The clinical terms "acute" and "chronic" have no fixed relation to the type of blood.

The red cells are diminished in number, as a rule, to about 2 millions per c.mm., and commonly include a few normoblasts and other forms signifying an accelerated output of red cells from the marrow; the hæmoglobin percentage and the colour index are both lowered. In more extreme cases the red cells may only number less than 500,000 per c.mm., megaloblasts are met with and the colour index is raised; this, however, is more significant of *lymphanæmia.* The white cells number about 100,000 on first examination, and may rise to over 600,000 per c.mm. In quite early cases the count may be much lower than 100,000, but these cases only come by chance under examination; but, from a consideration of the pathogenesis, which I have dealt with below, it is reasonable to think that the leucocytosis is sudden and very considerable. In early stages, the white cells are composed chiefly of *lymphocytes,* a few *prolymphocytes* and *large mononuclear cells,* the granular (neutrophil and eosinophil)

leucocytes being reduced to 5 per cent. or lower; *mast cells* are not usually found in increased numbers in the blood of this variety of **leukæmia.**

In later stages the *lymphocytes* are relatively fewer, whereas the *prolymphocytes* are increased in number, and the blood contains large numbers of *lympho-myelocytes* and *myeloblasts;* finally, in the extreme stage of the affection, lymphocytes are only rarely seen, the microscopic field being occupied with *myeloblasts* and *lympho-myelocytes.*

This series of changes in the cytology of the blood is an expression of similar changes taking place in the marrow; at first an excessive production of *lymphocytes,* later a failure of the *lymphoid* series to develop beyond the *prolymphocyte* stage, and partly not beyond the *lympho-myelocyte* stage, and, finally, complete failure to pass beyond the *myeloblast* stage; and the process is accompanied by a partial and finally a complete obliteration of the granular cells of the leucoid series, probably by substitution, and a limiting of the red cell production by crowding out.

Leucoid Leukæmia.

This variety of leukæmia presents similar blood changes to the preceding, but they affect the *leucoid* series of cells.

The number of red cells and the colour index are lowered, normoblasts are commonly met with even in the early stages, and later it is common to find megaloblasts and a raised colour index, though this is more significant of leukanæmia.

The white cells are enormously increased in number per c.mm., and they include different types of cells at different periods of the disease. In the early stage the *polymorphonuclear* leucocytes are predominant. They have several characteristic appearances: (*a*) the normal leucocyte, of which there are relatively few; (*b*) cells resembling the normal, but of much larger size which, as suggested above, have probably arisen from myelocytes that have passed through fewer generations to the proleucocyte type;

(*c*) degenerated forms with badly stained and swollen nuclei, and fewer neutrophil granules in the cytoplasm. There are usually a number of *proleucocytes* with halfmoon-shaped nuclei, and a few typical *neutrophil granular myelocytes.* The *eosinophil leucocytes* are also increased in number. The number of *lymphocytes* are relatively greatly diminished, and so also are the *large mononuclear cells,* but *mast cells* are relatively enormously increased in numbers.

At a later stage the normal leucocytes are few, the predominant elements being the *proleucocytes* and *myelocytes,* and there may be a few *promyelocytes. Lymphoid* cells are rarely met with, but *mast cells* are very numerous. At a yet later stage *myeloblasts* are present, and, finally, a condition is reached in which the microscopic field is almost entirely occupied with *myeloblasts,* and only occasional *granular myelocytes* and *mast cells* are to be seen.

This appearance is almost identical with that of the final stage of lymphoid leukæmia, and the finding of a few granular cells and mast cells, and the complete absence of lymphoid cells, are the only distinguishing signs between these two classes of leukæmia. This series of changes in the type of cells found in the blood expresses a similar progress of changes in the output of cells from the marrow. The fact that this form of leukæmia is commonly of longer duration than the lymphoid variety is probably accounted for by the greater length of the leucoid series of marrow cells.

Thus, there are six transitional phases:

1. An increased number of polymorphonuclear leucocytes, which means an increased production of myelocytes and proleucocytes.
2. The failure of proleucocytes to develop into leucocytes.
3. The failure of myelocytes to develop into proleucocytes.
4. The failure of promyelocytes to develop into myelocytes.
5. The failure of myeloblasts to develop into promyelocytes.
6. The simple increase of myeloblasts.

And, from the commencement of the process there has been a partial, and finally complete, obliteration of the lymphoid series, probably by substitution, and a limiting of red cell production by crowding out. The characteristic appearance of increased numbers of *mast cells* associated with the disappearance of *lymphocytes* and *large mononuclear cells* is interesting in connection with the suggestion, referred to above, that *mast cells* represent *large mononuclear cells* that have undergone some form of mucoid degeneration.

Lymphanæmia and Leukanæmia.

These two conditions are to be regarded really as those of *pernicious anæmia*, associated respectively with *lymphoid* and *leucoid leukæmia*. It is not intended to discuss, in this paper, the marrow aspect of pernicious anæmia, but in general terms it may be described as the production of *metrocytes* from *myeloblasts;* in other words, part of the potential valency of the *myeloblast* is distracted from its normal course, namely, the production of bivalent (lymphoid and leukoid) myeloblasts and their derivatives. The first effect of this, as might be expected, is a diminished production of both forms of white cells, and it is well known that *leucopenia* is commonly associated with pernicious anæmia. But it appears to me that the result of a prolonged or intense metrocytic development would probably necessitate an increased production of myeloblasts which will tend partly to increase the production of white cells, and the already disturbed potentialities of these myeloblasts would conceivably predispose to the production of a leukæmic fault, especially in the multiplication of the myeloblast phase.

In these variants of leukæmia the number of white cells is usually not so great as in true leukæmia. In a case of *lymphanæmia* I found only 15,000 per c.mm. on the first examination, but in a specimen taken a month later, 12 hours before death, there were about 280,000 per c.mm., composed almost entirely of *myeloblasts*. In many reported cases (vii.), and in one case examined by myself, of leukanæmia, the number of white cells was under 10,000 per c.mm.

Pathogenesis.

It has been made clear from the preceding description of the phylogeny of the white blood cells that myeloblasts give rise to two series of derivatives; and it is assumed that a single *myeloblast* may divide to form two cells, both of which are myeloblast in appearance, the one being potentially *lymphoid*, the other potentially *leucoid*. Now, it is conceivable that some developmental error may be caused whereby both the daughter cells of the parent myeloblast may be potentially the same: both will develop the same white cell series, and the number of derivatives, lymphoid or leucoid as the case may be, will be doubled. But this error would only account for the relative preponderance of one series of cells, and not for the enormous increase in the absolute number of these cells. But I have good reasons to believe that there is a variable number of generations of daughter myeloblasts before the promyelocyte phase is reached, and it is evident that if these intermediate generations are multiplied, the increase of their derivatives will proceed by geometric progression, and the total absolute increase of the cells will be enormous.

In an account of the development of the red blood cell in the chick (viii.), I suggested that the products of degeneration may constitute the stimulus whereby the development of less primitive forms may proceed to more evolved forms, and I would here further extend this notion to the production of mature cells from immature and more primitive cells. Normally, the white cells perform their functions and presumably give rise to certain products which suffice to stimulate the bone marrow to produce enough fresh cells to maintain the supply; but in leukæmia the white cells are stored up in the tissues of the body, some influence is at work whereby their normal functions are interfered with, and the more primitive marrow cells are unable to develop to mature cells, and repeated generations of myeloblasts are encouraged.

Conclusions.

1. Leukæmia is a condition in which white cells are stored up in the tissues and accumulate in the blood.

2. This condition interferes with the normal development of white cells in the bone marrow.

3. It encourages a multiplication of generations of primitive cell forms.

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HERPES AURIS.

By

W. M. MOLLISON, M.C.

During the last year two cases of herpes of the auricle in conjunction with facial paralysis have been seen in the Aural Department. Facial paralysis may be accompanied by herpes on various parts of the head or neck, but the conjunction of the paralysis with herpes on the auricle only occurs in quite a few cases. Ramsay Hunt has collected many cases, and discussed them fully in various papers. Among 147,600 cases collected from various clinics, 57 had herpes auris, or, roughly, ·04 per cent. This was in 1907; doubtless since then cases have been more frequently recognised, and this percentage will be raised.

Herpes has been shown to be due to an inflammation of posterior root ganglia in connection with the sensory nerve supplying the area over which the eruption is found. As is pointed out by Head and Campbell, and by Hunt, more than one ganglion is often involved; this gives the result that the crop of vesicles may not occur over the area supplied by the nerve giving the pain, but over an area of another nerve ganglion subsequently or simultaneously involved. When the eruption occurs on the auricle, the sensory nerve supply to that area gives the key to the nerve or, rather, ganglion affected. Several nerves supply the auricle, and their distribution has been traced anatomically in man, while Sherrington has mapped out the various areas and their appropriate nerves experimentally in the Macaque; the posterior part is supplied by the second and third cervical spinal nerves, and the fore part—

with the anterior wall of the external auditory meatus—by the auriculo-temporal. Between these areas is left the concha and the antihelix, and anterior part of helix, and this intermediate area is supplied by the facial, glossopharyngeal and vagus nerves. All these nerves have ganglia corresponding to posterior root ganglia on spinal nerves. It is probably the concha and floor of the external auditory meatus which are supplied by the facial nerve; this view is held by Hunt, and supported by a large number of his cases.

The facial nerve, then, contains not only motor fibres for the facial muscles and the stapedius, but also sensory fibres; the portio dura carrying the motor fibres and the pars intermedia the sensory fibres, while the geniculate ganglion is the "posterior root ganglion" of this sensory root. The distribution of this sensory root is in the chorda tympani and the branch supplying the concha.

Some of the cases of facial paralysis with herpes suffer from auditory nerve symptoms, deafness, or vertigo.

As in cases of herpes elsewhere, the eruption on the auricle is accompanied or preceded by pain, and the pain of herpes auris is referred to as earache. As long ago as 1871, Dr. Anstie, writing in the *Practitioner,* recounts his own experience of an eruption of vesicles on the "central fold of the pinna," coming on after a very severe attack of earache, and suggests that such cases may be more common than is usually thought, and may account for many cases of earache. The herpes, in his case, did not confine itself to the pinna, for a few vesicles appeared at the angle of the mouth and on the mucous membrane inside the cheek; there was no facial paralysis, but doubtless the eruption was dependent on an inflammation of the geniculate ganglion.

The inflammation affecting posterior root ganglia may be confined to the geniculate ganglion. This ganglion is described as lying at the first angle which the facial nerve makes in its passage through the Fallopian aqueduct, but on examining sections through the temporal bone, the cells composing the ganglion are found to lie scattered among the fibres of the

nerve almost from the internal auditory meatus to the genu; this anatomical arrangement may give partial explanation of the involvement of the motor part of the nerve when the ganglion is inflamed.

The following two cases are examples of the condition of inflammation of the geniculate ganglion, giving rise to herpes on the concha.

A. B., aged 28, a hairdresser, attended the Out-Patient Department in November, 1910, suffering from pain in the right ear and facial palsy. Ten or eleven days before attendance he had had shooting pain and aching inside the right ear, and four days later he woke to find his face paralysed on that side. He attended in the Nervous Out-Patient Department and was seen by Dr. Hertz; at this visit the right ear was distinctly deaf to the watch. A few days later the patient attended the Aural Out-Patient Department. On examination of the right auricle, a patch of reddened skin was seen in the concha and inner aspect of tragus; over this area were some small depressions as would be left by a previous crop of vesicles. On the floor of the meatus and extending up a little on the posterior and anterior walls was some scaliness of the skin, and over this area the sensitivity to touch was different (? increased) from other parts of the meatus and auricle. On the right side of the tongue taste sensations were diminished. The soft palate moved normally. The tympanic membranes were quite normal in appearance.

Hearing was tested, and found to be perfect. The deafness noticed in the Nervous Department had entirely gone. Whispered speech was heard equally well in both ears; the *lower tone limit* was normal, the patient being able to appreciate the sound produced by a tuning fork vibrating 16 times per second; the *upper tone limit* was also normal and equal in both ears, a note from Galton's whistle of about 30,000 vibrations per second being heard. Under electrical treatment, instituted by Dr. Hertz, the paralysis improved.

The deafness noted at first cannot have been due to any inflammation of the middle ear, else surely the effect would have

been left three or four days later, and would have been indicated by a raising of the lower tone limit. Neither is it probable that the auditory nerve was affected, for in that case some slight degree of nerve deafness would have been found, indicated by a lowering of the upper tone limit. There remains some temporary disturbance of function of the ear; perhaps this was brought about by paralysis of the stapedius muscle. Later, when the tensor tympani, which acts in opposition to the stapedius, accommodated itself to the new conditions, the hearing, disturbed by the paralysis of stapedius, was restored to normal.

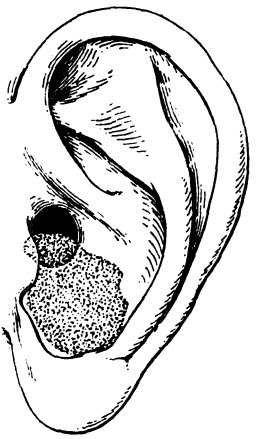

FIGURE TO SHOW DISTRIBUTION OF HERPETIC VESICLES.

The second case—

M. P., a girl aged 10, was brought by her mother to the Aural Out-Patient Department on November 10th, 1910, complaining of earache. For five days she had had earache on the left side, and for the same time that side of the face had been noticed to be "swollen." She was seen to have marked left facial paralysis of the infranuclear type, and this was the condition of face referred to as "swollen" by the girl's mother. On examination of the ear, a crop of vesicles was seen to occupy the concha and extend into the meatus, lying on the floor of the meatus, which was slightly narrowed by the swelling. The tympanic membranes were normal in appearance. There were some

enlarged and slightly tender glands in the neck, doubtless similar to those seen in connection with a typical attack of herpes zoster. Cultivation of the contents of the vesicles gave a pure growth of staphylococcus albus; this was said not to be due to accidental infection.

The hearing was good; a whisper was heard equally well in both ears, and, as in the previous case, both upper and lower tone limits were normal.

The palate was unaffected. Unfortunately taste sensation was not tested. Five days after the first attendance the vesicles had entirely disappeared, though the site was marked by some petechial spots and lines, and some excess of skin sensitiveness. Under electrical treatment the paralysis soon improved, and in six months was scarcely to be noticed. In this case, too, doubtless the stapedius was paralysed, but the temporary deafness not noticed.

Now, in these cases there were no symptoms except those referable to the one nerve—the facial; it therefore seems fair to say that the area over which the herpetic vesicles occurred represents the area supplied by the sensory part of the facial nerve. This area was the lower part of the concha, the inner aspect of the tragus, the floor and the lower part of the anterior and posterior walls of the meatus.

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OBSERVATIONS ON THE DEEP AND SURFACE TEMPERATURES OF MAN IN HEALTH AND DISEASE.

By

A. S. MORTON PALMER, M.A., M.D., B.C.

(Thesis for the Degree of M.D. in the University of Cambridge.)

Up to the present time little evidence exists of value for the comparative study of human temperature, in spite of the innumerable observations which have been collected in the course of medical routine. Of these, many have been recorded with unfortunate lack of care, and nearly all are based on mouth readings which, as shown by Pembrey (i.), "fail to give accurate or comparable readings of the internal temperature of the body." So long ago as 1877, Lorain (ii.) maintained that the rectal temperature is the only accurate measure of internal heat. It is also the only temperature of any value that can be taken in infants, comatose persons, and the like. Quite recently I met a case of rheumatic hyperpyrexia to which attention was only drawn by the suggestion to take the temperature in the rectum. The oral temperature had stood at 99·8°F. for two days, whereas the rectum showed that 108·0° was the true figure.

About 98·2°F. may be regarded (xiv.) as the mean internal temperature in health, with a range from 97·0° to 99·3°, but other data are needed if we are to throw any light on the mechanism by

which bodily heat is regulated. There are two main forces: heat loss and heat production; the rise of temperature in morbid states being due to a diminution of one or an excess of the other, the relative importance of the two being variously assessed by different schools. Traube (iii.) assumed the existence of an agent producing fever through a tonic effect on the vasomotor nerves. The peripheral arterioles contracting, the flow of blood to the surface rapidly diminishes, and the skin temperature drops, while there is a rapid rise of the internal temperature. The later fall of the latter he ascribes to the secondary relaxation of the cutaneous vessels. That some such sequence does occur in a typical rigor, I shall demonstrate later.

Liebermeister (iv.), on the other hand, argued that pyrexia is always due to excess of heat production. As to both heat production and heat loss we have very little information. The estimation of the former by calorimetry or by calculation from the respiratory quotient and food intake, etc., is unsatisfactory and of limited application. We may conclude, however, that heat production is raised in any given case if the internal temperature remains normal or above normal, while the heat loss is higher. Now, since of the total heat loss, 70 per cent. is dispersed by radiation and conduction from the skin, and 15 per cent. by evaporation, a good estimate of it may be arrived at if we learn the skin temperature. To apply thermo-electric methods to this purpose requires complicated apparatus and protracted observations, and is not easy in clinical work. Readings of sufficient exactitude and almost identical with those of thermo-electric methods may be obtained with a flat-bulbed mercurial thermometer. In the words of Waller (v.), "This thermometer does not, and need not, indicate the true value of the surface temperature, it acts as a heat-gauge receiving heat at its applied surface and giving off heat at its exposed surface, thus, in accordance with Newton's law, indicating the 'heat tension' of the surface to which it is applied, and, after graduation, the rate in calories per time per area at which that surface is giving off heat."

The earliest of such readings were obtained by John Davy (vi.), and are appended:—

Temperature of room	... ...	69·8°F.
,,	Sole of foot	89·9°
,,	Between internal malleolus and tendo Achillis	92·8°
,,	Middle of tibia	91·4°
,,	Middle of calf	92·8°
,,	Bend of knee	95·0°
,,	Middle of thigh	93·9°
,,	Middle of rectus femoris ...	90·8°
,,	Groin	96·4°
,,	One inch below navel	95·0°
,,	Left sixth rib over heart ...	93·9°
,,	Right sixth rib	92·8°
,,	Axilla (closed)	97·8°

As the result of 109 readings with the flat-bulbed thermometer, Pembrey and Nicol (vii.) find the mean temperature of the skin of the abdomen in health to be 93·0°F. (33·94°C.), there being in the protected parts of the body no regular variation between 5 a.m. and 12 midnight.

Dealing with the surface temperature in other parts of the body, they give the following chart:—

Time.	Temp. of Air.	Deep Rectal T.	Abdomen.	Dorsum of Hand.	Palm.	Forearm (Flexor).	Thigh.	Calf.	Remarks.
7 a.m.	67·1	97·7	93·2	87·8	90·5	92·1	89·6	89·6	Rest.
7.30 a.m.	65·3	98·4	95·0	91·4	93·5	91·9	91·9	91·7	In bed.
5 p.m.	64·4	100·7	91·4	90·6	94·2	92·3	92·1	93·2	After 20 mins. walk.
6 p.m.	65·3	99·3	94·2	91·7	93·2	93·5	91·0	91·4	After food.
9 p.m.	66·2	98·2	95·3	90·5	92·3	92·8	93·7	89·6	Rest.
10.30 p.m.	66·2	100·2	91·9	91·9	94·2	92·4	92·3	92·3	After 35 mins. walk.
4 p.m.	68·5	98·9	94·1	93·3	95·0	94·1	91·4	91·7	Rest.
10.30 p.m.	50·6	98·6 (urine)	93·2	79·1	86·0	87·4	91·4	87·8	Rest.
12.45 p.m.	37·4	99·8	93·2	—	—	91·4	—	—	Directly after rest.
6.15 p.m	65·3	100·0 (mouth)	—	91·4	—	91·4	92·3	—	Rest.

Time.	Air.	Fore-head.	Malar Bone.	Palm.	Lobe of Ear.	Alæ-nasi.	Cheek.	
4.5 p.m.	66·2	P. 93·5	91·0	92·1	84·9	89·2	92·8	Rest.
4.5 p.m.	64·4	94·1	93·9	—	84·7	—	—	Rest.
4.5 p.m.	66·2	N. 93·2	92·4	95·0	86·3	92·8	93·9	Rest.

Very little difference appears between these figures and those obtained by Kunkel (viii.) with a thermo-electric method, which he claims to be exact to about 0·1°. With this he made the following observations on a healthy muscular man 35 years of age, 179 cm. in height, and 84 kilos in weight—

Temperature of room	... ...	68·0°F.
,,	Forehead	93·3°—93·9°
,,	Over malar bone	93·2°
,,	Of cheek under malar bone	93·9°
,,	Lobe of ear	83·8°
,,	Back of hand	90·5°—91·7°
,,	Palm of hand (closed) ...	94·6°—95·1°
,,	Palm of hand (open) ...	93·9°—94·6°
,,	Wrist	91·5°
,,	Forearm	92·6°
,,	Forearm (upper part) ...	93·2°
,,	Arm	93·7°
,,	Sternum	93·7°
,,	Over pectoralis major ...	94·4°
,,	Over heart	94·2°
,,	Right iliac fossa	93·9°
,,	Left iliac fossa	94·2°
,,	Back (over sacrum) ...	93·5°
,,	Back (over ribs)	94·1°
,,	Buttock	89·6°
,,	Thigh	93·5°
,,	Calf	94·2°

My own work touches on a number of conditions both in health and disease. The skin readings have been taken with flat-bulbed mercurial thermometers (made by Mr. A. Deane of Hatton Garden), applied bulb downwards to the skin. The site, in most cases, and unless otherwise specified, has been on the abdomen, two inches to one side of the umbilicus, where the bulb was held till the mercury ceased to rise, which occupied some two minutes. If held there much longer, the column would start falling as the skin became chilled by the exposure. I give also contemporaneous readings of the temperature of the air, rectum, and, in some cases, the mouth, with a record of the pulse and respiration.

Observations on Healthy Persons in Bed.

The following observations were made for the purpose of control.

	Respiration.	Pulse.	Rectum.	Mouth.	Abdomen.	Air.
1. Girl, 9 years	18	84	98·8	97·8	93·2	61·7
2. Boy, 7 „	14	88	99·2	99·2	95·9	59·3
3. Girl, 10 „	28	76	99·8	98·0	91·9	57·2
4. Girl, 16 „	20	80	98·6	98·4	93·3	—
5. Man, 75 „	17	80	100·2	99·0	92·3	59·0
6. Woman, 27 „	—	—	99·6	98·6	91·5	60·8

These will be seen to agree substantially with those of Pembrey, the skin temperature ranging between 91·5° and 95·9°, and the excess of rectal over surface temperature between 3·3° and 8·1°.

The Temperature of the Newly Born.

We have as yet no evidence to show that the variation in skin temperature bears any ratio to age.

The following observations were taken on four new-born infants. Their rectal and surface temperatures were taken immediately after birth, before cutting the umbilical cord, and in two cases contrasted with later temperatures before and after a warm bath. In some cases simultaneous records of the temperature of the mother were taken.

	Rectum.		Surface.		Air.
	Infant.	Mother.	Infant.	Mother.	
1. 8 months child. At birth, 9.45 p.m.	101·4	100·8	96·8	—	68·0
10.45 p.m.	98·0	--	92·3	—	68·9
After 2½ mins. Bath at 105·8, 11 p.m.	96·0	—	95·3	—	—
Next morning, 11 a.m.	99·4	—	95·0	—	64·4
2. *Child at birth, 10 a.m.	99·4	98·8	89·6	86·0	64·4
10.15 a.m.	99·0	98·4	—	—	—
After bath at 100° F.	98·0	—	—	—	—
3. Mother 16 years old. Infant at birth, 2 a.m., 21/5/08	99·6	98·4	96·8	95·9	72·5
4. Before birth, 12.40 a.m.	—	99·4	—	94·1	76·1
At birth, forceps delivery. A.C.E. given, 12 mins.	101·0	99·8	92·6	94·6	—

* Records taken by nurse.

In all these the rectal temperature of the child when delivered was higher than that of the mother, the skin temperature higher in all except the fourth case where the normal ratio may have been upset by the anæsthetic. The effect of the hot bath in Cases 1 and 2 was to raise the surface and lower the internal temperature.

Raudnitz (ix.), in 1888, noted that the temperature of the infant before birth is slightly higher than that of the mother's uterus, and at birth averages 99·5° (rectum). Soon after birth, especially after the first bath, the temperature falls to about 98·15°, to rise somewhat during the next week and remain fairly constant at about 99·0°. The mechanism for heat regulation appears to be poorly developed in the infant.

Heart Failure.

The next series of observations refer to cases of failure of the heart in adults.

	Air.	Rectum	Mouth.	Skin.	Pulse.	Resp.
1. Failing heart	61·7	99·6	97·0	95·0	108	32
2. Failing heart. Mitral disease, 5 p.m., 8/4/08	59·0	98·3	97·6	92·3	44 to 52	20
11 a.m., 9/4/08	58·1	97·8	95·9	92·8	44	20
3. Aortic regurgitation, 6.15 p.m., 4/5/08	65·3	98·2	95·6	93·2	96	44
4. " "	—	98·3	Below 95·0	94·6	136	36
5. Mitral regurgitation, 8.30 p.m., 17/8/08	65·8	99·4	Below 95·0	93·9	68	28
6. Aortic aneurysm, 6 p.m., 27/4/08	54·0	99·0	98·0	91·0	76	16
7. Mitral stenosis and pregnancy (subsequent abortion)	59·0	99·1	97·6	91·7	—	—

All were grave cases presenting various degrees of anasarca, orthopnœa, and dyspnœa, the pulse of Nos. 2 and 4 being particularly bad, yet the internal temperature as shown by the rectum, though sometimes somewhat low, as in Case 2, fails

to show the subnormal character accredited to them by the text-books. Though the majority were not "mouth breathers," the readings taken in the mouth are much lower and approximate to that of the skin, which, however, is not lower than is often found in healthy persons. In other instances the excess of rectal over mouth temperature, though not often so great as in heart failure, ranges between 0·3° and 1·5°. Occasionally the two readings are identical.

Rigors.

The temperature of the skin was compared with that of the rectum and mouth in cases of rigor.

1. In a case of suppurating abdominal growth.

	Rectum.	Mouth.	Skin.
1.15 p.m., 25/3/08	103·2	102·8	97·7
2.30 p.m., 26th	103·0	102·5	100·4
6.40 p.m., 27th, during rigor	104·2	101·4	86·7
7.15 p.m., 20 min. after rigor	105·4	101·8	87·4
8.30 p.m., 28th	101·4	100·6	98·0

This shows the low skin temperature associated with vaso-constriction during the rigor. In spite of the high internal temperature, the patient feels cold and shivers. Later, the cutaneous vessels dilating, the heat of the skin rises and the internal temperature falls.

2. In a case of septicæmia following incomplete abortion, the patient had a rigor at the onset of pneumonia. Micrococcus tetragenus was found by Dr. Eyre in both the blood and sputum and appears to have been the infecting organism.

	Rectum	Skin.	Mouth.	Air.	Pulse.	Resp.
7.45 a.m., not more than 5 mins. after 1st rigor. Skin dry	106·0	103·1	103·0	60·8	136	40
8.15 a.m., recurrence of rigor, not severe. Skin dry	106·4	95·3	101·2	61·7	—	—
11.45 a.m., not shivering	103·0	94·1	101·2	61·1	140	25
11.45 p.m.	100·0	95·5	99·9	63·5	100	24

Unfortunately I did not reach the patient in time to take the temperatures during the first rigor. The reaction, which is very considerable, must have been rapid, as shown by my first observations.

During the rigor, the mouth, as in the previous case, entirely failed to give any idea of the internal temperature. As to the disproportion between the surface and internal temperature, it is great during the rigor, being 11·0° F. as contrasted with 4·5° fifteen hours later. When the rectal thermometer registered 106·4° the skin was actually cooler than when the former stood at 100·0°. The phenomena in these two cases agree with the teaching of Traube, though I doubt whether they are always present in a rigor, judging from the following case.

3. A case of pelvic peritonitis.

	Rectum	Skin.	Mouth.	Air.	Pulse.	Resp.
12.5 p.m., towards end of rigor. Still shivering	100·0	93·5	96·0	59·9	72	32
1.35 p.m., 25 mins. after end of rigor	—	93·5	100·6	—	—	—
5.30 p.m.	101·6	95·0	100·4	62·6	92	24

This rigor was far more severe than the second, yet the excess of rectal over skin temperature is small. The latter during the rigor was only 6·5° lower than the former, and afterwards 5·6°. That is to say, the difference of 0·9° was enough to provoke severe shivering, which raises a doubt whether some other factor may not arise than superficial vaso-constriction. Perhaps a rigor may be said to be due to the direct action of a toxin upon nerve cells generally, with or without some action on the vaso-motor centres.

Various Cases of Pyrexia.

In the continuous pyrexia of fevers, so protean are the conditions prevailing that to ascribe pyrexia always to diminished thermolysis is no more possible than it is to state that it is always due to excess of heat production. The method of

thermotaxis appears to vary with the disease, the one factor predominating in one, the other in another. Thus, in the typical cases of lobar pneumonia recorded in the next table, the skin temperature, as might be expected from the hot, dry character of the skin, is, relatively to the internal temperature, high. This, I might mention, has previously been dealt with by Dr. Hale White (x.), with whose results mine fully agree.

	Rectum.	Skin. (abdomen)	Mouth.	Air.	Pulse.	Resp.	Axillary.
1. 4 years old. 4.45 p.m., May 30, at height of fever	103·6	98·9	—	60·4	112	48	—
At crisis, 2.50 a.m., May 31 (dry skin)	98·2	92·3	—	63·1	96	34	—
6 a.m. Taken by nurse ..	98·0	94·1	—	--	100	36	—
2. 13 years. 4 p.m., 4/4/08, 3rd day	105·0	98·6	105·0	59·9	112	34	—
8.30 p.m., 5/4/08 ...	105·0	100·4	104·4	58·1	104	40	—
False crisis, 6 a.m., 7/4/08. Skin dry	100·2	94·6	99·4	59·9	72	32	—
12·45 p.m.	102·4	98·0	102·4	58·1	96	32	—
7 a.m., 16/4/08, when convalescent	98·0	92·3	97·4	59·0	64	20	—
3. Age 17. 6.15 p.m., 7/4/08, 3rd day	105·2	100·0	—	61·1	112	44	*103·6
4.35 p.m., 8/4/08 ...	104·6	100·0	--	61·7	108	36	103·6
9/4/08 ...	101·8	97·1	—	61·7	84	32	100·4
11 a.m., 11/4/08, 24 hours after crisis	99·4	94·1	--	59·9	72	32	98·5
4. 4.15 p.m., 6/4/08	103·2	98·6	103·0	59·9	112	34	—

* The axillary was taken instead of the oral, owing to nasal obstruction.

In the first case the excess of the rectal temperature at the height of the fever over the rectal temperature at the crisis was 5·4°, while the similar excess of skin temperature was 6·6°. In the second, the excess of rectal temperature at the height of the fever over the same after the crisis was 7·0°, while the excess of surface temperature was 8·1°, the skin thus rising 1·1° relatively more than the rectum. The skin in all these cases felt hot and dry. Sweating during the crisis was not invariable, being absent in No. 1. In atypical cases of pneumonia

other conditions prevailed, as seen in the next table, which shows some observations on 3 cases. No. 1 was a man, aged 72, suffering from glycosuria and lobar pneumonia, in whose case a very bad prognosis was given, though he eventually recovered. No. 2 was a rapidly fatal case of lobar pneumonia in an alcoholic patient. No. 3, a severe case with pregnancy resulting in miscarriage, presented an "up and down" temperature and some curious clinical features. They all show relatively low surface temperature.

ATYPICAL PNEUMONIAS.	Mouth.	Rectum	Skin of Abdm.	Air.	Pulse.	Resp.
1. Thorax on both right and left sides, 98·2	103·4	104·2	97·1	63·5	104	34
2. 10 a.m., 13/8/08, 1st day ...	—	99·0	—	—	116	26
10 p.m. " ...	—	102·0	96·4	68·0	132	30
10 p.m., 15/8/08	—	99·0	96·4	67·1	132	28
1 a.m., 17/8/08	—	100·4	96·3	67·1	128	20
2 p.m., 25/8/08, well convalescent	—	98·2	94·1	69·8	98	25
3. Previous chart "up and down." Bertha H., 37						
11.30 p.m., 7/3/09, ? 10th day	101·4	102·6	94·6	62·6	136	40
11.45 p.m., 8/3/09	102·2	103·4	95·5	64·9	136	—
5.45 p.m., 9/3/09	96·0	99·0	90·8	57·2	92	—
1 p.m., 3/4/09	98·2	99·6	94·8	59·0	88	20

Typhoid Fever.

Typhoid fever affords a contrast to the typical form of lobar pneumonia. Thus—

	Rectum	Mouth.	Skin.	Air.	Pulse.	Resp.
11.30 a.m., 12/4/08	101·6	101·4	96·4	58·6	96	20
6.20 p.m., 13/4/08	102·8	102·6	96·8	54·7	88	24

Another case of typhoid with meningeal symptoms gave a rectal temperature of 106·0° with a surface temperature of 98·6°. In the first case the rectal temperature was some 4·6° above the normal, the skin 3·8°; in the second, the rectal excess was about 7·8°, the skin only 5·6°.

Measles.

I have observed three cases of measles, all with a vivid rash, which show a surface temperature relatively lower than might be expected.

	Rectum	Skin.	Air.	Pulse.	Resp.
1. Child, 2 years. 1st day of rash, 9.20 p.m., 12/5/08	103·6	98·9	66·2	144	32
2nd day of rash, 1.25 p.m.	103·6	96·4	62·6	148	36
9 p.m., 14/5/08 ...	99·8	91·0	—	116	36
2. Child, 2 years. 1st day of rash, 9.20 p.m., 12/5/08	104·8	97·1	64·4	168	36
9 p.m., 14/5/08	96·4	91·4	62·2	80	28
3. Child, 3½ years. 1st day of rash, 9.30 p.m.	103·8	96·8	65·3	120	24

German Measles.

Observations in a case of this disease recorded on the second day of the pyrexia show the same features as in ordinary measles. The rash had disappeared.

	Air.	Rectum	Abdm. R. side.	Mouth.	Pulse.	Resp.
R. C. Male. 21 years	59·5	102·8	93·7	102·0	110	24

Uræmia and Eclampsia.

These conditions are usually apyrexial, and show such temperatures as the following:—

Eclampsia.	Rectum	Skin.	Air.	Pulse.	Resp.
11.30 a.m., slight convulsions, 3/3/09	98·2	91·4	61·7	92	—
12.45 a.m.	98·0	93·2	—	—	—
1.55 a.m.	99·6	95·0	—	—	—
Uræmia.					
8.45 p.m., 25/4/09	100	92·8	57·2	88	24

The following case of eclampsia shows some pyrexia (primipara, 16 years old)—

	Rectum	Skin.	Air.	Pulse.	Resp.
(a) Just before delivery. Conscious after convulsions	98·2	94·2	73·0	92	24
(b) After delivery, 5 p.m.	101·6	97·5	68·7	—	—

In one case of eclampsia hyperpyrexia occurred.

	Rectum	Skin.	Air.	Pulse.	Resp.
(a) In labour, 3.15 a.m., 11/4/08... ... Between the pains. No fit since 9 p.m.	102·2	97·3	72·5	138	52
(b) At birth of dead child, 3.30 a.m. ... Hot-air bath, 10.30 a.m.	102·4	—	—	128	36
(c) Sweating, 2.15 p.m.	103·8	98·0	63·5	124	40
(d) 11.45 a.m., 12/4/08 (axilla 104·8) ...	105·2	98·6	64·0	144	48
(c) 5 a.m., axilla 107·2	—	—	—	160	50
(d) Death at 5.29 a.m.	—	—	—	—	—
(e) Five minutes after death rectal temperature was at 108.					

At the autopsy no gross pathological changes were found. Observations (c) and (e) were made by the nurse, and were not sufficiently full. They, however, show post-mortem hyperpyrexia, as if, though the circulation has ceased and thereby there is less loss of heat by radiation, the tissues go on producing heat. It is unfortunate that we have no record of the skin temperature at the same time.

The only other post-mortem temperature which I have observed is also incomplete. A case of tuberculous meningitis—10 p.m., rectum 102·8°; 11.5 p.m., six minutes after death, rectum 102·0°; skin 94·6°; 11.50 p.m., rectum 99·2°.

Various Diseases.

The following are observations upon the deep and surface temperatures in various diseases:—

Pernicious Anæmia.	Mouth.	Rectum	Surface	Air.	Pulse.	Resp.
5 p.m., 11/3/08	105·0	105·6	99·5	55·0	126	32
9.30 p.m.	104·8	105·4	100·4	51·8	—	—
10.20 p.m.	105·6	105·0	102·56	52·7	120	32
11.25 p.m.	104·8	105·4	103·6	–	128	32

At 9.45 p.m. 10 c.c. of antistreptococcic serum were injected into the other side of the abdomen, well away from the point at which the thermometer was laid. It may perhaps account for the very high surface temperature, though even before it was considerable.

	Air.	Mouth.	Rectum	Skin.	Pulse.	Resp.
Infective endocarditis. Adult ...	—	103·4	103·4	97·7	120	40
Syphilis. Young woman ...	64·0	101·2	101·6	95·0	84	24
Gout. Male, 66 years	65·3	100·8	101·2	99·5	88	20
Rheumatic pericarditis. Boy, F. H., 16 years. 5.45 p.m. ...	56·6	—	100·6	93·9	96	30
Appendicitis. Adult. 4.30 p.m.	59·0	100·4	101·6	95·0	100	28

Empyema (Thoracic), left side.	Rectum	Mouth.	Abdom.	R. side.	L. side.	Air.	Pulse.	Resp.
Gwen, J., 13								
8.45 p.m.	103·2	102·2	98·6	98·2	97·5	61·7	128	40
10 p.m., 15 minutes after evacuation of 22 oz. of pus	103·0	102·2	98·2	—	—	62·8	120	40

Anæsthetics.

I have examined the action of anæsthetics on the temperature in four cases in which anæsthesia lasted one hour or longer. The air of the theatre was at about 68° or 70°, and the patient covered as much as possible with blankets, no other measures being taken to influence bodily heat.

Anæsthetics.	Rectum	Mouth.	Skin.	Air.	Pulse.	Resp.
1. Anæsthetic duration, 10.10—11.10 a.m. Girl, aged 9 years. A.C.E. and ether						
Before—9.50 a.m.	98·8	97·8	93·2	61·7	84	18
After—11.15 a.m.	98·0	—	95·9	—	120	24
2. Duration, 10.15—11.45 a.m. Girl, aged 10 years. A.C.E. and chloroform						
Before—10.5 a.m.	99·8	98·0	91·9	57·2	76	28
After—11.45 a.m.	97·6	—	90·5	—	120	28
„ 1.15 p.m.	97·0	—	93·5	58·6	92	28
3. Duration, 10.15—11.20 a.m. A.C.E. and ether						
Before—9.30 a.m.	98·6	98·4	93·3	—	80	20
After—11.25 a.m.	97·6	—	94·1	—	104	20
4. Duration, 2.55 to 4.40.... Woman, 27. Anæsthetic—Ether and A.C.E.						
Before—2 p.m. ...	99·6	98·6	91·5	60·8	—	—
After—4.53 p.m...	95·8	—	89·2	—	—	—
„ 6.45 p.m...	97·1	—	92·6	63·5	—	—

The most noticeable feature is the extent of the effect produced by the anæsthetic on the rectal as compared with that on the skin temperature, which may even rise. Thus—

In case 1.	Rectal temperature	fell	...	0·8
	Skin	„ rose	...	2·7
2.	Rectal	„ fell	...	2·2
	Skin	„ fell	...	1·4
3.	Rectal	„ fell	...	1·0
	Skin	„ rose	...	0·8
4.	Rectal	„ fell	...	3·8
	Skin	„ fell	...	2·3

In the first three cases the operation was for chronic mastoid disease involving practically no exposure of the body. The fourth underwent abdominal section for ovariotomy, the surgeon first dilating the cervix in the lithotomy position. Consequently, in addition to the long duration of the operation, there was much exposure. All the first observations after the operation were taken immediately the patient had been returned to bed

still unconscious, and before any hot bottles could be brought. The subsequent behaviour of the temperature was noted in two of the cases (2 and 4) nearly two hours later, after the application of hot bottles and blankets. In both, though the skin temperature is higher than before the operation, the rectal temperature does not show a commensurate rise, and in one case (No. 2) continues to fall.

Cases 1 and 3 show slight depression of internal temperature considering the length of the anæsthesia.

It is unfortunate that owing to the mixed nature of the anæsthetics employed, we can learn nothing of the respective influence of chloroform and ether on the temperature.

Spinal Anæsthesia.

The intraspinal injection of novocaine in a man with typhoid fever, who "had perforated," produced no change in skin or rectal temperature during forty minutes, in the course of which laparotomy was performed and the perforation discovered and sutured.

	Air.	Rectum.	Skin. Dorsum of R. Ankle.
8.10 p.m.	72·5	104·6	95·0
Injection 5 cc. given at 8.24 p.m. ...	—	—	96·4
8.27 p.m. ...	—	—	95·0
8.32 p.m. ...	—	104·6	95·0
8.50 p.m. ...	—	—	95·9

Local Changes of Heat.

Wunderlich (xi.), while telling us "that alterations of temperature may be confined to special regions of the body, which are the seat of diseased actions," also states "that such circumscribed variations are of very little practical moment." Personally, I believe them to be by no means unimportant, and should suggest that they are worthy of more careful study, with a view to the light which they would throw on the local factors in thermotaxis. I append a few instances.

(*a*) **Purulent ophthalmia induced in left eye by the installation of jequiritol.**

	Upper Lid.		Abdom.	Rectum	Mouth.	Pulse.	Resp.
	Right.	Left.					
6.15 p.m., 17/3/08 ...	95·0	97·16	96·4	100·0	99·8	88	18
6 p.m., 18th	93·2	96·8	95·9	100·0	99·8	60	20

(*b*) Arthritis with acute gonorrhœa. Both knees affected, especially the right.

	Rectum.	Air.	Patella.		Pulse.	Resp.
			Right.	Left.		
2 p.m.	102·0	67·1	96·8	94·1	88	24

In both cases are seen local as well as a general rise of temperature. In case (*b*) the excess of temperature on the right knee was not obvious to the touch. The right knee was considerably more painful and tender than the other.

(*c*) **Herpes Zoster.** Attention is drawn by Fuchs (xii.) to the local elevation of heat in the case of trigeminal Herpes Zoster, a point to which I cannot find reference in other textbooks. I have two cases verifying his statement as to this phenomenon, which I also found present in a case of intercostal herpes. This rise of temperature is present not only during the actual stage of inflammation, but also for some months after. It cannot be sufficiently explained as due to simple local vascular changes, and is more probably due to some obscure nervous influence. We might conjecture that the nerve ganglion, which is the probable seat of the disease, has also some share in local thermotaxis.

1. Left trigeminal herpes. Third day of vesicles—right temple, 97·7°; left, 98·0° (air, 69·4°).

2. Right trigeminal herpes. (*a*) Fourth day, 11 p.m., 2/7/08—right temple, 97·7°; left, 95·7° (air, 72·5°). (*b*) Nineteenth day—right temple, 92·3°; left, 89·6° (air, 65·8°).

3. Intercostal herpes. Scars of left first and second spaces nearly two months after attack—left second space, 96·0°; right, 92·8° (air, 64·0°).

Hemiplegia.

Apart from infective fevers, a rise of temperature occurs in other conditions, *e.g.*, poisoning by certain drugs, as belladonna, or in damage to the central nervous system, especially the corpus striatum. Of 100 cases of hyperpyrexia collected by Dr. J. H. Bryant (xiii.), 29 were due to lesions to the brain or cord. An obscure case of injury to the cord, recorded later, gives a temperature of 106·1°.

In connection with these lesions we must also consider the local changes of temperature which occur in association with paralysis. In his Croonian Lectures, Dr. Hale White (x.) records three cases in which the temperature was always higher in the axilla of the paralysed side. In one case, the surface temperature of that arm was for over a month higher than that of the sound arm; in another, though the surface temperatures on the two sides were equal, the amount of sweat secreted on the paralysed arm was greater, and, therefore, he concludes, the loss of heat was much the greater. Hence, he argues that in these cases there is a greater production of heat in the paralysed than in the sound limb, which "would be an instance of a lesion paralysing the motor, and at the same time exciting the thermogenetic functions."

Without discussing the cogency of these deductions, I will simply detail the results of my observations in eight cases of paralysis, which differ in many respects from those of Dr. Hale White. The readings are all taken at corresponding points on the two sides and under corresponding conditions.

Case 1.—Cerebral hæmorrhage setting in on 9/7/08, and producing paralysis of left arm and leg with unconsciousness. The readings taken that day were rendered difficult by peculiar rapid movements of the right arm and leg. The movements of the arm were almost purposive in character, *e.g.*, the patient kept on slapping his leg.

8 p.m., 9/7/08.

Air	64·7° F.	
	Left.	Right.
Upper arm	86·9	89·6
Knee	84·2	82·4

The paralysed leg shows a higher surface temperature than the sound limb in spite of the activity of the latter.

Two days later, at 12 noon.

Air	68·9	
	Left.	Right.
Wrist	94·6	95·5
Knee	92·8	94·1
Abdomen	96·26	93·56
Rectum	101·6	—

Resp. 40. Pulse 128

Slight movements—not convulsive—of right arm and leg still occurred. The surface temperature of both paralysed limbs was now the lower, that of the abdomen on the same side being higher than on the other. There is a rise of rectal temperature. Next morning the patient died, and a hæmorrhage into the internal capsule was found post-mortem.

Case 2.—A man of 37 suffering from mitral stenosis and right hemiplegia due to cerebral embolism, beginning now, eight weeks after the onset, to improve.

12 noon, 10/9/08.

Air	63·5	
	Right.	Left.
Abdomen	88·5	87·4
Elbow (olecranon)...	78·8	84·7
Tip of ext. malleolus	78·4	80·6
Mouth	97·4	—
Rectum	99·0	—

Pulse 76. Resp. 26

The paralysed limbs show a lower temperature than the sound, while the sides of the abdomen show the reverse. The difference between rectal and oral readings previously commented on in cases of heart disease is well shown.

Case 3.—W. S., male, aged 45. Cerebral softening (?hæmorrhage). Left hemiplegia.

12.30 p.m., 10/9/08.

Air 62·2 Rectum 98·0

	Right.	Left.
Abdomen	91·04	95·0
Elbow (olecranon)...	79·1	87·8
Tip of ext. malleolus	77·36	74·3

The temperature of the abdomen and arm on the paralysed side is higher, of the leg on the same side, lower.

Case 4.—S. F., male, aged 26. Right hemiplegia (leg, arm, lower part of face) due probably to laceration of the brain following a fall.

5.45 p.m. 76 days after the accident.

Air 58·6 Rectum 100·0 Mouth 99·0

	Right.	Left.
Dorsum of foot ...	66·2	68·0
Outer side of great toe	60·8	61·7
Elbow (front) ...	91·7	93·2
Abdomen	93·7	96·4
Outer end of eyebrow	91·4	92·3

The whole of the paralysed side is the cooler.

Case 5.—Right hemiplegia involving both upper and lower limbs and to a slight extent right side of face. Aphasia.

5.15 p.m. 20 days after onset.

Air 55·4 Mouth 96·6 Rectum 100·4

	Right.	Left.
Front of elbow ...	91·0	90·5
Between fingers ...	79·1	80·6
„ toes ...	71·6	78·8
Abdomen	88·7	89·9
Thorax (near nipple)	87·0	89·8
Outer end of eyebrow	88·5	88·5

Though in the antecubital fossa the paralysed arm is 0·5° warmer than the other, the fingers on the same side are 1·5° colder. Apart from the elbow and the forehead, the body is

throughout colder on the paralysed side. At the post-mortem nothing pathological could be found in the brain. The paralysis was probably due to some latent encephalitis.

Case 6.—A man, aged 39, suffering from general paralysis of the insane. Unconscious when admitted to the hospital on February 25th, he developed left hemiplegia, which rapidly cleared up.

6.15 p.m., March 3rd.

Air 55·4 Mouth 96·6 Rectum 99·6

	Right.	Left.
Inner side of thumb	85·1	83·1
Abdomen	88·7	91·4
Inner side of great toe	80·6	77·0

Power had returned to a great degree, the left knee being nearly as strong as the right, though there was still considerable difference between the grip on the two sides. The limbs on the paralysed side show the lower, and the abdomen the higher, temperature.

Case 7.—Woman, aged 20. Sudden onset of aphasia and paralysis of right arm and leg on August 18th. Babinski's sign was present, and the hemiplegia appeared definitely organic, though no definite cause could be ascertained.

	Air.	Rectum	Skin of Abdomen.		Skin of Elbow.		Skin of Tip of Ext. Malleolus.		Pulse.	Resp.
			Right.	Left.	Right.	Left.	Right.	Left.		
8.30 p.m., August 24th	65·3	99·0	93·2	93·2	88·8	89·6	92·1	92·1	72	28
Sept. 15th	67·1	98·6	93·3	93·7	91·0 (anterior 93·2)	87·8 (anterior 91·4)	75·9	78·8	—	—
10.30 a.m., Sept. 24th	65·8	98·6 mouth 98·4	92·3	93·5	83·3 (anterior 89·6)	86·1 (anterior 91·9)	80·7	79·3	104	24

In the course of a month we here see curious variations. Six days after the onset there is little difference between the two sides, the abdomen and lower extremities being equal in temperature, and the arm on the paralysed side only 0·8° lower

than the other. Twenty-two days later we find the paralysed side of the abdomen slightly the colder, as also the leg, while the paralysed arm is the warmer by several degrees. At this time, the leg was beginning to recover movement, while the arm remained powerless. Speech was returning. When the temperatures were next taken there was a remarkable reversal of the preceding. The paralysed leg was now slightly warmer than the sound limb, and the arm and abdomen of the affected side cooler than those of the other. Power was returning rapidly, especially in the leg, and the woman could walk, and speech was returning. These observations were made with special care, and were confirmed by another medical man. The readings were made on the two sides under identical conditions of exposure, no hot-water bottles being near the patient. There is a marked difference between the readings taken anterior to the elbow and those taken over the olecranon. The former were taken in the antecubital fossa, comparatively near to the main blood vessels. A similar ratio, however, is present between the two sides.

Case 8.—G. B., a man 57 years of age, on the 1st of June fell six feet on to his head, and came to the hospital complaining of stiffness of the right arm. He was admitted at 10 p.m., and soon lost all power in the right arm and in both legs, some power remaining in the left arm, which also jerked occasionally. His temperature steadily rose, and, as taken in the mouth by the nurse, read as follows:—

10 p.m.,	1st June	... ...	96·4°
6 a.m.,	2nd „	... ...	100·4
10 a.m.,	„ „	... ...	103·8
2 p.m.,	„ „	... ...	103·2

When seen by me at 6 p.m. he presented the symptoms of a lesion low down in the cervical cord, viz., the paralysis above mentioned, folding of the arms across the chest, priapism, and incontinence. I took his temperature from that day to the 11th of June.

	Air.	Mouth.	Rect.	SKIN. Abdomen, Left side.	SKIN. L. Wrist.	SKIN. R. Wrist.	SKIN. L. Knee.	SKIN. R. Knee.	Pulse.	Resp.
6 p.m., 2/6/08...	74·6	105·2	105·8	101·6	98·9	99·8	102·3	101·8	84	24
7 p.m., after cold sponging	73·4	103·4	104·0	96·4	—	—	—	—	—	—
11.35 p.m. ...	71·6	102·6	103·0	95·9 / Rt. 97·7	—	—	—	—	80	28
5 p.m., 3/6/08, semi-comatose.	—	102·6	—	97·7	—	—	—	—	—	—
Left arm completely paralysed	76·1	mouth breathing	106·1	Rt. 97·7	99·3	98·9	—	—	93	32
5 p.m., 4/6/08 ...	77·9	100	102·6	97·7	—	—	—	—	64	16
4.50 p.m., 5/6/08, general condition much better. Paralyses unchanged	20·4	96·6	99·7	94·6	—	—	—	—	52	12
6.10 p.m., 11/6/08	68·9	96·4	97·8	91·7	—	—	—	—	52	16

The ward chart recorded the oral temperatures of 95° to 95·6° from the 6th June continuously onwards till death on June 21st. Post-mortem, nothing pathological was found except a small round body the size of a small shot in the central canal just below the fourth ventricle. On section, it showed only granulation tissue. There was no trace of hæmorrhage in the brain or spinal cord and no injury to or displacement of the vertebræ.

I may point out first the height, 106·1°, reached by the internal temperature two days after the accident, and the subsequent drop to subnormal. On the first day the rectal temperature was 4·2° above the surface temperature, the former being 8·0°, the latter 9·9° above the level recorded nine days later. Cold sponging reduced the skin 5·2° and the internal temperature only 1·8°. Next day the rectal temperature was 3·5° above the oral and 8·4° above the skin, being 8·3° higher than that of the 11th, while the skin was only 6·0° over the corresponding temperature.

As to the inequality of the two sides, the day after the accident the surface of the right wrist, which had completely lost power, was 0·9° warmer than that of the left, which had only partly done so and was still moving. Next day the left had

become completely paralysed, and was now slightly warmer. As to the abdomen, the temperature of the more paralysed side was, on the second day, 1·8° the higher, though when on the next day the paralysis on both sides was complete, they were also equal in temperature.

The slowness of the pulse rate (52) on the 5th and 11th is striking, considering the subsequent failure to discover any lesion within the skull.

In five of my cases the paralysed arm was the cooler, in the other three the warmer externally, while in the eighth case the temperature appeared definitely to follow in its course the extent of the paralysis. In the 7th case the arm was only temporarily the warmer. In the same case when, 35 days after the onset, the arm dropped relatively in temperature, the affected leg became warmer than the other. The leg was then rapidly recovering movement. In one other case the affected leg was temporarily 1·8° warmer than the sound, which two days later showed the higher temperature, the legs having been at first equal in surface heat. In five other cases the paralysed leg was markedly the lower in temperature. In Case 8, where the loss of power was equal in both legs, there was little difference in temperature. The abdomen presents a noticeable inequality between the two sides in surface temperature, though not in motor functions. In three cases the temperature on the paralysed side is higher, in two it is lower. In No. 7, for twenty-eight days the two sides are equal, though seven days later the paralysed side is the cooler. In Case 8, when there was a difference in the amount of paralysis present in the limbs, the abdomen on the more affected side showed the higher surface temperature, which became equal to that of the other side when the paralysis became equalised. It would appear that the disturbance of the temperature is more extensive than that of the motor functions. So far as my own observations show, the surface temperature is more often raised on the paralysed side of the abdomen, though it may be lowered; that of the limbs may be raised, but is more often lowered, the limbs

often varying, since the arm may be relatively lower and the leg higher or vice versa. In cases of long standing, both limbs and abdomen on the paralysed side appear definitely lowered in temperature.

The variability of the results is only what is to be looked for when we consider how many and how changeable are the factors involved, the primary loss of central control, the internal stasis induced by shock, and later the recovery both of the general circulation and of local tone, and also the local response to external influences.

Summary.

1. To gain any knowledge of the regulation of bodily heat we need many more data as to internal (*i.e.*, rectal) and surface temperature, a record of which in different pathological conditions should furnish valuable information as to the cause of pyrexia in the individual case. Pyrexia is the resultant of excessive heat production and diminished loss, or, in the majority of cases, a combination of the two. The skin temperature may be taken with sufficient exactitude by a flat-bulbed mercurial thermometer, which furnishes results almost identical with those of thermo-electric methods. The mean temperature in health of the skin of the abdomen is 93·0°F. (33·94°C.), that of the rectum being about 98·2°F.

2. The rectal and surface temperatures of the child at birth are higher than those of the mother. The effect of a hot bath on the child is to lower the rectal and raise the surface temperature.

3. In heart failure the internal temperature is not, as a rule, sub-normal, the mouth readings being particularly misleading.

4. Two cases of rigor show a relatively low surface temperature due to cutaneous vaso-constriction, and associated with a high internal temperature. The patient feels cold and shivers. Later there is a reversal of the conditions. These phenomena were not observed in a third case.

5. In typical lobar pneumonia, the skin temperature is, relatively to the internal temperature, high, though in atypical and grave cases it may be quite low.

6. In typhoid fever heat loss appears to be low, the rise in skin temperature being much less than that of the internal parts of the body.

7. In measles and German measles the skin temperature is, considering the rash, unexpectedly low.

8. Though uræmia and eclampsia are usually not associated with pyrexia, it occurs in two of my cases, in one of which there was a post-mortem temperature of 108·0° (rectum).

9. A case of pernicious anæmia gave a high skin temperature (103·6°) with a reading of 105·4° in the rectum.

10. The pyrexia of infective endocarditis, pericarditis, syphilis, gout, appendicitis, empyema, show nothing noteworthy in the relations of the two temperatures.

11. As a result of general anæsthesia induced with ether, chloroform, or A.C.E. mixture, the rectal temperature in four cases fell and remained low for several hours, while the skin fell considerably less, varying in degree with the exposure of the patient, and in one case even rose 0·7°.

12. Following intra-spinal injection of novocaine in a case of typhoid with perforation of the bowel, no change of temperature (skin or rectum) occurred during the operation of laparotomy.

13. Local Changes of Heat:—

(*a*) A local rise is shown in purulent ophthalmia and gonorrhœal arthritis, also in the case of Herpes Zoster, where the temperature remains raised for months subsequently. This appears to be due to nervous influences.

(*b*) There may be important heat changes, both local and general, in lesions of the central nervous system, cerebral hæmorrhage, etc., an association with hyperthermia being not infrequent. I record a temperature of 106·1° reached in a case of obscure injury to the spinal cord.

As to the local changes, Dr. Hale White in three cases found the heat loss consistently the greater on the paralysed side. In my own investigation of eight cases there is considerable variation in skin temperature. My personal deductions are that frequently the paralysed side does show some elevation of temperature which is only temporary. The paralysed arm may be raised in temperature and the paralysed leg lowered as compared with the limbs of the sound side or conversely, the temperature ratio completely changing sometimes in a few days and appearing often to follow no definite rule.

The disturbance in thermotaxis appears to be more widespread than it is in motor function.

In the abdomen no difference in motor power can be detected between the two sides, yet nearly all show a difference in temperature which, in the majority, is raised on the paralysed side, being relatively lowered on the other. In cases of long standing both limbs and abdomen on the paralysed side show a definite fall in heat.

In conclusion, I must express my warm thanks for his kind help and advice to Dr. Pembrey of whose published work I have made extensive use. I am also much indebted to the Croonian Lectures of Dr. Hale White; and, further, to the Physicians and Surgeons of Guy's Hospital for permitting me to make observations on the patients in their wards. The special thermometers used were provided by Dr. Pembrey out of a grant made by the British Medical Association.

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THE ADMINISTRATION OF RADIUM AND ITS DERIVATIVES WITH REFERENCE TO THEIR POSSIBLE APPLICATION TO CANCER.

By

E. BELLINGHAM SMITH, M.D.,

(Douglas Research Student, Guy's Hospital, 1909—1910),

AND

W. WILSON, M.Sc.,

(Hon. Fellow of the University of Manchester, 1909—1910).

So much has been written in reference to the external application of radium in the treatment of carcinoma, and the quantities of radium used have been so far beyond any at our own disposal that we have felt that any repetition in this direction alone would be not only unnecessary, but useless. On the other hand, but little work has been done in regard to the internal administration of this element and its derivatives, and that which has appeared has failed to deal quantitively with the subject.

We propose, therefore, in this paper to explain the methods which we have adopted to ascertain the actual distribution and fate of radium and its derivatives after their introduction into the body, and incidentally to mention any changes which may have occurred in the course of these experiments. As the later experimental work dealing with the application of the knowledge

so obtained has been carried out on cancerous mice, we have, in these preliminary experiments, made use of the same animals.

Let us, then, first of all consider the chemical properties of radium. Briefly, we can say at once that it is a member of the group of alkaline earths—barium, strontium, calcium—having an atomic weight of about 226, which is separated by a long and tedious process from various uranium residues, and is obtainable for use in the form of bromide, chloride or sulphate.

In dealing with the physical phenomena exhibited by this element, we shall try to explain how these changes occur, in what way they may be studied and measured, and how they may be made available for use.

Radium is a substance constantly undergoing disintegration, during which process heat is generated and energy liberated in the form of a rapid discharge of minute particles, to which have been given the name of *alpha* and *beta* rays.

The first group of rays have been shown to be atoms of helium charged with positive electricity, while the second group are negative electrons. These particles are ejected with great velocity, the speed of the *alpha* particle being of the order 10^9 cm. sec. and that of the *beta* particle, 10^{10} cm. sec. In addition to these radiations, a third group is recognised, which is known as the *gamma* rays. Whether these are uncharged particles or merely ethereal vibrations similar to X-rays set up by the motion of the *beta* rays is at present unsettled. They have the power of producing secondary rays, similar to the *beta* rays, when they are allowed to fall on matter. Further, about 90 per cent. of the total activity of radium is due to the *alpha* rays, 9 per cent. to the *beta* rays, and only 1 per cent. to the *gamma*.

The three groups of rays vary greatly in their power of penetrating matter. The *alpha* rays are all stopped by 7 centimetres of air. The *beta* rays are more penetrating, and can be detected after passing through 2 mm. of aluminium, while the *gamma* rays will readily pass through several centimetres of lead.

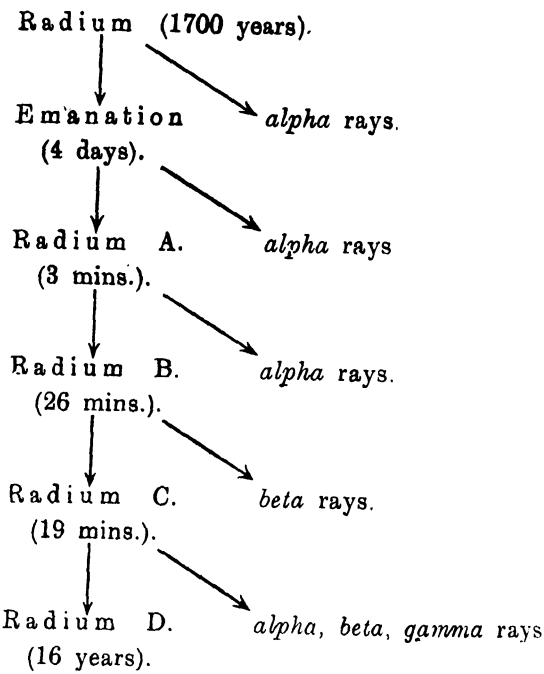
The disintegration of radium, however, represents something more complicated than the mere discharge of particles. Moreover, these rays are not only emitted from the radium itself, but also from other bodies which are formed during the changes which the radium itself is constantly undergoing.

When the radium atom emits an *alpha* particle, the residue is found to be an atom of a gas of high atomic weight, which is called the emanation. This gas in turn disintegrates, giving rise to a further body, which is called radium A ; in this process the emanation also emits *alpha* rays.

Radium A in turn breaks up to form radium B, with the liberation of an *alpha* particle, while radium B, giving off *beta* rays, gives rise to radium C, which yields *alpha*, *beta*, and *gamma* rays. With the terminal products D, E, F, if terminal they be, we have here no need to deal. These bodies—radium A, B, C—have been called the active deposit of the emanation. Their name arises from the fact that, if any substance be brought in contact with the emanation, these bodies are deposited on its surface, inducing an activity which exists during their lifetime. When substances possessing such induced activity are removed from the exciting agent they rapidly lose their radio-active properties. In fact, the activity dwindles to half its original value in half an hour, and after four hours has practically disappeared. Further, the emanation itself tends in the same way gradually to lose its activity, so that at the end of four days its radio-activity is only half what it was when first collected.

It should be mentioned that this gas is not formed in any appreciable quantity, and it is only by the most refined methods that it can be obtained in anything approaching a pure state. This emanation or gas can be obtained by heating the radium salt, by passing a current of air over the radium, or bubbling it through a solution. Prepared in this way it may be collected in a sealed tube, or as a solution in various liquids. Such solutions, if kept tightly sealed, will obey the above law, and the solution will gradually lose its activity, until at the end of four days it is only half value. Now, we have seen that the radium

itself gives off merely *alpha* rays and that it is from the products of the emanation which is left behind that the *beta* and *gamma* rays are ultimately formed. It is, therefore, at this point essential to note how much of the total activity pertains to the radium and how much to the emanation. Experiment has shown that, if a radium salt be thoroughly de-emanated by a prolonged current of air, then the *alpha* ray activity of that salt will have fallen to quarter of its original value, while the *beta* and *gamma* ray activity has entirely disappeared. The emanation and its products, therefore, at any time, are responsible for three-quarters of the radio-activity of the radium in question.



The transformations of radium and its derivatives, with the respective periods during which they retain their radio-activity, can be shown, perhaps, more clearly in a table, found in all text-books of radio-activity and which we reproduce above. The

type of radiation emitted by the bodies and the time taken to decay to half value are given.

The radium is continually producing emanation which in turn is continually decaying, so that from a given quantity of radium only a certain maximum amount of emanation can be obtained. If we consider a quantity of radium which has been deprived of its emanation, at first more emanation is being formed than is decaying, since this latter is proportional to the amount of emanation present. As more and more emanation is produced, however, the amount which decays continually increases, while over ordinary periods of time the amount of radium which disintegrates, that is, the amount of emanation which is being formed, remains constant. We thus finally reach a certain stage when just as much emanation is being formed as is splitting up, so that the actual amount present is then constant. This state is reached after about one month's time. Thus, there is a definite quantity of emanation in equilibrium with a definite amount of radium, and if this quantity be determined it is a measure of the amount of radium present.

It now remains to explain the methods employed for the detection and measurement of these activities, and the principles on which they are founded. It is known that gases are feeble conductors of electricity, and that under the influence of various agencies this conductivity can be increased. Amongst those agents we find the rays of radio-active bodies. The radiation in passing through the gas splits it up into negative and positive ions, and these in the presence of an electric field move towards the positive and negative respectively. Consequently, if a substance such as radium be introduced into a charged electroscope, ionisation of the contained air occurs, and the rate of discharge of the gold leaf is increased. The rapidity of this discharge is proportional to the activity of the radium. To express this activity conveniently a standard must be sought, and for this purpose a body of feeble radio-active properties has been chosen, known as uranium. The activity of this metal being taken as unity, we can express the activity of a preparation in terms of

uranium. Thus, if we say the activity of uranium is one, and that of radium 2,000,000, we mean that the ionising power of the latter is 2,000,000 times greater than that of uranium.

The most convenient way of estimating this activity is by means of an instrument known as the electroscope. In the experiments which we have undertaken we have made use of two different types.

The first, or *alpha* ray electroscope, consists of two small aluminium chambers, placed one above the other. The lower or ionising chamber B contains two horizontal metal plates, separated by a distance of 5 cm. The upper plate is in connection, through an insulating plug C with an upright metal rod and attached gold leaf, which occupy the upper chamber A. The fall of the charged leaf can be watched by means of a reading telescope through the two windows in A. The material, the activity of which it is desired to determine, is placed in a receptacle on the lower of the horizontal plates. Ionisation of the air between the plates occurs with consequent discharge of the electroscope.

This instrument is not applicable to those substances which emit emanation. Its use is restricted to finding the available *alpha* ray-activity of a given specimen, and cannot be applied to determine the total radium content, as the rays employed only proceed from a superficial layer. In dealing, therefore, with the emanation, and also in practically all estimations requiring a quantitative and accurate result, we have made use of a second instrument, which is an emanation electroscope. In this instrument the quantity of radio-active material present is gauged by the measurement of the emanation in equilibrium with it.

The apparatus consists of a silvered glass flask with side tube; the upper opening is fitted with a rubber cork through which pass two copper wires. One of these supports the gold leaf and metal rod, with the intermediation of an insulating sulphur bead. The second, bent twice at right angles, acts as the charging rod. The portions of wire outside the flask are

carefully earthed, and a small wire attached to the first copper wire is in contact with the silvered surface of the glass. The side tube, by means of a T-shaped junction, is in connection, on the one hand, with a water pump and mercury pressure gauge, and, on the other, with the vessel or vessels containing the emanation or radio-active body of which it is desired to measure the activity.

The method of procedure is as follows:—

The glass flask, which must be air tight, is exhausted by means of the pump, and carefully clamped. The material of which it is desired to record the activity is placed in a flask which is attached to two wash bottles in series, and is then boiled. This drives off all the emanation contained in the active material, which is then collected in the wash bottles. These are in turn clamped and attached to the previously exhausted electroscope. The clamps are then released, and the emanation allowed to enter the electroscope. When all the emanation has passed in, air is allowed to enter until atmospheric pressure is attained. The leaf is then charged and the rate of the leak determined. It is found that the rate of discharge rises at first rapidly, and then slowly, until a maximum reading is obtained at about the end of four hours.

The readings in both instruments are taken by watching the leaf through a telescope, with a scale in the eyepiece. By the latter means extremely small amounts of radium can be measured. From the observed rate of fall of the leaf must be taken the rate of fall before any active material is introduced into the vessel.

It now remains to be seen, firstly, in what way radium and its derivatives may be administered; secondly, to determine the methods adopted by the body for the elimination of the substance after its absorption; and thirdly, the effects, harmful or otherwise, which may accrue from such administrations; while lastly, we must judge how we can apply the knowledge so obtained to therapeutic uses.

Administration of Radium.—Most substances can be administered externally, internally, or by injection, and radium forms no exception. But the internal administration of pure radium, owing to its scarcity, is as yet prohibitive. Also, it is difficult to believe—even if it could be obtained abundantly—that a large dose, however transitory its residence in the intestinal canal, would do aught otherwise than produce those effects which we know it capable of in its external application to the skin. As a drug for internal administration, therefore, it must be used in very small doses, and it is even now possible to make use of it in this way.

It may, then, be given in small doses of pure radium bromide or radium chloride; if absorption is not required, as an insoluble radium sulphate. On the other hand, it can also be obtained admixed with barium salts, a condition in which it occurs in the later stages of its purification and preparation from uranium ores. In this latter case, however, it must be remembered that barium is an acute gastro-intestinal irritant, and in large doses causes cardiac paralysis. These so-called impure salts are measured in the same way, and according to the quantity of radium they contain are called salts of 250, 1,000, 20,000, etc., activity. They are obtainable in the same way as the pure salts, as mixtures of radium barium bromide, and radium, and barium sulphate.

We will, first of all, consider the fate of a pure radium salt after its administration by the mouth. In this case we have had to content ourselves with a single experiment on account of the costliness of the material. For the experiment 1/22 mg. of pure radium bromide was dissolved in 2 c.c. of water; to this solution was added a very small quantity of bread. A mouse was then placed by itself in a case at 12.45 p.m., July 14th, with no other food than the radio-active sop. At the end of four and a half hours the sop had all disappeared. A very small quantity of fresh sop was then placed in the bowl, so as to avoid any loss of radium; this was partially eaten by 5.30 p.m. of July 14th. The animal was then killed. The stomach,

small intestine, and large intestine were each separately tied off and placed in different vessels. The other viscera were treated in the same way and sealed up. Each separate portion of the gastro-intestinal tract was then carefully washed in normal saline until as far as possible free from any contents.

On the following day an estimation of the activity of the various organs was commenced by means of the emanation electroscope. The viscera were finely minced in water and heated in separate flasks, and the products collected and drawn in turn into the emanation electroscope. An examination was made in this way on the two following days, 15th and 16th July, and the maximum leak in each case recorded. The table below shows the various organs examined, their respective weights, and the activity of each in scale divisions per minute. In the final column the activity in scale divisions per gramme of tissue is given:—

Organ or Tissues.	Weight wet in grm.	Activity of organ examined in divisions per minute.	Activity in scale divisions per gramme.
Kidneys	0·418	15·3	36·6
Liver	1·780	3·75	2·1
Stomach	0·191	2·2	11·5
Small intestine ...	1·352	7·05	5·2
Large intestine ...	0·559	3·75	6·7
Lungs	0·534	5·12	9·6

From this we see that the greatest activity is present in the kidneys, and is most marked next in the stomach and lungs. There are, however, evident inaccuracies in this experiment. One is the extreme difficulty in entirely freeing the intestinal canal from its contents. Secondly, the values which are given are below full value, as the radium, after exposure to the body temperature, will probably have parted with a large proportion of its emanation, and, as the examinations were made on different days directly after death, they are not strictly comparable. Consequently, to correct the two latter fallacies, the organs were sealed up for a month, and a further examination made when the emanation had attained its equilibrium value.

The next table shows the great alteration which occurs in the figures after the organs and radium contained have been kept for a month:—

Organs	Weight in grm.	Activity after 2nd Estimation in divisions per minute.	Activity in scale divisions per gramme.
Kidneys ...	0·418	562	1340
Liver	1·780	138	78
Stomach ...	0·191	44	230
Small intestine	1·352	214	150
Large intestine	0·559	327	580
Lungs	0·534	75	140
Muscles, Bones, Skins ...	24·400	1529	62
Intestinal contents	Not weighed	Too great an activity for accurate estimation. Circ. 6000 divisions per min.	—
Quantity left after feeding	Not weighed	804	—

The activity of the kidney is still the greatest, and the large intestine now occupies the second place. We shall discuss these figures later when dealing with the estimation of the radio-activity of various organs after injection.

It would not seem reasonable to expect any absorption to occur after the administration of the insoluble salts of radium by the mouth, but, as we have known them given as a therapeutic agent, we feel it necessary to settle this point definitely.

Experiment.—Three full-grown mice with small carcinomata were given 30 mg. of radium barium sulphate daily for three consecutive days. On the evening of the third day two of these were separated and placed in a cage specially adapted for the collection of their urine and fæces. The accumulated fæces and urine passed during the subsequent 17 hours were then taken and examined separately in the emanation electroscope, as described above. The urine failed to show any activity. The fæces, on the other hand, were markedly active. Radio-active material was, therefore, being consumed and excreted by the two mice under observation. A fourth dose of 30 mg. was then given, and a similar examination yielded a like result: fæces active, urine not.

A fourth mouse was now taken, and the administration of radium barium sulphate was continued with the third mouse of the other experiments. During the following 27 days 210 mg. of 250 salt were given by the mouth. On three separate occasions the urine and fæces were collected for periods of 24 hours and examined. The activity of fæces was marked, while none existed in the urine. On the 27th day both animals were killed, the whole gastro-intestinal tract was carefully ligatured and removed; the other viscera were then treated in the same way.

The organs selected for examination were the kidneys, liver, and spleen. All these viscera showed a slight temporary activity, which, however, disappeared after a few hours, and was probably due to a trace of circulating emanation and not to radium. This estimation was made with the *alpha* ray electroscope. The bowels were then taken and carefully freed from their contents, and both were saved. An examination was then made of the bowel and contents respectively. It was found that, while there was marked activity in the intestinal contents, none existed in the bowel itself. The whole of the viscera of the animals were then examined together to detect, if possible, a trace of activity, but with a negative result. These last estimations were made with the emanation electroscope. Therefore, while the contents of the bowels themselves are exceedingly active, the bowel wall and the other viscera show no evidence of any trace of radium. Absorption, therefore, in the case of insoluble salts does not occur after administration by the mouth.

The next question that arises is the fate of these salts after subcutaneous injection. We must consider this under three headings:—

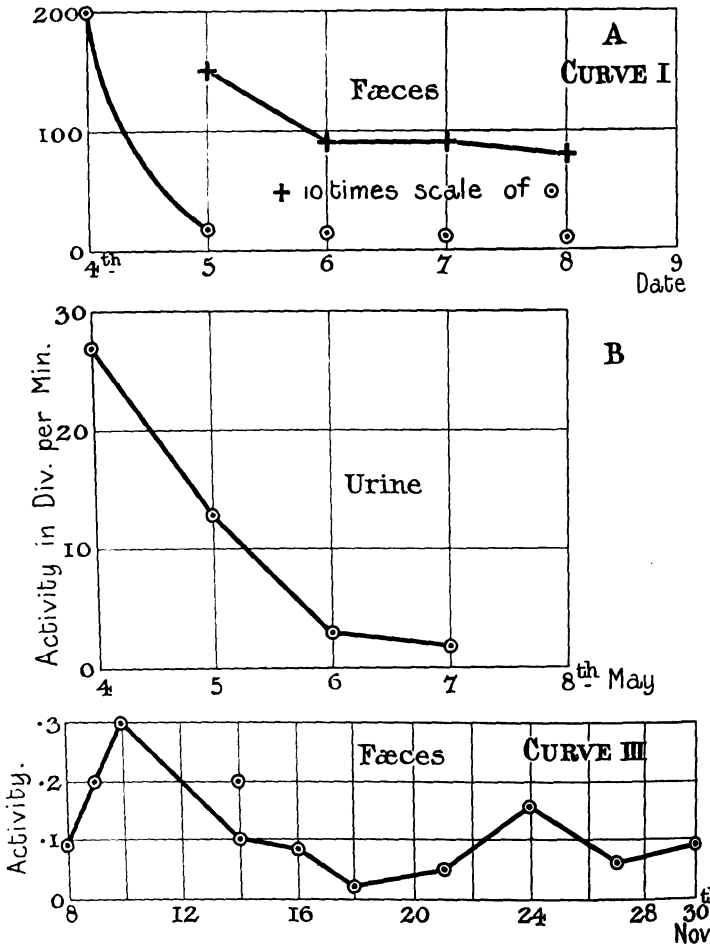
(1) The elimination of soluble salts of radium admixed with barium salts.

(2) The elimination of insoluble salts of radium.

(3) The distribution and elimination of pure radium salts.

(1) *Experiment.*—To determine the direction of excretion of soluble salts of radium admixed with barium.

For this purpose two mice, A and B, were taken and injected subcutaneously with 0·5 mg. of radium barium bromide of 20,000 activity (uranium taken as unity). Both points of injection were painted with a solution of collodion in acetone, to prevent any risk of escape of fluid. Both mice were then placed in a cage



specially constructed for the separation and collection of urine and fæces, which were removed at the end of every 24 hours. The excreta were examined in the emanation electroscope, and the daily activity recorded. The chart above, Curve I. (A and

B), shows the radio-activity of the urine and fæces for each succeeding 24 hours.

From this we see that 60 to 70 per cent. of the radium excreted appears in the fæces during the first 24 hours, and only 10 per cent. in the urine. At the end of the third day the amount has fallen to 2 per cent. in the fæces and practically nothing in the urine.

(2) In the same way, to study the elimination of an insoluble salt injected subcutaneously, a mouse of 16 grm. weight was injected with 50 mg. of radium barium sulphate of 250 activity. A daily examination of the urine and fæces was made in all cases. The urine was negative, and the fæces showed a very feeble radio-activity. Curve III. indicates the daily record of active material passed by the bowel. In all these experiments a control experiment was performed before the injection was given, to test the normal urine and fæces for activity. The chief features of this chart are the exceedingly small quantity of radio-active material eliminated each day, and the long time over which this excretion is prolonged. In this case the animal was still passing active fæces 23 days after injection.

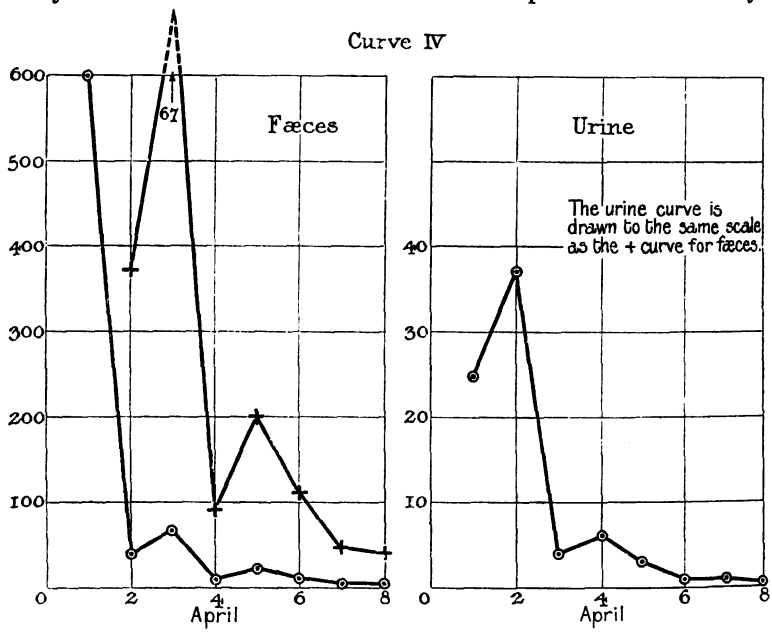
In a second experiment a mouse was injected with the same quantity of radium barium sulphate, and the accumulated fæces were examined at the end of the first 14 days, at the end of the third week, two days later again, and then at the end of the fourth week. The table shows the total radio-activity for each period:—

Excretion.		Natural leak. Divisions per minute	Period of Collection.	Activity (total) Divisions per minute.	Activity in scale divisions per day.
Urine nil	Fæces	0·18	Dec. 21—Jan. 4	0·70	0·05
—	—	0·22	Jan. 4—Jan. 11	0·84	0·12
—	—	0·21	Jan. 11—Jan. 13	0·26	0·13
—	—	0·22	Jan. 13—Jan. 20	0·85	0·12

We see that the amount excreted daily is constant, and identical with that excreted in the previous experiment. Again, if these figures really represent the presence of radium, we should expect

to find that salt present at the seat of injection at a late date. In the last experiment, 4 days after the last estimation, or 32 days from the initial injection, the animal was killed, the tissues at the site of injection were cut up and examined in the *alpha* ray electroscope. There was marked activity present. An examination in a similar way, of the other viscera, showed a feeble activity in the liver alone.

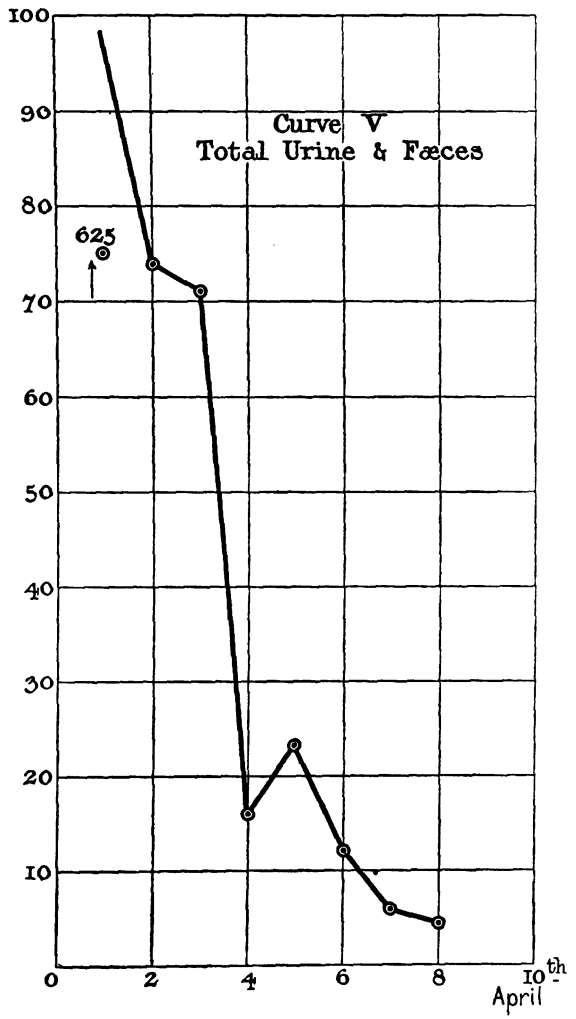
In the above injection experiment radium has been used, diluted with barium. Now it has been shown by Gustave Meyer that elimination of this metal takes place almost entirely



NOTE. + Scale 10 times that of ⊙

by the bowel, and only slightly in the urine when the animal is fed by the mouth. It is, therefore, possible that the excretion of radium might be influenced by the presence of the barium. A further experiment was therefore performed with a small quantity of pure radium bromide, and the curve of excretion, Curve IV., can be compared with that of radium barium bromide, Curve I. It will then be seen that excretion takes place in almost the identical way, and at the same rate in the two cases.

In this experiment two mice were used, and an injection of 2 c.c. of distilled water containing 0·0036 mg. of pure radium bromide was given in each case. The radio-activity of this



quantity of radium was estimated previous to use at about 800 div. per min. (0·2 c.c. of the original solution discharged an

electroscope at the rate of 40 div. per min.). If the activity for the various periods be added up, we find the total is 825. So that apparently all the radium originally given appears either in the urine or fæces, if we allow a small margin of 25 in a large number of readings to be due to an extra 0·1 c.c. having been injected or as due to repeated small errors of observation.

Of the total quantity, 91 per cent. appears per rectum and only 9 per cent. in the urine.

From repeated experiments we can say that the excretion of radium, whether given by the mouth or by injection, appears to take place principally by the bowel, and to a slight degree by the urine. It then only remains to examine the distribution of the radium after injection, and to discover whether the whole, or only a part, of the intestinal canal excretes radium, and whether any other organ, such as the liver, plays any part in the process.

William Salant and Gustave Meyer (i.), working on the elimination of radium, found that in dogs and rabbits the kidneys, liver, and small intestine eliminate radium, while in rabbits elimination also takes place through the large intestine.

In these experiments radium barium bromide of 1000 activity was used, and a dose of 10—30 mg. given on each occasion.

The means employed were the formation of a biliary fistula, on the one hand, and ligature of the different portions of the intestinal canal, on the other. These ligatures were placed at the cardiac and pyloric end of the stomach, below the duct of Wirsung and above and below the cæcum. An injection of radium was then given, the bile was collected at varying periods, and a few hours later the animal was killed. By this means, in dogs, they found the bile radio-active, as also the contents of the small intestine. The stomach, large intestine, and contents of both, showed no activity.

The same features held true for rabbits, with the exception that there was some slight activity in the contents of the large

intestine. In no case was any activity detected in the intestinal wall. These estimations were conducted by means of a quadrant electrometer, and are of a purely qualitative order, and give no indication of the quantity of radium present. In other words the activity was measured by observing the ionisation of the air in which the various organs were exposed, which does not give the total radium content, but depends on the area of the specimen exposed, and its density. Further, the mere evidence of activity in an organ or secretion does not indicate necessarily that that organ or secretion is actively eliminating radio-active material, unless it can be shown that the activity present is greater than the average activity elsewhere. As will be seen from the experiments below, activity is present everywhere in the body and tissues generally, both with large and small injections of radium, after 4 hours or after 28 hours from the time of injection.

Although with mice it is impossible to conduct an experiment on the same lines as those of Meyer and Salant, yet we have attempted by another method to determine the quantity of radium present in the various parts of the body after an injection of a quantity subcutaneously. These experiments depend for their result on the measurement of the radium by the estimation of the emanation in equilibrium with it, a factor which we have seen is constant. This method is, therefore, quantitative and not qualitative alone, and if the weights of the different parts of the body be taken, the percentage of radium present in each part can be deduced from the measurement of the emanation liberated.

There is, however, a difficulty in these experiments which, after repeated trial, we have found insurmountable, and that is the introduction of an exact quantity. It is obvious that the injection of the smallest fraction, more or less than the amount calculated for, will upset by many figures the total of the activities present in the body at the end of the experiment. We have, therefore, not been at any great trouble to save and

measure the excreta, or to determine what is practically an impossibility, the value of the amount injected, but have contented ourselves with a series of careful observations on the distribution of the element throughout the body after administration.

Experiment 1.—Three mice were taken on June 29th, and injected each with 2 c.c. of pure radium bromide solution. The total quantity of radium injected was about 1/100 mg. The three mice immediately after injection were placed in a cage, so arranged that no excreta might be lost. Eighteen hours later they were killed, and the rest of the experiment was carried out in the following stages:—

(1) The bodies were opened, the stomach, small intestine, and large intestine were separately ligatured at their extremities, and divided and placed in separate vessels.

(2) Each in turn was then repeatedly washed, until free from its contents, which were saved.

(3) The other viscera were then removed and placed in a small glass specimen tube, previously weighed.

(4) The skin was carefully removed from the rest of the trunk, and each was similarly preserved in a separate receptacle.

(5) The weights of the various organs and structures were then immediately taken in the wet state.

(6) After some days each separate organ and portion of tissue was taken, minced finely in distilled water, placed in a small flask and gently heated. The products so obtained were collected in a wash bottle series and conveyed to the emanation electroscope, in the method previously outlined (page 137). By this means a measurement of the quantity of radium contained in each organ was obtained by the estimation of the emanation liberated.

(7) The tissues were then all carefully dried in a water bath and afterwards in a sulphuric acid desiccator until the weight

was constant. The percentage activity in dry and wet substance respectively was thus obtained.

The following table shows the radio-activity exhibited by the different parts of the body:—

FIRST ESTIMATION CONDUCTED JUNE 30TH—JULY 8TH.

Parts of Body or Excreta.	Weight wet in grm.	Weight dry in grm.	Activity in scale divisions per minute.	Activity in scale divisions per minute per 100 mg. of organ wet.	Ditto in dry.
Bones and muscles...	40·400	15·000	428	1·06	2·85
Skins...	12·850	7·000	26	0·20	0·37
Liver...	5·887	1·644	13·3	0·23	0·81
Kidneys	1·452	0·400	8·5	0·58	2·12
Spleen	0·722	0·201	3·6	0·49	1·79
Lungs	1·000	0·265	7·2	0·72	2·71
Hearts	0·602	—	0·04	0·01	—
Genital organs ...	4·687	3·123	10·00	0·21	0·32
Stomach	0·752	0·138	1·39	0·18	1·01
Small intestine ...	4·057	0·899	17·1	0·41	1·90
Large intestine ...	1·677	0·342	2·1	0·12	0·61
Contents of stomach	Not weighed	Not weighed	0·3	Practically nil	Nil
Contents of small intestine	—	0·357	4·5	—	1·23
Contents of large intestine	—	0·200	11·1	—	5·5
Urine passed before death	—	—	30·00	—	—
Fæces passed before death	—	—	41·00	—	—
Washings of trays and cage	—	—	218·00	—	—

These figures are open to the same objections as those previously mentioned in the feeding experiment, viz., the fact that they were carried out too soon after death, and that therefore the radium and emanation in equilibrium with it was not at a full or constant value. The same remedy was therefore taken of sealing up the dried organs and tissues and keeping them for a month. They were then estimated for a second time.

SECOND ESTIMATION AFTER ONE MONTH.

Part of Body or Tissues examined.	Weight wet in grm.	Weight dry in grm.	Total activity in divisions per minute.	Activity in scale divisions per minute per 100 mg. of organ.	
				Wet.	Dry.
Skins	12·850	7·000	68·5	0·53	0·98
Trunk (muscles and bones)	40·400	15·000	2100	—	—
Liver and gall bladder	5·887	1·644	23	0·39	1·40
Kidneys	1·452	0·400	8·5	0·59	2·12
Spleen	0·722	0·201	4·7	0·65	2·33
Lungs	1·000	0·265	11·3	1·13	4·26
Hearts	0·602	—	0·04	—	—
Genital organs ...	4·687	3·123	18·1	0·39	0·58
Stomach	0·752	0·138	1·66	0·22	1·20
Small intestine ...	4·057	0·899	25·0	0·62	2·80
Large intestine ...	1·677	0·342	10·3	0·62	3·01
Contents of small intestine	—	0·357	4·5	These were not estimated a second time.	
Contents of large intestine	—	0·200	11·1		
Contents of stomach	—	—	0·3		
Fæces passed before death	—	—	41		
Urine passed before death	—	—	30		
Washings of cage, trays, food, etc.	—	—	218		

A second incomplete experiment shows features which are similar to above. In this experiment the same number of mice were taken, and the same quantity of radium was administered subcutaneously. Injected on May 10th; killed 10 hours later.

TABLE SHOWING VARIOUS RADIO-ACTIVITIES.

Organs or Tissues examined.	Weight wet in grm.	Weight dry in grm.	Activity in scale divisions per minute.	Activity in scale divisions per minute per 100 mg. in wet organ.
Liver and gall bladders ..	4·807	0·977	8	0·16
Lungs	1·027	0·168	6·3	0·61
Spleen	0·962	0·158	2·0	0·21
Kidneys	1·060	0·145	25	2·40
Small intestine	0·780?	Not weighed	1·09	0·14
Large intestine	1·022	"	6·0	0·58
Stomach	0·397	0·040	0·38	0·10
Contents of stomach ...	Not weighed	Not weighed	0·34	—
" of small intestine...	"	"	109·00	—
" of large intestine ...	"	"	150·00	—
Rest of body	20·009	12·00	400·00	2·0

These figures will be commented on when the two next experiments have been described. For the present it suffices to draw attention to apparent enormous differences in the activity of the contents of the bowel in the two experiments. This is easily explained by the fact that two of the mice in the previous experiment developed diarrhœa after the injection, and the bowels post-mortem were virtually empty. In the second experiment the bowels were normal and contained a quantity of fæcal material, and consequently a quantity of radio-active material. In order to confirm these results, and also partially to see whether larger doses of radium are poisonous after injection, a third experiment was carried out. In this case 1/44 mg. of pure radium in 0·5 c.c. distilled water was injected subcutaneously into a mouse on August 5th. No distress or ill effects of any kind were noticed during the following 28 hours. The mouse was then killed, and the organs and tissues were weighed separately, and then dried, weighed again, and kept sealed for a month in small glass specimen tubes. At the end of that time they were examined by means of the emanation electroscope for radio-activity. The table appended gives the figures:—

Female mouse, weight 18·300 grm., injected with 0·5 c.c. of radium bromide solution (4 mg. in 88 c.c.), August 5th, at 1 p.m. Killed 5 p.m. August 6th, 28 hours after injection.

Organs or Tissues examined.	Weight wet in grm.	Weight dry in grm.	Activity in scale divisions per minute.	Activity in scale divisions per minute per 100 mg. of organ.	
				Wet.	Dry.
Liver and gall bladder	1·526	0·463	3·3	0·22	0·71
Lungs	0·579	0·135	24·0	4·15	17·8
Kidneys	0·406	0·125	19·3	4·75	15·4
Spleen	0·197	0·052	4·4	2·23	8·5
Genitalia	0·507	0·383	1·01	0·20	0·26
Stomach	0·215	0·065	0·67	0·31	1·03
Small intestine ...	1·162	0·240	2·07	0·18	0·86
Large intestine ...	0·397	0·078	1·07	0·27	1·37
Skin, body, muscles and bones	12·000	—	600	5·00	—
Contents of intestine and excreta	Exceedingly active.		No accurate estimate obtained.		

In the fourth experiment of the series 1/22 mg. of pure radium bromide was injected subcutaneously on August 8th. As before, no ill effects or changes appeared as a result of the administration. The animal was killed $6\frac{3}{4}$ hours later. No changes post-mortem could be demonstrated. The organs were treated as above.

Female mouse, weight 19,500 grm., injected subcutaneously with 1 c.c. radium bromide pure (4 mg. in 88 c.c. distilled water), at 11.15 a.m. August 8th. Killed 6 p.m., August 8th, $6\frac{3}{4}$ hours after injection.

Organs or Tissues examined.	Weight wet in grm.	Weight dry in grm.	Total activity in scale divisions per minute.	Activity in scale divisions per minute per 100 mg. of organ.	
				Wet.	Dry.
Liver and gall bladder	1·526	0·518	4·2	0·28	0·81
Lungs	0·187	0·045	10·3	5·5	22·9
Kidneys	0·302	0·077	50·0	16·5	65·0
Spleen	0·287	0·070	1·17	0·41	1·67
Genitalia	0·232	0·128	0·83	0·36	0·65
Stomach	weight lost	0·050	1·24	—	2·48
Small intestine ...	1·715	0·375	8·0	0·47	2·13
Large intestine ...	0·490	0·180	7·25	1·48	4·02
Skin, muscles and bones	12·500	not weighed	1875	15·0	—
Blood	0·109	0·022	10·0	9·2	45·5

Now, in all these four experiments a fact obtrudes itself constantly, and that is, the high activity which is present in the lungs and kidneys whether death has taken place shortly or some hours after injection, or whether the injection has been a powerful dose or a small dose. In three out of the four experiments the percentage is higher in the kidney than in the lungs.

The next feature is the total absence apparently at any time after injection of an accumulation of radium in the liver and gall bladder. If this organ and the bile took an active part in elimination we think it would be natural to expect at some period a percentage higher than the average to be present. This is not the case. When we come to deal with the spleen we find the percentage activity is little, if at all, above the average in three cases, while in the fourth there is evidence of

quite a marked radio-activity. Had the activity in the spleen been constantly of a high character, we might have assumed that along with the lungs such activity was due to the great vascularity of these organs. Now, it will be shown later that the lungs are the chief path in the elimination of the emanation, and consequently, failing other explanation, we must assume that accumulation takes place in these organs for the purpose of freeing the radium from its active principle, the emanation.

The genitalia and stomach, with the liver, show no evidence in any of the experiments of any activity higher than the average. Further, the contents of the stomach, which are estimated, are practically nil, showing that no elimination takes place through the wall of the stomach. When we come to the small and large intestine, one or both of which must assuredly excrete the major quantity of the element, we are met at once with a difficulty, for the activity of the bowel wall, though it is generally slightly greater than the average, and is more marked in the large than the small intestine, at no time shows any accumulation of radio-active material. Seeing, however, the great activity which is exhibited by the contents, we must assume that excretion takes place with such rapidity that the quantity present is never much above the average quantity present in the blood stream elsewhere. Whether excretion takes place by both the large bowel and small intestine or by the small intestine alone can hardly be settled from these figures. But the greater activity of the large intestine throughout rather suggests that it also plays some part in elimination. Against this must be weighed the fact that the cleansing of the sacculated large intestine from its contents is more difficult than the same process in the small intestine.

The remaining structures to be dealt with are the skin, muscles and bones. In the second experiment there exists no evidence that the skin plays any part in excretion. With the muscles and bones there appears to be a higher activity, but this is due to the fact that death has occurred in all cases before the absorption of the radium injected into the tissues has been completed.

For the normal distribution of radium in these tissues after administration, reference must be made to the experiment in which this element was given by the mouth. We have noticed here the same features: the high activity in the kidneys, a much less activity than usual in the lungs, but greater than that represented by the liver and tissues generally: while, further, there is a greater activity in the large intestine than in the small; as in the injection experiments.

It appears, then, that however given, the absorption and elimination of radium salts takes place always in the same direction, and in the same ratios. That, further, the evident channels of excretion are the small and large intestine primarily, the kidneys next, and that for some reason or other an accumulation takes place in the lungs, which is only explicable by the theory that it is an effort on the part of the body to free the radium contained in the blood from the emanation in equilibrium with it.

Administration of Emanation.—So far we have dealt with radium and its salts, their absorption, distribution and elimination. There now remains the emanation. The emanation is capable of administration in several ways:—

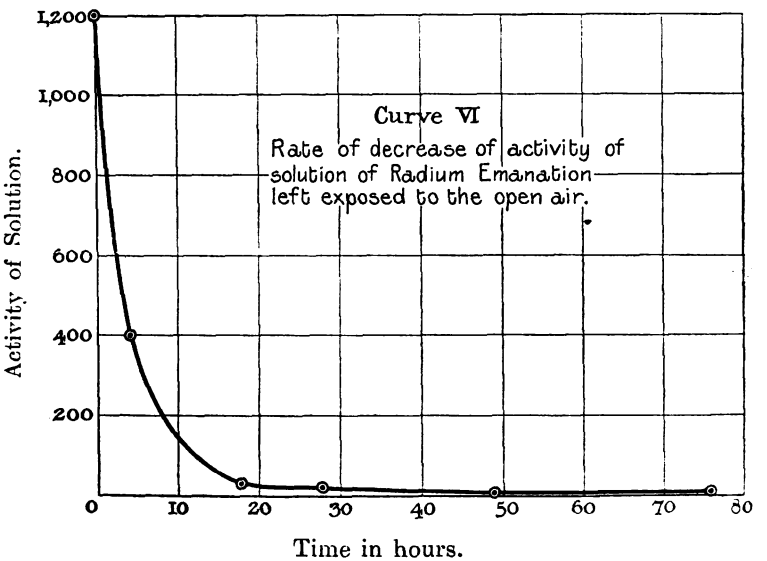
(1) By inhalation.
(2) In solution:—
    (a) By the mouth.
    (b) By injection.
(3) As an external application.

The emanation can be inhaled by breathing air that has been drawn through a solution of radium. The absorption and distribution of the emanation after this procedure we will deal with later when discussing the effects produced by this inhalation of the gas.

The next question is the administration in solution. We must first of all discuss the simple method of obtaining it. A glass vessel fitted with rubber cork and glass tubes containing the liquid, in which it is desired to obtain the emanation in solution, is exhausted, clamped, and attached to the apparatus containing

the radium itself in solution. The clamps are now released gradually, the air contained in the radium flask is drawn over and allowed to bubble slowly through the liquid. When bubbling ceases, a further supply of air is admitted to the emanation vessel, which is allowed to bubble through the radium solution and thence to the exhausted vessel. By this means a thorough de-emanation of the radium in solution is obtained. The radioactive liquid so prepared is drawn off from the vessel by means of a side tap. As this occurs, further emanation and air pass over to replace the liquid withdrawn. By this means the liquid will be found to remain at a fairly constant activity. Kept in a closed vessel, the solution of the emanation loses its activity at the usual rate, *i.e.*, half value in four days. Exposed to the atmosphere, on the other hand, it diffuses into the air according to the laws of gases.

The following chart exhibits the loss of activity which the solution undergoes when exposed in a watch glass:—



From this we see that, starting with a high activity, the solution, at the end of four hours, has decreased to one-third of its

original value. At the end of 24 hours there is still a considerable activity which, even after 76 hours, is appreciable. The quantity used in this experiment is only 0·2 c.c. of a solution of the emanation in oil. Consequently, if the solution be administered at fairly frequent intervals, a highly active state of the body should be maintained, provided absorption and circulation of the emanation takes place. Moreover, without in any way affecting the original supply of radium, we are by this method in possession in moderation of an inexhaustible supply of activating gas.

To determine whether absorption of the gas takes place after administration of the radio-active liquid by the mouth, the following experiment was performed:—

A full-grown mouse was fed on seed and radio-active water, or sop made with radio-active water, from September 3rd to October 7th, during which period 90½ c.c. were supplied. On the latter date the mouse was killed two and a half hours after the last administration. A rapid examination of the viscera was made, by means of the *alpha* ray electroscope, to determine whether any activity was present. A feeble but widely distributed radio-activity was found to be present.

With a view to testing the duration of this activity, a second experiment was conducted with a mouse B, fed in a similar manner, from September 20th to November 15th. During this period 240 c.c. of the radio-active solution were given. In this case the animal was not killed until 24 hours after the last food had been given.

An examination on the same lines as before showed a total absence of any activity in the body. At the end of two or three hours, therefore, there is a very feeble activity, which is totally absent at the end of 24 hours. In other words, the activity induced in the different tissues of the body by feeding an animal on a solution of the emanation is only of a temporary nature. Now, we know that the emanation only decays to half value in about four days, and that this rate is a constant; consequently if it is absorbed and has disappeared in less than 24 hours, we

must assume that it is either destroyed or is rapidly eliminated. As the first is impossible, excretion of the gas evidently takes place in some direction. Now, in the feeding experiments it is impossible to obtain the excreta or respiratory gases without previous contamination with the food material. Further, the quantity consumed at any one time is probably so small, and is spread over so large an area after absorption, that any appearing in the excreta would be infinitesimal in quantity.

A number of observations, however, have been made by us on the urine and fæces and respiratory gases, but no radio-activity was forthcoming. With the injection of large doses subcutaneously it is different. And it is possible to demonstrate that, when the gas is introduced in this manner, both the direction and rate of elimination can be detected.

The first experiments were undertaken to determine whether any active gas appeared in the urine or fæces. A mouse, weight 25 grm., was placed in a cage for collection of urine and fæces. The specimens for the first 24 hours were examined, and found to be free from any trace of activity. The mouse was then injected subcutaneously with 1 c.c. of radio-active distilled water at 10.45 a.m. December 2nd. The urine was collected over short periods, and the activity estimated in the usual way by the emanation electroscope. The following table gives the various figures:—

Quantity of radio-active fluid injected.		Time of Injection.	Duration of Collection.	Natural leak of Electroscope. Divisions per minute.	Activity of Urine. Divisions per min. Natural leak deducted.
(1)	1·0 c.c. (40 divisions per minute)	10.45 a.m. Dec. 2nd	10.45—12.45	0·133	1·59
(2)	"	"	12.45—4.45	0·22	0·07
	"	"	6.30 p.m. Dec. 2nd 10.30 a.m. Dec. 3rd	0·18	0·05

It would appear, then, that when the emanation is introduced subcutaneously in water, a very small quantity appears in the

urine of the first two hours, while after that period the activity of that excretion is scarcely perceptible. Further, as a previous estimation of the radio-active liquid used showed that 1 c.c. possessed an activity capable of discharging an electroscope of 40 divisions per minute, it is clear that the greater portion of the emanation must escape otherwise than through the kidneys. The fæces gave no evidence of activity. The two following experiments show similar results, but not so marked, owing to the fact probably that a larger interval occurred before the urine was collected in the first instance.

Experiment 1.—A mouse was injected on October 18th at 10.45 a.m. with 2·5 c.c. of radio-active distilled water. (Activity of 1 c.c. equals 433 divisions per minute.) (Vide Table A.)

Quantity injected.		Time of Injection.	Period of Collection.	Natural leak. Divisions per minute.	Activity of Urine. Natural leak deducted.
A.	2.5 c.c.	10.45 a.m. Oct. 18th	10.45 a.m. to 5.45 p.m.	0·13	0·10
B. (1)	2.5 c.c.	11.5 a.m. Oct. 26th	11.5 a.m. to 4.20 p.m.	0·11	0·08
(2)	"	"	6.30 p.m. Oct. 26th to 10.30 a.m. Oct. 27th	0·12	No activity. —

Experiment 2.—The same animal was injected again on October 26th, and the result is shown in Table B (1 and 2). As in these experiments the direction of excretion of the radio-active gas was probably influenced by the presence of an excess of water in the tissues, tending to diuresis, a second experiment was made with an active solution in oil, a vehicle which is hardly or not at all absorbed, and is therefore incapable of influencing the excretion of the gas contained in it.

Experiment 3.—A mouse was injected on December 13th at 12.30 mid-day with 1 c.c. of oil having an activity of 1000 (1 c.c. equals 1000 divisions per minute). The Table C below gives the times during which the excreta were collected and the activities of each respectively.

Quantity and Activity of Oil.		Time of Injection.	Period of Collection.	Natural leak. Divisions per minute.	Activity (Natural leak deducted)	
					of Fæces.	of Urine.
C.	1 c.c.	12.30 p.m. Dec. 13th	6.30 p.m. Dec. 13th—10.30 a.m. Dec. 14th	0·18	Nil.	Nil.
	1000 divisions per minute	"	Dec. 14th—16th	0·16	Nil.	not estd.

Experiment 4.—On February 18th at 5.30 p.m. a second mouse was injected with 1 c.c. of oil (activity equals 1600 divisions per minute). Table D shows the activity of the excreta. The injection was repeated on February 21st. (Vide Table E.)

Quantity and Activity of Oil.		Time of Injection.	Period of Collection.	Natural leak. Divisions per minute.	Activity (natural leak deducted)	
					of Fæces.	of Urine.
D.	1 c.c. (1600 divisions per minute)	5.30 p.m. Feb. 18th	5.45 p.m. Feb. 18th—3.30 p.m. Feb. 19th	0·15	Nil.	0·27 possibly contaminated.
E.	1 c.c.	11.30 a.m. Feb. 21st	11.30 a.m. Feb. 21st—10.30 a.m. Feb. 22nd	0·066	not estd.	Nil.

From these we see that, while the specimen of urine collected for 22 hours after injection on the 18th gave evidence of high activity, that on the 21st gave none. Similarly the excreta in C show no radio-activity. The mouse injected on the 18th and 21st February was killed on February 24th, and the tissues at the point of injection were carefully examined. Although oil was present, there was no radio-active material. That is, by the third day all the active gas had escaped. It is possible in the experiments that, as no examination was made of the urine until a good many hours after injection, the little radio-active gas passed by the kidneys might have previously escaped. Consequently, a third mouse was injected with 1·2 c.c. of oil on

February 25th at 12.35 p.m. The urine was collected for the following five hours. (Vide Table F.)

On February 28th a fourth mouse was injected with 1·6 c.c., and the urine passed in the following three hours estimated. (Vide Table G.)

It will be seen in both cases that a very feeble activity exists, which, as we shall be able to show later, is possibly due to some absorption by the exposed urine of the emanation excreted by the lungs.

Quantity and activity in divisions per minute per c.c.		Time of Injection.	Period of Collection.	Natural leak of Electroscope.	Activity (natural leak deducted)	
					of Urine.	of Fæces.
F.	1.2 c.c. 1600	12.35 p.m. Feb. 25th	12.35–5.35 p.m. Feb. 25th	0·055	0·105 very feeble	Nil.
G.	1 c.c. 1600	12.30 p.m. Feb. 28th	12.35–3.35 p.m. Feb. 28th	0·086	0·044 as above	"
	"	"	6.30 p.m. Feb. 28th— 10.30 a.m. March 1st	0·067	0·031 as above	"
	"	"	6.30 p.m. March 1st— 10.30 a.m. March 2nd	0·071	— nil	"

In only one of these experiments is there definite evidence of activity in the urine, while the fæces were negative throughout. Two other channels of excretion remain, namely, the lungs and skin. The latter we have seen after the administration of radium bromide by mouth exercises no excretory function (page 140). We are left, then, with much the most probable channel, namely, the lungs.

Before estimating the activity of the exhalations of an animal injected subcutaneously with radio-active liquid, it is perhaps advisable to see how long this activity persists at the site of injection. We have seen from the above experiments that from four to seven days after injection there is no evidence of activity in the oil left at the point of injection. Further, when the

emanation was injected in water, such activity as appeared in the urine was only evident during the first two hours of excretion.

With these data, on June 6th at 2 p.m. a mouse was injected with 1 c.c. of oil (having an activity of 6000 divisions per minute). The animal was killed at 5 p.m. the same day. The tissues at the seat of injection were removed *en masse,* heated in a flask, and the products so obtained admitted into an exhausted electroscope. It was then found that the oil left after three hours possessed an activity of 88 divisions per minute; the entire viscera discharged the electroscope at only 4·2 divisions per minute. The rest of the body was not examined. It is evident, therefore, when we compare the activity of the oil previous to injection and three hours after injection, that the elimination of the emanation is exceedingly rapid.

The following experiment shows that this elimination takes place almost entirely, if not completely, by the lungs:—

Experiment 5.—A large glass vessel of 1200 c.c. activity, fitted with an air-tight stopper and two glass tubes bent at right angles, was taken, and in it was placed a mouse, previously injected subcutaneously with 1 c.c. of oil (activity 6650 divisions per minute). No attempt was made in this experiment to collect all the emanation expired from the lungs. The jar was in communication, on the one hand, with the air of the room, and by the other tube with an emanation electroscope. The mouse was injected at 12.15 and placed in the jar at 12.23. At varying periods after this time samples of contained air and emanation were withdrawn into the electroscope, and the activity of the sample so removed was estimated. The following table indicates how the activity of the air contained in the vessel falls as the quantity of emanation expired begins to decrease. The first column shows the times at which a sample was removed for estimation. Thus, the first estimation was made 15 minutes after the mouse was placed in the vessel; the second, 15 minutes after that; the third, 40 minutes later, and so on. The second column gives the average activity of the amount discharged per minute of each period of time.

Sample.	Time at which Sample was withdrawn.	Activity of Sample. Divisions per minute.	Activity of amount discharged per minute.
1	12.38	545	36
2	12.53	436	29
3	1.33	920	23
4	2.05	568	18
5	2.42	683	18
6	3.12	428	14
7	3.44	428	14
8	4.42	262	4

This experiment gives no idea of the total quantity of emanation excreted by the lungs from hour to hour. Accordingly, a second experiment was prepared to measure the actual rate of elimination after the injection of a known quantity. For this purpose a large jar of 1205 c.c. capacity was taken and fitted with an air-tight stopper and entrance and exit tubes, each tube having a tap. Two wash bottles containing water and connected in series were also fitted up. A mouse was then injected subcutaneously with 1 c.c. of oil (activity 3000 div. per min.). The injection was given at 3 p.m. and the mouse was immediately placed in the jar, which was then tightly closed and clamped. After a period of twenty minutes the exit tube of the jar was attached to the entrance tube of an exhausted emanation electroscope. The taps between jar and electroscope were opened, and a portion of the emanation and air contained in the jar was thus drawn into the electroscope. The partially exhausted jar was now attached to the wash bottles, and the taps between these and the jar were in turn opened and air was withdrawn from the wash bottles to replace that which had passed into the electroscope. By measuring the quantity of water displaced from one wash bottle into another the amount of air and emanation withdrawn by the electroscope could be estimated.

The jar containing the mouse was now rapidly cleaned out and dried, the mouse replaced, and after a further period of time had elapsed a further quantity of emanation was withdrawn, and so on until three hours had passed since the injection. By this means, knowing the quantity of emanation and air removed on

each occasion, and the total capacity of the jar, it was possible to determine the quantity of emanation excreted during each period, per hour or half hour as the case might be. The various readings for the three hours are shown below:—

TIME OF INJECTION, 3 P.M. CAPACITY OF JAR, 1205 C.C.

Period of Collection.	Quantity withdrawn in c-c.	Activity in divisions per minute.	Total amount exhaled.	Average amount exhaled per minute during period of collection.
3.03—3.23	390	200	618	30·9
3.33—4.28	390	345	1065	19·9
4.33—5.03	370	89	290	9·7
5.14—5.54	340	78	278	7·5
6.03—6.18	207	9	52	3·5

Hence, we see that the total activity of the emanation collected amounts to 2,303 divisions per minute when the quantity injected had a value of 3,000 divisions per minute. But we have not yet calculated for the short periods during which the animal was removed from the jar for cleaning purposes, and during which time the emanations would consequently be lost. We can, however, arrive at a rough determination of the value of this amount in the following way :—The total activity of the quantity excreted in the first 20 minutes is 618, that is to say, in every minute a quantity is discharged having an activity equal to 618/20, or about 30 divisions per minute. Similarly, in the next 55 minutes the quantity eliminated per minute has an activity equal to 1,065/55, or 20 divisions per minute. Between these two readings there is an interval of 10 minutes. If we take the mean of the two readings above as the value of emanation emitted per minute during the interval, we shall arrive at a total quantity of activity lost equal to 25 multiplied by 10, equal to 250 divisions per minute. In the same way, by taking the mean of the reading before and after each interval, we can estimate the values of the amounts lost on each occasion. These happen to be 250, 70, 99, and 114 respectively, or a total of 553 divisions per minute. If we add this to our previous total of 2,303 we shall have accounted for 2,856 of the 3,000 injected. The two totals, therefore, closely agree, and we

see then that the elimination of the emanation takes place entirely by the lungs.

The various effects produced by the administration of the salts and products of radium have yet to be discussed. Next, to conclude from the above experiments in what directions the administration may be of most value, and lastly, to review the results obtained by such treatment.

When we come to deal with the question of the effects produced by the administration of radium, we have to consider them under two headings:—

(1) Effects on metabolism.

(2) Effects on various systems, circulatory, respiratory, etc.

As before, we shall neglect the question of the external application of radium in massive doses. Moreover, the results must be studied after the introduction of the radium by the mouth, or by injection, and in the case of the emanation after inhalation.

Changes produced in the Metabolism of the Animal after Administration of Salts of Radium by the Mouth.

In an exhaustive paper, Berg and Walker (iii.) conclusively prove that the administration of radium barium bromide by the mouth is without any influence on the metabolism of the dog. In their experiments careful controls were first carried out with barium bromide, both as regards the quantity necessary for a toxic dose and also with regard to its influence on metabolism. The salts used in the radium experiments are radium barium bromide of 240, 1,000 and 10,000 activity respectively. The animal upon which the experiment was performed was a dog of 6·5 kilo weight. The quantity of radium administered by the mouth was 1·10124 grm. of 240 salt given in divided doses on six consecutive days, followed by 0·240 grm. of 1,000 salt in three divided doses, which in turn was immediately succeeded by 0·140 grm. of 10,000 salt also administered in three separate doses on three consecutive days. No abnormal changes were noticed in behaviour, appearance, weight, or in quantity and quality of excreta, either during or after the experiment.

In the same paper these writers have considered very fully the effect of injecting radium barium bromide subcutaneously. The animal was again a dog of 5·6 kilo weight. The quantity of salt injected was 0·0762 grm. of 10,000 activity, given in three separate doses on three consecutive days. As before, they found this proceeding had no appreciable influence on the general metabolism of the animal.

These experiments are so thorough and complete as to need no corroboration from us. Moreover, mice offer no facilities in the analytical examination of their excreta.

However, in 15 out of the following 17 experiments which were conducted for various purposes, we can say that no ill effects were noticed during or after the administration of the different radium preparations used. In two cases untoward results were noticed, but require confirmation before being attributed to radium.

The following table shows briefly the method of administration, the quantity administered, and its effects:—

METHOD OF ADMINISTRATION—BY MOUTH.

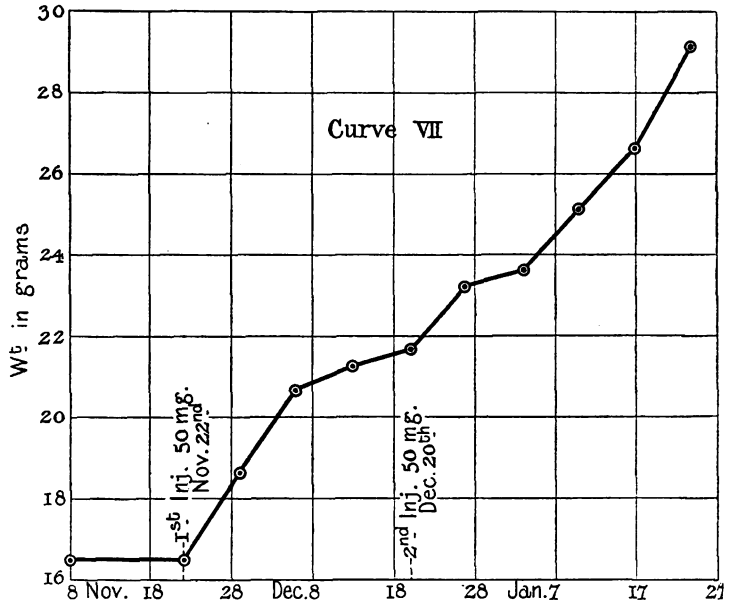
Experiment.	Mouse and Weight.	Quantity administered.	Duration of Treatment	Effects.
1	Three mice—			
	(a) 20 grm.	150 mg. Rad. Ba. SO_4 (250 units)	10 days	(a) gained weight.
	(b) 16 grm.	—	—	(b) gained weight.
	(c) 15 grm.	—	—	(c) lost weight.
	Three controls—			
	a^1 22 grm.	Ordinary diet	—	a^1 lost weight.
	b^1 19 grm.	—	—	b^1 gained weight.
	c^1 16 grm.	—	—	c^1 stationary.
2	Two mice	210 mg. Rad. Ba. SO_4 (250 units)	26 days	Nil.
3	One mouse	$\frac{1}{2\frac{1}{2}}$ mg. pure Rad. Bromide	In 1 dose, $4\frac{3}{4}$ hours	Restlessness 2 hrs. after food. P.M. $4\frac{3}{4}$ hours after food showed multiple hæmorrhage in lungs, injection of cardiac end of stomach and two small hæmorrhages.

METHOD OF ADMINISTRATION—BY SUBCUTANEOUS INJECTION.

Experiment.	Mouse and Weight.	Quantity administered.	Duration of Treatment.	Effects.
4	One mouse, 16.500 grm.	2 × 50 mg. Rad. Ba. Sulphate (250 units)	At intervals of 1 month	Nil.
5	One mouse	"	"	Nil.
6	One mouse	3 × 20 mg. Rad. Ba. SO_4 (250 units)	14 days	Nil.
7	One mouse	6 × 20 mg. Rad. Ba. SO_4 (250 units)	6 weeks	Nil.
8	One mouse	4 × 20 mg. Rad. Ba. SO_4 (250 units) 1 × 0·4 mg. (20,000 units) Rad. Ba. Brom.	—	Nil.
9	One mouse	2 × 0·4 mg. Rad. Ba. Be. (2,0000 units)	7 days	General effects. Locally, hæmorrhage into tumour.
10	Two mice	0·5 mg. Rad. Ba. Br. each	1 injection	(1) nil. (2) died of diarrhœa on 6th day after injection.
11	One mouse	5 × 20 mg. (Rad. Ba. SO_4 250)	16 days	Nil.
12	One mouse	5 × 0·5 mg. Rad. Ba. SO_4 (20,000 units)	16 days	Nil.
13	Three mice, total wt. 73 grm.	$2\frac{1}{10}$ mg. pure Rad. Bromide each	1 injection	Slight diarrhœa in 2 mice.
14	Three mice, total wt. 30 grm.	"	"	Nil.
15	Two mice	"	"	Nil.
16	One mouse	$\frac{1}{44}$ mg. pure Rad. Bromide	"	Nil.
17	One mouse	$\frac{1}{22}$ mg. pure Rad. Bromide	"	Nil.

The weight of No. 4, which was a young growing mouse, was taken every week for 12 weeks. The chart below shows that no alteration in the weight took place. In this experiment the radium was very slowly absorbed and excreted after each injection, over a period of many weeks. So that the animal was under the influence of radium in very small doses for practically the whole period of observation. In the one fatal case (No. 10), death occurred six days after injection, from diarrhœa. It is possible that the excretion of radium through the bowel induced it. However, it does not occur when large doses are given.

In No. 3, the administration of 1/22 mg. pure by the mouth produced hæmorrhages into lungs and stomach. It will be noticed that in No. 17 a similar quantity injected subcutaneously produced no similar change. If reference be made to the experiments (pages 140 and 152), it will be seen that the quantity of radium in circulation in the first case is enormously greater than in the second. In other words, absorption from the intes-



tinal canal occurs more readily than after subcutaneous injection. It should be remembered that the examination was made a little later after the initial injection in the case of No. 17, but hardly late enough to account for the enormous difference in question.

While these administrations by mouth and by injection subcutaneously of small doses appear to have little effect, the consideration arises as to what may happen after direct intravenous injection. Burton, Opitz and Meyer (iv.), making use of salts of radium barium bromide in varying strengths—240, 1,000 and 10,000, and comparing the results with control experiments

with barium bromide, came to the conclusion that the toxic symptoms of respiratory and cardiac paralysis manifested by the first were of the same nature as those caused by barium bromide alone. Further, with the higher power salts of radium and barium mixed, that is, where the quantity of radium present is greater, the toxic effects were less marked. They therefore assume that radium given intravenously in small doses possesses no harmful properties.

With this review of the distribution, elimination and properties of radium and its salts, we must next turn to the question of the properties pertaining to the emanation and the effects that are manifested after its administration, whether it be by inhalation, feeding or injection.

It has been shown by Bouchard, Curie and Belthazar (v.) that the inhalation of the emanation in large quantities and administered over a long period was fatal to mice and guinea-pigs. Thus, death was caused after nine hours' exposure to 15 gramme-heures of emanation. Exposure to 28 gramme-heures of emanation produced a fatal result in six hours (28 gramme-heures—emanation of 200 mg. of radium).

On the other hand, E. S. London (vi.), working at St. Petersburg, found that the inhalation of the emanation from only 10 mg. of radium bromide caused death in very young sucking mice of 2—3 grm. weight after an exposure of 4—5 hours. In this case death, which took place from congestion of the lungs, did not occur till two days later. In these latter experiments we think it open to doubt as to whether death may not have occurred from other causes than the emanation when the extreme delicacy of so young an animal is taken into account. However, the difference between these doses is considerable, and the question immediately arises as to whether the gas is capable of inhalation in any quantity whatever. From this point of view experiments were undertaken as follows:—

Experiment 1.—To show the effect of inhaling small doses of the emanation freely diluted with air.

Two large glass jars of 1200 c.c. capacity were taken and fitted with air-tight corks. One of them was attached to a flask in which a solution of 4 mg. of pure radium bromide had been dissolved and kept sealed for some weeks. The second jar, which was for the control experiment, was connected to a flask of the like capacity, containing an equal quantity of water. Both these flasks were fitted with entrance tubes and taps, so that air could enter and bubble through the liquid contained in each. In the other direction the jars were joined to a third jar by two separate tubes. This jar contained water to act as a trap, and was in turn connected to a water pump. In each jar were placed three mice, æt. 2 months, all of the same litter. The pump was then set working, and a current of air drawn slowly through the two jars. The rate of flow of air was controlled by means of the taps in the flasks, and the amount of air flowing through each jar could be determined relatively by observing the bubbles in the trap. This experiment was continued for six hours, and no ill effects were noticed at the time or afterwards.

It was now necessary to assure ourselves that the emanation derived from small quantities of radium and inhaled in a comparatively concentrated form was also innocuous. For this purpose a jar of similar capacity to that used in the previous experiment was taken, and in it were placed two mice, six weeks old, of the same litter, and weighing 14 grm. apiece. A wire cage containing 56 grm. of soda lime was then introduced, the jar tightly closed and sealed and exhausted to half an atmosphere without any ill effects. It was then rapidly attached to a flask containing 4 mg. of pure radium bromide in solution. The clamps of the jar were released, and the emanation contained in the flask was drawn into the exhausted jar. Air was then allowed to bubble through the radium solution until equilibrium was attained. At the same time, throughout the whole experiment a free communication existed between the emanation flask and the jar containing the mice.

A control experiment was also arranged with flask and jar of the same capacity as above, but without any radio-active contents. The mice were of the same litter as above, and weighed respectively 12 and 14 grm. In both cases wool was placed in the jar, and the temperature of the surrounding air was kept at 24° C. After $3\frac{1}{4}$ hours' exposure to the emanation, one mouse suddenly collapsed and died before the jar could be opened. The second exhibited considerable muscular weakness, but rapidly recovered in the open air. Previous to the termination of the experiment, the symptoms were increasing drowsiness, failure to react to external stimuli, and slow deep breathing, tending to be irregular, and occasionally Cheyne-Stokes in character. In the control experiment the same symptoms were not manifested markedly until some $4\frac{3}{4}$ hours had elapsed.

It would appear, therefore, that distress, and in one animal death, occurred earlier in the case of the emanation than in the control. But the symptoms which were revealed were such as are compatible with a deficiency of oxygen. The experiment was therefore repeated at a later period. The two mice used as a control in the above experiment were in this experiment exposed to the emanation in the same way as before. A control experiment was conducted also with the two remaining mice of this litter whose weights were respectively 16 and 15 grm.

Drowsiness and respiratory distress were noted at the end of 4 hours in the mice exposed to the emanation, while in the control experiment the same symptoms were manifested, and became urgent as early as $3\frac{1}{2}$ hours. These latter results are, therefore, the exact reverse of the previous experiment. Moreover, symptoms of distress occurred almost at the same time in the two experiments with animals, either when exposed to the emanation or used as controls.

Small doses of emanation would seem, therefore, to be possessed of no deleterious properties. In the case of the mouse that died, an examination with the *alpha* ray electroscope showed marked activity in the lungs, liver, kidney and spleen. No other parts of the body were tested.

Natural leak of Elect:	Liver.	Lungs.	Kidneys and Spleen.
0·20 divisions per minute	8·5 divisions per minute	6·7 divisions per minute	5·0 divisions per minute

If prolonged exposure to the inhalation of the emanation in small doses is not fatal, it is difficult to imagine that the administration and absorption of like smaller doses by the mouth or by injection will be productive of any serious effects.

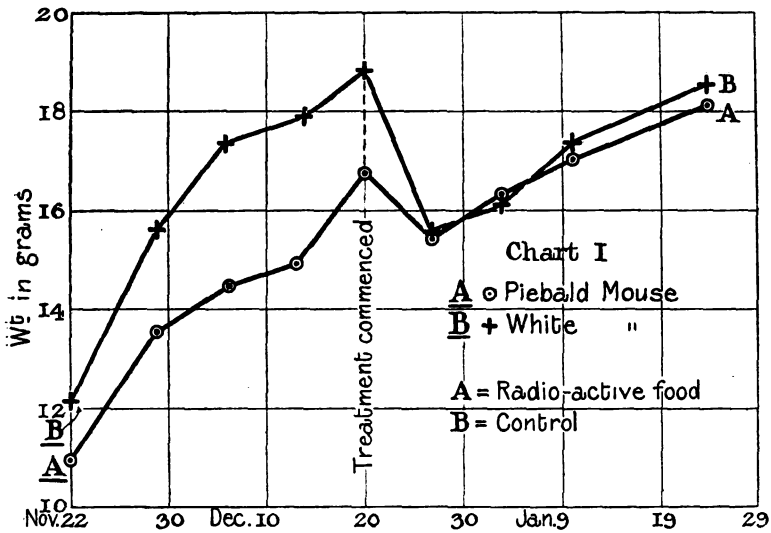
Victor Henry and Mayer (vii.) have shown that the rays of radium exert an influence on the activity of various ferments. Invertin exposed to the rays for 13 hours was reduced to one-third of its activity. Emulsin, after 20 hours, became affected, while the pancreatic juice, after 48 hours, became completely inactive. It is, therefore, possible that what happens in the test tube may be produced in the body by the continual administration of highly active materials.

We have shown, however, that the administration of salts, whether given subcutaneously or by the mouth, has no influence on the growth and metabolism of animals. Similarly, if the emanation in solution possesses the power of influencing the digestive secretions, we should expect some change to be shown in the appearance or weight of a young growing animal. It is, however, more likely that, where the more slowly excreted radium salt is powerless, the quickly eliminated emanation will be also devoid of activity.

The following chart shows the weight of animals fed on solutions of emanation of varying strength.

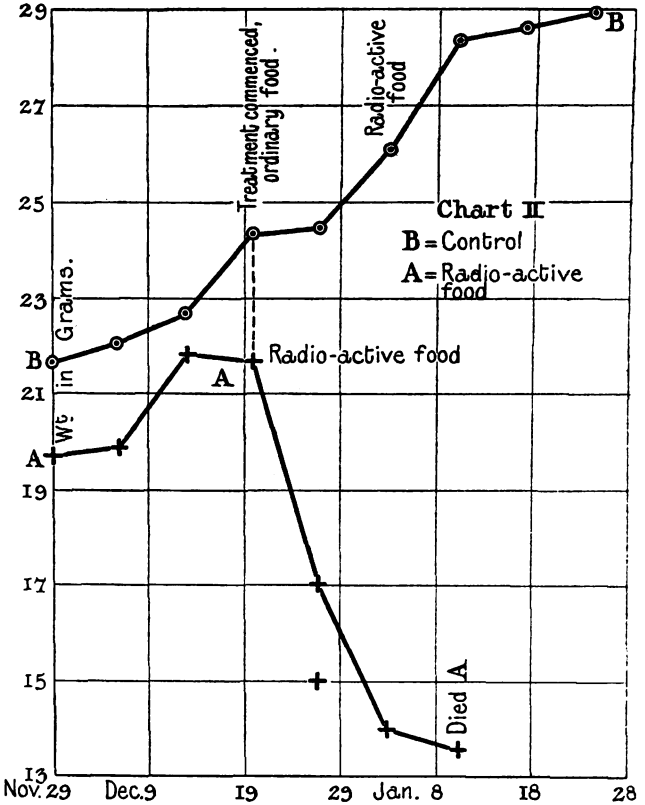
In Chart 1 the weights of the animals were taken weekly for one month before treatment was commenced. At the end of the fourth week A was fed on sop made with radio-active water, and B was kept as control. It will be noticed that with the commencement of change of diet, there is a drop in weight, but also that the loss in the case of the control is greater than in that of the animal under treatment, and was, therefore, due to external causes not associated with the radio-active food.

From that date, gain in both cases is equal. At the end of three weeks both mice were on ordinary sop, and no radio-active material included; there is no sudden increase in weight in the case of A.



In Chart 2 the solution was given in oil, which takes up a much greater quantity of emanation per volume than water. Here, as before, the period before treatment was commenced shows a fairly steady gain. On the day that treatment was commenced the weight of A has, however, dropped slightly, while that of B continues to rise. After the first week of radio-active food, A has lost enormously, while the control mouse B continues to gain. At the end of 14 days the animal was extremely emaciated. The treatment of A then ceased, and three times the quantity was administered to B. A continued to lose weight and died 10 days later, while, after three weeks' continued treatment, B showed no alteration in continued gain in weight. The slight gain during the last 14 days is due to the fact that the animal had attained practically to full growth. A post-mortem on A showed intestinal parasites and a cyst in the liver, sufficient to account for wasting and death.

It appears, then, that if the emanation be inhaled in massive doses, it is capable of producing fatal results. On the other hand, we have not succeeded with the small quantity at our



disposal in reproducing these effects, either after introduction through the lungs or by the mouth. There yet remains a third method of administration, namely, by injection.

Changes produced by the Administration of Salts of Radium by Injection.

Bouchard, Curie and Belthazar (v.) injected the gas in large quantities into the peritoneum of guinea-pigs and rabbits without any deleterious result. Bashford (viii.), on the other hand, reports three cases of death in mice on the third, fourth and

sixth day after injection respectively of 2 c.c., 1·5 c.c., and 2 c.c. of very strong emanation solution; no indication of quantity or activity is given. Post-mortem showed hæmorrhages in lungs and kidneys or congestion of the same organs, and in all cases enteritis. In 21 other cases where the solution was apparently not so strong, no ill effects were noticed.

For our part, the following table briefly epitomises the results of injecting the emanation in various media—distilled water, saline, and oil:—

No. of Mouse.	Media.	Quantity injected.	Result.
1	Distilled water	1 × 1 c.c.	Nil.
2	"	1 × 1 c.c.	Nil.
*3	Olive oil	5 × 1 c.c. in 9 days	Nil.
*4	"	5 × 1 c.c. in 9 days	Nil.
5	"	2 × 1 c.c. in 3 days	*1st injection*—nil. *2nd injection*—dyspnœa and diarrhœa for 3 hours afterwards.
6	"	1 × 1·2 c.c.	Nil.
7	"	1 × 1·6 c.c.	Nil.
8	Normal saline	2 × 2·5 c.c.	Nil.
9	Olive oil	1 × 1 c.c.	Nil.
10	"	1 × 1 c.c.	Nil.
*11	"	1 × 1 c.c.	Died suddenly 12 hours later. P.M.—lungs congested, no hæmorrhage.
12	"	1 × 1 c.c.	Drowsiness and dyspnœa for 4 hours afterwards.
13	"	1 × 1 c.c.	Nil.
*14	"	3 × 1 c.c. in 6 days	Nil.
*15	"	3 × 1 c.c. in 6 days	Nil.

* Indicates tumour mouse.

We see, then, that in only three were any untoward symptoms noticed. In one case death appeared to follow the injection of highly radio-active oil. There was congestion of the lungs, and hæmorrhages into the tumour. In the other two cases both showed respiratory distress.

It will be noticed that in all these cases we had used the emanation in oil; the symptoms, therefore, could not have been due to any sudden alteration in the circulatory mechanism as the result of the absorption of a large quantity of fluid, or to the destructive effects of distilled water. Further, it will be

noticed that in all three cases the symptoms and changes take place in the respiratory organs, which is what we should expect, seeing that the emanation is excreted entirely by the lungs, when administered in a medium which is not absorbed.

In the three cases reported by Bashford, where the emanation was given in water, the kidneys were also affected, indicating that in these cases the excess of radio-active fluid has passed through the kidney. In other words, pathological changes take place at those points where concentration of the emanation occurs.

It is interesting at this point to go back to examine the post-mortem findings in the case of the mouse (No. 3, page 165) who had an internal administration by the mouth of 1/22 mg. of pure radium bromide. Here, after $4\frac{3}{4}$ hours, we find multiple hæmorrhage in the lungs, also two hæmorrhages in the stomach, and considerable congestion of the cardiac end of that organ. Here it may be the emanation of the radium that is responsible for the changes.

While, therefore, hæmorrhage would seem to be the result of large and powerful doses of radium, whether applied internally or externally, so far no reasons have been found to explain its occurrence. Clearly it is due either to some change in the blood or in the blood-vessels. Now Mayer and Henry (vii.) have stated that blood after exposure to the rays of radium is hæmolysed. If this is so, it is possible that the hæmorrhages are in some way dependent on this change. But, on the other hand, if destruction of the blood corpuscles were taking place owing to circulation of radio-active products, the hæmorrhages could not be localised as in the cases mentioned, but would be diffused, and, moreover, would give rise, not necessarily to hæmorrhage, but assuredly to the presence of hæmoglobin in the urine. Now, in none of the animals to whom we have given injections have we been able to determine the presence of hæmoglobin in the urine. Again, if hæmolysis occurs in the body, we should expect it possibly to occur outside as stated by Mayer and Henry. We have, however, exposed freshly drawn rat's blood in saline for a long time to the rays of 5 mg. of radium,

and have also bubbled emanation from a like quantity of radium through the blood in an exhausted vessel; in neither case did any change take place earlier than was noticed in the control experiments.

In these experiments small graduated cylinders with cork and tubes were filled with equal amounts of rat's blood, and the colours of the solutions of the controls and radiated blood were contrasted at varying periods after exposure to the radium and the emanation. If no change occurs in the blood, we are left with possible—and more probable—changes in the blood vessel walls. While we have been unable to observe these changes ourselves, there is yet a quantity of evidence to show that endothelial changes do occur as the result of the influence of radium. That being so, the cause of the extravasation of blood corpuscles is not so far to seek. Moreover, the strictly localised nature of the changes found could be explained on those grounds, as such changes would only occur where concentration of the radio-active material occurs, which, as we have shown in previous experiments, is in the kidneys and lungs. In a similar way, it will occur from the same cause in the tumours themselves after prolonged exposure.

As to what influence such hæmorrhage may have in the reduction of cancers, or in their actual disappearance, if such ever occurs, it is difficult to say. Bashford (viii.) thinks that such hæmorrhages precede and produce a connective tissue proliferation which is the causal factor in the reduction of the tumour. He admits, however, that such changes occur as a natural phase, independently of any exposure to radium.

It would, perhaps, be convenient at this point to sum up those facts which seem definitely settled in regard to the absorption, circulation, and distribution of radium, and also as regards the effects after administration in various ways.

We can say:—

(1) That radium can be safely administered internally by the mouth, or by injection in small doses.

(2) That such administrations produce no alterations in the metabolic processes of the body, and are without influence on the respiratory, circulatory, or nervous systems.

(3) That after such treatment a widespread degree of radio-activity is evident throughout the body.

(4) That elimination of radium takes place principally by the bowel, in a minor degree by the kidneys, while in mice, at all events, there is no evidence that the liver or skin plays any part in excretion. As regards the elimination of the element by the bowels, it is certainly excreted by the small intestine, and there are indications that the large bowel also assists in that function.

(5) That the high activity in the lungs is possibly due to the extreme vascularity of these organs, but its constant presence at all times after inoculation, and the fact that the emanation is entirely eliminated by the lungs, suggests that an accumulation of radium takes place with a view to the more ready excretion of the emanation.

(6) The administration of a large dose by the mouth has produced hæmorrhage into the lungs and stomach.

(7) The causes of such hæmorrhage are not evident, but would appear to be due to some change in the blood vessel wall rather than in the blood itself.

(8) That the emanation can be obtained in solution in various media, and can be introduced into the body in small doses by inhalation, feeding, or by injection, without materially affecting the animal in question.

(9) That after such administration, however introduced, a general radio-activity of very brief duration is caused throughout the body.

(10) That elimination of the emanation takes place principally and almost entirely by the lungs, and to a very slight extent by the kidneys.

(11) That the administration of the emanation by injection in a powerful dose has, in one case, proved fatal with us. Other observers, however, have noticed similar changes to those recorded after administration of large doses of radium, viz., hæmorrhage into the lungs and kidneys.

(12) That the duration of the activity induced in the body, or, in other words, the time taken in excretion, differs with the nature of the preparation used. Soluble salts of radium are rapidly eliminated, however administered. The insoluble salts, *per os*, are excreted directly by the bowel, and there is no evidence of any temporary absorption and circulation. When given by injection, however, an exceedingly slow elimination takes place by the bowel. The time taken is so great, that for all intents and purposes the salt may be considered to be permanently present at the site of injection.

(13) The elimination of the emanation occurs with great rapidity, and was complete with us after administration in powerful doses in so short a time as four hours.

It had been our hope, previously expressed in this paper, that, while working on these lines, further information might be forthcoming which might enable us to apply to carcinoma freshly discovered properties, or from some new direction, those already attributed to radium. The experimental work above, however, adds nothing to what is already known as to methods of applying radium, while it suggests that radium possesses no therapeutic values beyond those which are already known to belong to it as an external applicant.

The administration of radium in a soluble form internally can be obviously only wasteful, and more or less useless, if directed to a local object, such as cancer. The amount which arrives at the carcinoma is infinitesimal as compared with the quantity excreted, while larger doses could only produce a fatal result by intestinal burning.

With insoluble salts we have already alluded to the absurdity of such being administered by mouth. They are excreted by the bowel directly, and the only influence they could have would be

by their radiation, which would be practically nil, or by the absorption of any emanation possessed by them, which would be negligible in quantity. The injection of the insoluble salts, however, opens a fresh field. They may be injected into or around a tumour, and will then act for an indefinite period. Further, such a method enables one to use the enormous *alpha* ray activity, which is practically always absent in external application, owing to the thickness of the supporting material containing the radium, or the mere interposition of the skin itself. Such a line of treatment has been recently suggested by Wickham (x.).

The entire excretion of the emanation through the lungs may be perhaps more applicable some day to certain diseases of these organs, but it must be remembered that large quantities show a tendency to induce local vascular disturbances. On the other hand, the brief residence of the emanation in the body makes it hardly applicable to cancer, where a long-continued influence only could be of value. This might possibly be obtained by frequently repeated doses, and would then necessitate each patient having a separate apparatus. In spite of these obvious disadvantages it has been advocated in the treatment of many diseases, and occasionally in cancer.

In the following tables we have epitomised the results of some months' treatment of mouse cancer by means of radium and its derivatives, with special reference to the internal administration of these substances.

1ST SERIES. DATE OF INOCULATION, OCTOBER 29TH, 1909.

Size of Tumour.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Result.
1. 3×2·1 cm.	Nov. 8, 1909	Dec. 7 to Dec. 30, 1909	5 mg. pure. No screen	21	Total 16½ hours from 15–60 min. each	Very rapid growth. Killed Jan. 3, 1910
2. 1·8×1·5	Nov. 16	Dec. 14 to Dec. 31	Tube 5 mg. introduced into tumour. No screen	13	Total 4½ hours, 15–60 min. each	Rapid growth. Killed Jan. 17.
3. 1·5×1·5	Nov. 16	Dec. 14 to Dec. 23	Injections of radio-active oil	5	1 c.c. each	Rapid growth. Killed Jan. 11.
4. 1·6×1·5	Nov. 20	Dec. 14	5 mg. No screen	25	Total 9 hours, 15-60 min. each	Steady growth. Superficial hæmorrhage controlled by applications. Died Jan. 10.
5. 1·8×1·7	Nov. 20	Dec. 14, 1909, to Jan. 6, 1910	(*a*) Injections of radio-active oil (*b*) Insertion of tube 5 mg. into tumour	5 16	1 c,c. each 10 hours total	Softening and liquefaction of tumour. Killed Jan. 8.
6. 1·4×1·7	Nov. 20	Dec. 20, 1909	50 mg. of Rad. Ba. SO_4 (250 units) injected beneath tumour	1	—	Steady growth. Killed Jan. 21.

All controls to this series died.

2ND SERIES. DATE OF INOCULATION, DECEMBER 21ST, 1909

Size of Tumour.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Result.
1. 0·5×0·5 cm.	Jan. 3, 1910	Jan. 13 to Mar. 11, 1910	Fed on radioactive liquids (solution of emanation)	Daily	Constant supply	Nil. Killed Mar. 11
2. 0·6×0·7	Jan. 3	Jan. 13 to Feb. 7	do.	do.	do.	Nil. Killed Feb. 7
3. 1·2×1·5	Jan. 1	Jan. 17 to Feb. 8	5 mg. pure. Screen of ½ mm.	6	Total 18 hours	Nil. Death Feb. 18
4. 1·0×1·4	Jan. 3	Jan. 21 to Feb. 21	do.	12	Total 48½ hours	Nil. Death Feb. 26

All controls to this series died.

3RD SERIES. DATE OF INOCULATION, JANUARY 11TH, 1909.

1. 0·2×0·3 cm.	Jan. 20	Jan. 21 to April 19, 1909	Fed on solution of emanation	Daily	Constant supply.	Grew steadily for a few days, then decreased in size, and on Feb. 3 had almost disappeared. Feb. 12 commenced to grow again. Tumour removed March 19. Mouse died of a recurrence April 19.
2. 0·1×0·2	Jan. 20	Jan. 21 to Feb. 26	do.	do.	do.	Grew steadily. Killed Feb. 26.

N.B.—One control appeared January 20th, grew steadily until Feb. 3rd, but had disappeared by February 12th, and did not reappear. Temporary improvement in 1, Series 3, therefore not due to treatment.

4TH SERIES. MICE INOCULATED FEBRUARY 7TH, 1910.

Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Result and Comments.
1a. 0·3×0·3 cm.	Feb. 21, 1910	Feb. 24 to Mar. 11, 1910	5 mg. screen of ½ mm.	8	Total exposure 28½ hours, 3–5 hours each	Steadily growing. Removed March 12. 2×1·5 cm. Recurrence March 29.
1b.	Recurrence Mar. 29 in scar	April 4 to April 14	5 mg. No screen	6	Total exposure 16 hours	Death April 26.
2. 0·4×0·4	Feb. 24	Feb. 28 to Mar. 11	5 mg. screen of ½ mm.	7	Total exposure 26 hours	Tumour removed Mar. 12. Size 2·1×1·6 cm. and growing steadily. No recurrence. Mouse still alive (Oct. 1910).
3a. 1·4×1·2	Feb. 28	March 9 to April 8	5 mg. No screen	17	Total exposure 42 hours	March 21 there appeared a marked Radium reaction. Loss of hair, small vesicular erosions, and eventually a small area of ulceration. On April 8 the white surface had healed and was covered with a thin white flexible scar, but no hair reappeared. On April 21 tumour still growing, 2·8×2·5. Removed surgically. April 29 recurrence.
3b.	Recurrence April 29th	April 29 to May 6	5 mg. No screen	3	Total exposure 7 hours	Death May 15.

N.B.—These tumours were removed for microscopical examination.

Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Result and Comments.
1. 0·3×0·3 cm.	Mar. 8, 1910	March 10, 1910 (one day)	5 mg. tube screen of ½ mm.	1	16 hours continuously	March 14—Smaller. March 18—Palpable. March 21—Nil. No reappearance.
2. Do. approx.	Mar. 8	Mar. 10 to Mar. 21	Fed on Radium Bar. Sulphate (250 units)	5	30 mg. in sopped bread on each occasion	March 14—Slightly larger. March 18—Smaller. March 23—Nil. No return of growth.
3. Just palpable	Mar. 8	do.	do.	5	do.	March 14—Larger. March 18—Much smaller. March 21—Nil. No return.
4. 0·2×0·3	Mar. 8	Mar. 10 to Apl. 20	do.	12	do.	March 14—Smaller. March 21—Growing again. April 4—Growing rapidly. April 21—Killed. Very large tumour.
5. 0·3×0·4	Mar. 24	Mar. 24 to Apl. 20	do.	7	do.	Grew steadily. Killed April 21.
6. 0·3×0·4	Mar. 7	Mar. 10 to Mar. 24	Injection beneath tumour. Rad. Bar. Sulph. (250 units)	3	20 mg. on each occasion	March 21—Slightly larger, 0·5×0·6. March 23-29—Stationary, 0·6×0·7. April 7—Much smaller. April 11—Disappeared. No return.

5TH SERIES—*Continued.*

Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Result and Comments.
7. 0·3×0·3 cm.	Mar. 8, 1910	Mar. 10 to Apl. 26, 1910	Injection beneath tumour. Rad. Bar. Sulph. (250 units)	6	20 mg. on each occasion	March 18—Larger. 0·6×0·6. March 21–29—Stationary. April 7—Slightly larger. April 11—Growing steadily. May 13—Very large. Killed.
8. 0·3×0·3	Mar. 21	Mar. 23 to Apl. 11	5 mg. pure. Screen of ½ mm.	5	Total exposure 72 hours	Steady growth. Killed May 11.
9. 0·6×0·7	Mar. 18	Mar. 23 to Apl. 12	do.	7	Total exposure 78½ hours	do.

IN THE CONTROLS TO SERIES 5 NOTE THE FOLLOWING :—

1. 0·2×0·2 cm.	Mar. 8, 1910	No treatment	Tumour was still present on March 15, but had disappeared on March 18.
2. 0·2×0·2	Mar. 8	do.	Tumour grew steadily until March 16, but had disappeared on March 21.
3. 0·2×0·3	Mar. 17	do.	Grew steadily until March 19th, then gradually decreased in size, and had disappeared on April 7th.

6TH SERIES. MICE INOCULATED MARCH 19TH, 1910.

Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Results.
1. 1·2×0·5 cm.	Mar. 29, 1910	Apl. 12 to Apl. 19, 1910	Injection into tumour. Rad. Bar. Brom. (20,000 units)	2	½ mg. on each occasion	After second injection there was an enormous increase in size of tumour due to hæmorrhage. Died May 7.
2. 1·0×0·6	April 4	Apl. 12 to May 10	(a) Injection of Rad. Bar. Sulph. (250 units)	4	20 mg. of Rad. Bar. SO_4 on each occasion	Steady growth. No sloughing or liquefaction. No hæmorrhage.
			(b) Injection of Rad. Bar. Brom. into tumour (20,000 units)	1	½ mg. of Rad. Bar. Brom.	Death May 21.
3. 1·1×0·6	April 1	Apl. 6 to Apl. 22	External application 5 mg. pure. No screen. Fed on solution of emanation.	7 daily	Total exposure 22½ hours Constant supply	Died May 7.
4. 0·9×0·4	April 4	Apl. 13 to June 13	External application 5 mg. Rad. pure. No screen. Fed on solution of emanation April 6 to June 13	29	Total exposure 97 hours	A brief account of the course of this tumour is given at the end of this Series, as it is one in which "Radium" seemed undoubtedly to influence the growth.
5. 0·4×0·3	April 4	Apl. 15 to May 6	External application 5 mg. pure. Screen of lead	7	Total exposure 110 hours	Tumour grew steadily. Killed May 19.

6TH SERIES—*Continued.*

Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Results.
6. 0·2×0·3 cm.	April 26, 1910	April 26 to July 4, 1910	External application 5 mg. pure. Screen of lead.	10	120 hours	Tumour grew steadily until May 10.
			Injections of emanation in oil	3	1 c.c. each	May 10–19—Decreased in size. May 26—Just palpable. June 1—Harder and larger. June 6—Growing steadily. June 6–13—Applications repeated. June 29 to July 4 – Injections of emanation in oil. July 10—Tumour rapidly growing. July 12—Killed. Softening and liquefaction of tumour commencing.
7. 0·5×0·5 cm.	April 20	April 25 to May 9	External application 5 mg. pure. No screen.	6	Total exposure 17 hours	Died of diarrhœa May 20.
			Injection of emanation in oil	1	1 c.c. each	No change in tumour.

6TH SERIES—*Continued.*

	Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Results.
8.	0·5 × 0·5 cm.	April 20, 1910	May 3 to June 21, 1910	(a) Injection of radioactive oil	2	1 c.c. each	Steady growth
				(b) External application 5 mg. No screen	5	30 hours	Died June 23
				(c) External application with screen	6	51 hours	
				(d) Internal application through central excavation	4	17 hours	
						Total 98 hours	

From April 13th to 21st there were five applications of four hours each. Tumour remained *in statu quo* until April 27th. On the 22nd there was a slight radium reaction present, which was very severe and general on the April 27th.

On May 2nd slight growth was apparent, extending dorsally from tumour, and applications were renewed; the rest of the tumour seemed flabby and inactive. Applications were continued to May 12th, and no increase in size took place.

On May 18th the Radium burn had healed, giving rise to thin white flexible scar.

On May 24th there was a further slight growth in dorsal direction. No activity manifested elsewhere. Repeated applications were given to whole of tumour, the bulk of which remained inelastic, flattened, and apparently atrophied.

On June 13th an extension of growth took place in a ventral direction, and became inaccessible to treatment.

Mouse killed June 23rd.

7TH SERIES. INOCULATED MAY 12TH, 1910.

Approximate size of Tumour at beginning of Treatment.	Date of Appearance.	Duration of Treatment.	Nature of Application.	Number of Applications.	Duration and Quantity of each.	Results.
1. 1·1 × 1·1 cm.	May 28, 1910	June 29 to July 15	Injection of emanation in oil	3	1 c.c. each	Softening and liquefaction of tumour. Killed July 28th.
			Application of 5 mg. No screen	6	30 minutes each	
2. 1·0 × 1·2	June 9	July 10 to July 26	Injection into tumour Rad. Bar. Sulph. (20,000 units)	5	0·5 mg. each	Extensive sloughing of tumour. Killed August 8.

Mice in this series treated by external application alone, all gave negative results.

8TH SERIES. INOCULATED JUNE 23RD, 1910.

1. 0·5 × 0·5 cm.	July 4th	July 10 to July 26	Injection of Rad. Bar. Sulph. (250 units) into tumour	5	20 mg. each	Extensive sloughing and softening of tumour. Killed August 8

Mice in this series treated by external application alone, all gave negative results.

It will be seen from these Tables that we have utilised radium and its products in every way possible: external application, the introduction of insoluble salts into and beneath the tumour, the injection of radio-active fluids, that is, solutions of the emanation, into and around the tumour, administration of salts of radium and the emanation in solution, by mouth, and a combination of all these methods have been tried. The effects produced are varied, but cannot be said ultimately to lead in any way to a disappearance of the growth.

In Series I. death occurred in every instance. It will be noted, however, that in No. 4 a quite considerable tendency to hæmorrhage appeared to be checked by the application. In No. 5 there was extensive softening and liquefaction of the tumour, which we shall allude to later. These tumours were of large size and rapid growth, and the quantity of radium used was small.

In Series II., III. and IV. the result of treatment is entirely negative. In these three series, treatment was commenced at a much earlier date than in Series I., in some cases directly the growth was noticed.

In Series V. we found a change. Here, again, treatment was commenced as early as possible, and we see that four of the tumours, though treated each on entirely different lines, have disappeared. Five tumours, on the other hand, have grown steadily, and death has occurred. In this series the inoculations had been made into mice of a different type to the previous series, a fact which seems to indicate that radium had no part in the disappearance of the growth, but that rather some lessened susceptibility to cancer in the animal itself was responsible for the change. It must be noted also that in the controls to this series there are three cases of apparently spontaneous disappearance.

In Series VI., however, there is distinct evidence in the case of No. 4 that radium, while not curing the carcinoma or ulti-

mately checking its growth, does, on the other hand, tend to delay the fatal termination by inhibiting growth. The flabby, inelastic feel of that portion of the tumour which had been thoroughly treated, and over which there were signs of a radium reaction was in marked contradistinction to the tense elastic growth which took place in directions it was impossible to treat.

Again, No. 6 decreased steadily in size under treatment until it had almost disappeared. After a short period, however, growth recommenced, and further application proved of no avail. This appears at first as if it had occurred under the influence of radium, and is comparable to some cases of carcinoma in human beings, which, under treatment, show a tendency to decrease in size, and then ultimately grow again in spite of continued treatment. However, it must be remembered that in mice it is not uncommon for a temporary reduction in the size of the tumour to take place—without any radium application.

The only cases in Series VII. and VIII. are those in which repeated injections were made *into* the tumour. We have seen that in the previous cases where radio-active substances were injected around or beneath the tumour no apparent alteration took place. In these latter, however, where the injection is into the tumour itself, there is to be found the most marked necrosis and liquefaction of the tumour, which is ultimately discharged through the skin. That these changes were produced by the introduction of highly active materials, and were not part of the ordinary necrosis and ulceration that occurs, was shown by the fact that the whole of the skin, except at the point where the discharge of necrotic material took place, was intact. These changes are not unlike those discussed by Morton as occurring in sarcomatous growths after the introduction of tubes of radium into the substance of the tumour. In these cases there was intense reaction and destruction of the tissues locally, and a general febrile disturbance of varying severity in the patient. In some later series, not reproduced here, we have treated these

mouse tumours with increasing quantities of radium up to 9 mg. pure. In a few cases small injections of radio-active preparations—salts of radium and barium sulphate—not sufficient to cause extensive sloughing have been used in combination with the external applications. In some, the "feu croisé" method, so strongly recommended by Wickham (x.), has been employed. So far we have seen nothing to cause us to modify our previous opinion that the external application of radium in small doses does nothing further than inhibit the rate of growth and delay the natural course of ulceration to which these tumours are subject.

We do not, on these grounds, feel justified in stating definitely that the external application of radium is without effect on malignant tumours. Such an opinion can only be given after the use of the element in such quantities as will indicate its value without any possible doubt.

In conclusion, we can say:—

(1) That the internal administration of radium and its derivatives in a number of cases has not shown any tendency to check the growth present.

(2) That internal administration in combination with external application yields no better results than can be obtained by external application alone.

(3) That in some cases internal application has proved, not only useless, but even harmful.

In conclusion, we wish to express our indebtedness to the great generosity of Dr. James Douglas, who has afforded us all the materials and many other facilities necessary for an undertaking of this nature.

Our best thanks are also due to Mr. W. C. Ball for his arduous work on our behalf, in the extraction of 4 millegrammes of pure radium from a solution of oil and water; and to many other friends for much advice and kind assistance.

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RHEUMATIC FEVER IN THE LAST DECADE.

By

ALEXANDER SANDISON, M.B., B.C., B.A., B.Sc.

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Introduction.

The following essay is divided into two parts :

Part I. deals with the subject from an historical and critical point of view. The condition of medical knowledge at the commencement of the decade (1900—1909) with regard to the disease is first considered at some length. A chronological survey is then made of the various advances made in all directions in the study of acute rheumatism, and special attention is paid to the development of the bacteriology of the subject. The whole question is then summed up, and certain general conclusions are drawn.

Part II. is concerned with a personal analysis of the cases admitted to Guy's Hospital during the period 1900—1909, inclusive. Various statistics with regard to age-incidence in relation to number of attacks, family history, diathesis, and similar factors have been worked out and presented, some with the aid of diagrams. Especial and detailed attention has been paid to the question of the influence of weather conditions upon the prevalence of the disease, both annually and in each month

during the decade. The variations in rainfall, rainy days, humidity, sunshine, mean air temperature, and prevailing winds have all been investigated fully, and several charts are appended to illustrate the relations thus brought out. As the result of this research the author puts forward a possible explanation of the influence of climate on the disease.

The details of mortality in the disease have been carefully analysed, and statistics relating thereto are given. Similarly, the occurrence of rheumatic nodules and of salicylism have been studied, and the results set out at some length.

Comparison with other work on the same lines is made throughout, and a few general deductions are stated with regard to these special results.

PART I.

Historical and Critical.

Scope of Enquiry and Definition.—This essay deals only with questions relating to acute rheumatic fever, and is not concerned with others of the medley of diseases which, in both the lay and the medical mind, make up the concept "Rheumatism." Most physicians, however, make no clear distinction between "acute" and "subacute" rheumatic fever, and in consequence the two varieties are here treated as essentially identical.

Sir William Church (i.) defines rheumatic fever as "equivalent to a synovitis accompanied by pyrexia, and generally multiple." Dixon Mann (ii.) describes it as "a febrile condition attended by inflammatory affections of the joints and serous membranes caused by the presence of an unknown infective agent." Other authors introduce into their summary some comment on the frequency with which the heart is involved in the pathological picture, but the above short descriptions are sufficient for all practical purposes.

Views on Rheumatic Fever ten years ago.—Dr. Mitchell Bruce, in his article on "Acute Rheumatism" (Quain's "Dictionary of Medicine," 3rd edition, published in 1901), gives a full account of the ideas prevalent with regard to the disease at the commencement of the decade under consideration here. His definition is interesting from a present-day standpoint, because of its vagueness in regard to any bacteriological explanation of the disease. He describes it as "an acute disease caused by certain infective, diathetic or climatic influences, and characterised by fever, sweats, acute shifting inflammatory and other nutritional changes in connection with the joints and related structures, and certain of the viscera, particularly the heart, as well as the serous membranes."

In regard to his remarks on etiology, the same character is noticeable. The allusions to bacteriology are as brief as they are vague. In one place he states that "different micro-organisms have been described in connection with the disease, but an etiological relation between any one of them and the disease is not established"; whilst on another page he remarks: "Certainly the present trend of opinion is that the disease is due to the presence in the blood of a micro-organism or a variety of micro-organisms." It is clear, then, that at this date a bacteriological conception of rheumatic fever was only beginning to exert much influence. Stress is laid, however, on the importance of the inheritance of "a rheumatic diathesis" as a predisposing factor; whilst "exposure to cold and wet, or exposure to cold after severe exertion" is emphasised as the most common determining circumstance. The possibility of "rheumatic districts" or "houses" is also considered worthy of note.

An interesting summary is given of the principal pathological conjectures either then or previously in vogue with regard to the disease, admission being made that the whole subject is very obscure. This summary may be suitably abstracted here:—

(i.) *Lactic acid hypothesis.*—The disease is directly due to the accumulation of this poison in the system.

(ii.) *Nervous hypothesis.*—Chill of the peripheral parts of the body, especially of the skin and joints, causes disturbance of corresponding parts of the central nervous system, and this gives rise to pain and (?) vaso-motor or trophic changes of the same peripheral parts, and to fever.

(iii.) *Neuro-toxic hypothesis.*—Chill causes accumulation or retention of lactic acid; this acts on the central nervous system, which in turn reacts upon the joints and other parts. A further modification of this conjecture was, that as chill disturbs the nervous system, and as this, again, disturbs metabolism generally, lactic or uric acid, or both, are retained and act as poisons. Bastian considered that chill produced some toxic product within the system, which, according to various external and internal circumstances, excited acute articular affection, multiple neuritis, or acute spinal paralysis.

(iv.) *Microbic hypothesis.*—It was suggested by Heter, several years ago, that rheumatism originated with the entrance of micro-organisms into the system, resulting in endocarditis with secondary joint symptoms due to embolism.

In summing up the position, Dr. Bruce states: "While the true pathology of acute rheumatism is still unsettled, the most promising directions from which we may expect light to be thrown upon it are, first, bacteriology; secondly, the actions of organic poisons, whether introduced from without, or produced within the body as the intermediate products of nutrition; and, thirdly, the intimate relation of the nervous system to the body heat, to the skin, and to nutrition." As will be shown later, it is in the first of these directions that progress has been chiefly made, and, at the present day, attention is almost entirely concentrated on that aspect of the subject.

With regard to the relation of the various "complications" of the disease, the author considers cardiac inflammations, pneumonia, pleurisy, peritonitis, erythema nodosum, chorea, and meningitis as having an intimate genetic relation to the affection. Albuminuria, hyperpyrexia, and mental disorder; scarlatina,

dysentery, and profuse hæmorrhages, he thinks, are possibly etiologically related to rheumatism, whilst bronchitis and delirium tremens are merely intercurrent conditions.

The account given of the symptoms, post-mortem appearances, clinical characteristics, and complications differs but little from the description given in a text-book of the present day, and, therefore, it is unnecessary to quote it in detail here. The acute rheumatism of childhood is separated from that of adults, as being more characteristically a disease of the heart than of the joints, and this distinction is now even more emphasised by clinical workers. Cardiac affections, acute and chronic, are stated to be present in 50 per cent. of all cases, acute carditis being present in at least 33 per cent. The close relationship between tonsillitis, chorea, and rheumatism is specially commented on, but "Peliosis rheumatica" is not regarded as true rheumatism.

In diagnosis in the early stages special stress is laid upon the factors of family history or previous attacks; the absence of specific eruptions or coryza, the development of pain and tenderness in a definite joint; acid sweats, and, most important of all, the discovery of cardiac inflammation. In the later stages, the transient and erratic course of the arthritic symptoms and the probable presence of cardiac lesions are cited as helpful in the differential diagnosis from "gout, rheumatoid arthritis, gonorrhœal arthritis, pyæmia, glanders, and acute synovitis, or arthritis of traumatic or diathetic origin." First attacks of rheumatoid arthritis are stated to be "readily confounded with acute rheumatism."

Prognosis is "necessarily most uncertain." In old subjects it is stated to be "good," in others, the extent or absence of cardiac lesions is a determining factor, especially in children; whilst the danger of relapses and recurrences is great. Nodules are regarded as of grave prognostic significance, indicating considerable cardiac involvement.

The question of treatment is discussed at length. Rest in bed, between blankets to absorb the sweat, and efficient nursing are

laid down as essential principles. In regard to dietetics and drugs, there are two main indications: first, the control of the morbid process; and, secondly, the relief of local symptoms and general distress. The use of salicylates is described as orthodox routine treatment, sod. salicyl. gr. xv.—xxv. being given every one, two, three, or four hours until the temperature falls to the normal; after this the dose is gradually reduced, but kept sufficient to maintain the apyrexia, and to control the joint symptoms for seven to ten days. No mention is made of acetyl-salicylic acid. As defects of this treatment the following points are raised:—

(i.) The rheumatism frequently returns after the drug is stopped.

(ii.) The salicylates, though undoubtedly controlling the arthritis and pyrexia, yet often fail to prevent the onset of carditis and other complications.

(iii.) The occurrence of salicylism, and the depressant action of the drug on the heart. Dr. Bruce, however, thinks these toxic effects comparatively unimportant, and may be counteracted by digitalis, ammonia, etc., but he does not specially mention the utility of combining carbonates with the salicylic acid in preventing salicylism.

Mention is made of the alkaline treatment, which was in general use previously to the introduction of salicylates, and which consists in the administration of sufficiently large doses of alkaline salts (carbonates, citrates, etc.), to render the urine quickly alkaline, and in maintaining this reaction so long as the rheumatic symptoms continue. No opinion is expressed on the relative value of this treatment, but Garrod is stated highly to recommend a combination of quinine and large doses of alkalis. As a general remedy for relief of pain and distress, opium is given a prominent place, and is said to be regarded by some as almost specific. It is stated to be falling out of use, however, at any rate in large doses; and Bruce does not recommend its general application.

Use of the cold bath or wet pack is strongly advised in cases of hyperpyrexia.

Amongst purely empirical remedies the following are mentioned:—Lemon-juice (up to viii. oz. in 24 hours), propylamine (iv. to viii. m. every 2 hours), Potassium nitrate (up to i. oz. in 24 hours), guaiacum and potassium bromide. The pain of the affected joints may be relieved by absorbent cotton wool, opium lotions, and hot fomentations.

The diet is of the ordinary type for febrile complaints. Special and careful attention must be paid to the heart during convalescence, and release from rest must be very gradual. In other respects there is nothing noticeable in the treatment advocated as compared with that in vogue at the present time.

In the above summary of Dr. Bruce's article the prevailing views with regard to rheumatic fever have been briefly stated, and will now be used as the basis for the study of the progress made in the ensuing ten years.

Historical Survey of Rheumatic Fever: 1900—1910.—The progress in the accumulation of facts and the promulgation of opinions during these years will be first considered from a chronological standpoint, and an attempt made to outline the advance in all directions year by year. The results of special value and interest will then be discussed in more detail and from a general point of view.

Chronological Account.—Previously to 1900 several observers reported the discovery of some micro-organism, regarded as specific, in rheumatic fever, and amongst them the following are worthy of note :—

(i.) *Examination of Joint Lesions.*—Sahli (iii.), in 1892, isolated staphylococcus pyogenes citreus, fourteen hours after death, from the synovial membrane. Maragliano (iv.), 1897, found staphylococci and streptococci. Melkich (v.), 1899, described a sporing, anærobic bacillus (bacillus of Achalme) in the periarticular fluid of four cases. Chvostek (vi.), 1897, reports seventeen negative and no positive results; and several other observers give negative results.

(ii.) *Examination of the Blood and Heart Lesions* (ante- and post-mortem).—Achalme (vii.), 1897, found a large sporing, anærobic bacillus before and after death. Confirmed by several observers, but many negative results also reported.

(iii.) *Post-mortem Examinations of Heart Lesions.*—Triloubet and Coyon (viii.), 1897, found Achalme's bacillus and a diplococcus in a case of endo-pericarditis. Apert (ix.), 1898, found Triloubet's coccus during life. Westphall, Wassermann, and Malkoff (x.), 1899, found a streptococcus in the blood, brain, and valves from a girl, aged 19, who died of endocarditis and nephritis, associated with chorea. The coccus grew best on alkaline media, and, in a series of 80 rabbits, inoculation of the culture after an incubation period of 9—10 days produced multiple arthritis.

(iv.) *Examination of Chorea and Cerebral Rheumatism.*—Triloubet and Coyon (viii.), 1897, found Achalme's bacillus in a severe case of rheumatic endocarditis and chorea forty hours after death. Apert (ix.), 1898, found Triloubet's coccus in two cases of chorea.

(v.) *Experimental Work.*—Thiroloix (xi.), 1897, by injecting the pleural exudate of guinea pigs inoculated with Achalme's bacillus into rabbits, a condition superficially resembling acute rheumatism, especially in its cardiac manifestations, was produced. Triloubet and Apert (ix.), 1898, produced mitral disease in a rabbit by injection of the blood from a rheumatic patient.

These, then, were the chief results produced on the bacteriological side previous to 1900. In that year, Paine and Poynton (xii.) made their now famous isolation of a diplococcus which has since received the name of diplococcus (or micrococcus) rheumaticus, and which is now believed by these observers to be the chief, if not the sole, specific bacterial agent in rheumatic fever. It was owing to the work of these observers that the microbic hypothesis first gained a definite recognition in the medical world. The rapidity of progress in this direction during the first few years of the century was considerable, and the change in ideas is well exemplified by a comparison between

the survey of rheumatism in the "Medical Annuals" for 1900 and 1903 respectively. In 1900 the reviewer writes, "Nothing has been added to our knowledge during the past year (1899) on the pathology or bacteriology of rheumatism"; and he even commits himself to the assertion that, "There is nothing in the etiology or pathology of acute rheumatism to render necessary the intervention of a bacillus." Turning now to the volume for 1903 we find that "important evidence has been forthcoming in favour of the microbic theory of this disease," and a lengthy account of the evidence is given. Moreover, in Pribram's monograph on the disease (Der Acut. Gelenkrheumatismus), published in 1899 and containing a bibliography of 68 pages, the only reference made to the microbic theory is a mention of Sahli's view that acute rheumatism is an attenuated pyæmia caused by streptococci, and especially staphylococci of slight virulence.

The year 1900 was, therefore, specially noteworthy for the publication of Paine and Poynton's (xii.) communications. They reported the isolation of a diplococcus from eight successive cases of acute rheumatism, and considered it to be identical with the organism previously reported by Triloubet (1897) and Wassermann (1899). Furthermore, intravenous inoculation of large doses of these cocci into rabbits produced lesions typical of acute rheumatism, and, in most cases, the coccus could be re-isolated from these lesions, these results being published in 1901 (xiii.). Hewlett (xiv.) in 1900 published a paper in which he maintained that "Achalme's bacillus" was identical with bacillus enteritidis sporagenes (Klein), and had nothing to do with acute rheumatism. Later, the correctness of this opinion was partially acknowledged by Achalme himself.

During 1901 numerous observations regarding the etiology of the disease were published. Poynton and Paine recorded their inoculation results mentioned above at a meeting of the British Medical Association, and also stated that they had been unable to immunise against the coccus. At the same meeting, Foulerton pointed out that valvulitis was common in normal rabbits, and that in considering these experiments this must be borne in mind.

Meyer (xv.) reported his isolation of a strepto-diplococcus from the tonsils in five cases of acute rheumatism; and stated that by its inoculation into rabbits he had produced arthritis and endocarditis. He surmised that this organism was identical with that described by Wassermann. Menzer (xvi.), on the other hand, strenuously denied the existence of Meyer's microbe, and urged that the disease "is an infective process due to ordinary cocci (especially streptococci), which have become pathogenic owing to some special reaction of the body." Infection, he thought, occurred viâ the naso-pharynx, and especially the tonsil. Allaria (xvii.) described three cases of acute rheumatism transmitted by tonsillitis, and in which the throats contained a non-pathogenic staphylococcus, with a streptococcus resembling that of Meyer. Inoculation into guinea-pigs produced arthritis. Triloubet and Coyon reiterated their belief in a specific microbe, probably a diplococcus, and put forward the view that endocarditis is a secondary infection viâ the gastro-intestinal tract. Singer (xviii.), however, continued to advocate the hypothesis, based on his discovery of streptococcus pyogenes in the blood in five cases of acute articular rheumatism and one of chorea, that the disease is a modified pyæmia. Thelberg (xix.) urged that a condition of diminished alkalinity of the blood, due to increased production of lactic acid, lessened the resisting power of the body to micro-organisms, and recommended on that ground the use of calomel and alkalis in the treatment of acute rheumatism.

In regard to treatment, Strügel reported three good results from the use of anti-streptococcic serum, and also strongly recommended the use of aspirin. Ewart and Douglas Powell (xx.) advocated large doses of salicylates combined with alkalis and opium in bad heart cases. Caton (xx.) recommended the use of blisters over the joints and heart, and considered that if applied during the first few weeks in this way, endocarditis could be somewhat abated. Kerr (xxi.) confirmed this statement as regards the heart, but not for the joints. Abrahams (xxii.) stated that he was able to avert nervous symptoms by combining iii.—v. grs. of sod. bromide with the salicylates. Stengel

(xxiii.) advised a simultaneous use of methyl salicylate externally, as a 10—20 per cent. ointment, with large doses of salicylates internally.

In connection with the general symptoms of the disease in children, Still (xxiv.) emphasised the importance of "growing pains" as an indication of rheumatism, a contention previously advocated by Brockbank (xxv.) in 1900. Still (xxiv.) also supported the opinion that chorea was an undoubted sign of rheumatism, 55·7 per cent. of 226 cases of this disease showing marked rheumatic signs. Amongst other slight manifestations of the disease he mentioned stiffneck, headache, night-terrors, somnambulism, and habit spasms.

During 1902 and 1903 many further observations with regard to bacteriology were reported, but of these it will be sufficient to mention the following—

Meyer (xxvi.) continued his researches with regard to his particular coccus. From cultivations of the blood and inflammatory exudate of more than 30 cases of acute rheumatism he obtained only negative results. In 26 cases of acute rheumatic angina however, he obtained a strepto-diplococcus which, when injected into rabbits, produced the symptoms of acute articular rheumatism, and could be re-obtained in pure culture from the joints. He is, therefore, of the opinion, that this coccus is the cause of the disease, and the tonsils its point of entry.

Beaton and Ainley Walker (xxvii.) published a confirmation of Poynton and Paine's work, having isolated the diplococcus from 15 cases, including 8 of acute rheumatism, 3 of chorea, and 4 of acute endocarditis in rheumatic subjects. The source of their cultures was various, comprising the heart-blood, the knee-joint (in life), the urine, and blood from the ear. The coccus was Gram-positive, and in ordinary culture media could not with certainty be distinguished from streptococcus pyogenes, but grew abundantly in broth filtered from that organism. By inoculation, large doses being required, 17 positive results were obtained in rabbits, including arthritis and endocarditis. They conclude, therefore, that acute rheumatism is an infective process, and,

moreover, that its specific bacterial cause is single and determinate.

Subsequently, in 1903, Walker and Ryffel (xxviii.) announced with regard to this coccus that—

1. In a blood-agar culture the colour change characteristic of the pneumococcus and influenza bacillus is produced.

2. The hæmolytic action upon red blood corpuscles is greater than that of any other streptococcus.

3. It produces considerable quantities of formic acid, produced probably by oxidation of sarco-lactic acid.

They further reported the presence of appreciable quantities of formic acid in the urine of cases of rheumatic fever, whereas it is absent or only present in traces in normal urine. Under salicylate treatment this acid disappeared from the urine.

Vernon Shaw (xxix.), also in 1903, showed that monkeys were susceptible to inoculation with the diplococcus of Poynton and Paine, arthritis, endocarditis, and other "rheumatic" lesions being produced.

As opposed to these researches, McCrae (xxx.) reported entirely negative bacteriological results from the urine, blood, and joint effusions of 270 cases. Philipp (xxxi.) similarly records 30 negative and no positive results, and concludes that "neither the circulation nor the joint fluid contains any micro-organisms which are demonstrable by ordinary bacteriological methods, or can be successfully inoculated into guinea-pigs, rabbits, or monkeys."

Webster (xxxii.), in a summary of the whole position, concludes that all cases of acute articular rheumatism are due to infection, but that the infective agent may give rise to other pathological conditions, and is not specific. Individual susceptibility and other extraneous conditions are, he thinks, the chief factors in the production of the local manifestations of rheumatism.

Drechsfeld and Dixon Mann (xxxiii.) similarly considered the specificity of any rheumatic micro-organism as unproved.

Carey Coombs (xxxiv.) suggested a classification of the disease into three clinical types: transient, malignant, and intermediate; and thought the occurrence of relapses at very long intervals was in favour of the microbe possessing great powers of latency, comparable with the tubercle bacillus.

In regard to diagnosis, Achalme (xxxv.) emphasised the "pre-articular" signs of rheumatism, particularly cardiac irregularity.

Terc (xxxvi.) put forward the use of bee-stings as a means of diagnosis from gonorrhœal rheumatism, and further believed that the bee-sting exercised a specific effect on the rheumatic virus, and that those immune to stings were also refractory to rheumatism.

Macalister (xxxvii.) emphasised the close similarity of many cases of rheumatoid arthritis to acute rheumatism, the distinguishing features being the absence of reaction to salicylates or of cardiac complications. In the former disease, also, the temperature is remittent, the joint pains tend to be symmetrical and to spread to other joints without leaving those originally affected. He considered this type of disease to be due to toxic absorption.

Questions of treatment at this date were mainly concerned with the use of sera. Menger (xxxviii.) published four papers on the use of his anti-streptococcic serum obtained from animals immunised to the streptococci of rheumatic throats. He considered the serum improved the natural resistance of the body, and prevented relapses and endocarditis. The serum was also of value in cases of chronic streptococcic bronchitis, a fact which he places in favour of the non-specificity of acute rheumatism.

Poynton (xxxix.) recorded wholly negative results with an anti-streptococcic serum in rheumatism and chorea.

Much difference of opinion continued to be expressed with regard to the use and abuse of salicylates, Thomson (xl.), for instance, believing them to increase the frequency of cardiac trouble, and recommending alkalis and aconite instead, or lemon

juice, whilst Huchard (xli.) maintained that sodium salicylate acts both as a cure for acute rheumatism and a preventive of carditis.

Serafide (xlii.) brought forward massage with petroleum as an efficient therapeutical measure, both as to fever and pain, whilst O'Conor (xliii.) reported successful results in 20 cases of the performance of arthrotomy.

The years 1904 and 1905, though not producing any results which could be pointed to with certainty as elucidating the etiological problem of rheumatic fever, yet added considerably to the rapidly growing store of knowledge regarding the possible bacterial origin of the disease. From America, Lewis and Longcope (xliv.) reported the investigation of a fatal case of chorea and endocarditis from the blood of which (14 hours after death) a streptococcus was isolated which, when injected into rabbits, gave rise to multiple arthritis. They discussed, however, the possibility of this microbe being the ordinary streptococcus pyogenes, and pointed out that, as they never succeeded in obtaining a coccus from the living subject, streptococcal infection may supervene as a terminal event in rheumatic fever.

In this country, Dr. Beattie (xlv.) isolated an organism, identical with that described by Poynton and Paine, from the synovial membrane of a girl with acute rheumatism, and, after inoculating a rabbit from it, re-obtained it from the vegetations of the resulting endocarditis. Other "rheumatic" symptoms were similarly produced, and the author concluded that, "Micrococcus rheumatica is a specific organism, and is causal in acute rheumatism."

Cole (xlvi.), however, obtained arthritis in rabbits with six strains of streptococci isolated from cases in no way resembling rheumatism, viz., peritonitis following cancer of the stomach, puerperal fever, septicæmia, empyema, appendicitis, and scarlatinal adenitis. The arthritis produced, moreover, closely resembled the typical acute rheumatic arthritis of man, and endocarditis, though not chorea, was also demonstrated. These

results were in harmony with those of Menzer, mentioned above, in which he obtained similar results from the inoculation of streptococci, whether procured from puerperal sepsis, a mammary abscess, or a rheumatic tonsil.

On the other hand, Poynton (xlvii.) continued to maintain his position, and reported positive results as regards his and Paine's diplococcus in 32 total cases, various rheumatic lesions, including the nodule, having been investigated. In 1905, however, he appeared to consider that though the diplococcus is the only bacterial cause of the specific disease, rheumatic fever, yet the coccus itself need not be specific.

About this time several writers advocated the use of mesotan, which contains 71 per cent. of salicylic acid, as an inunction, and claimed that by its use better results were obtained than by the administration of salicylates by the mouth. Mendel also recommended intravenous injections of a double salt of caffeine and sodium salicylate, but a special technique was required in its use.

In the volume of the "Medical Annual" for 1906, it is stated that the existence of the micrococcus rheumatica is now generally acknowledged, and in this year Bullock's summary of the evidence was published in Clifford Allbutt's "System of Medicine," and from this article quotation is opportune as expressing the current opinion half way through the decade under consideration. Accepting, for the moment, the infective hypothesis, the author draws special attention to the striking divergencies amongst the experimental results, and especially to the very numerous definitely negative results in the attempt to recognise Paine and Poynton's diplococcus. The principal opposing opinions are summed up as follows:—

i. Rheumatic fever is the result of an infection with a specific anærobic bacillus. (Achalme.)

ii. Rheumatic fever owes its origin to staphylococcus and streptococcus, and is merely an attenuated form of pyæmia. (Singer.)

iii. Rheumatic fever is not due to any particular microbe, but is a particular reaction in predisposed persons to various microbes, especially streptococci. (Menzer.)

iv. Rheumatic fever is the result of an infection with a specific diplococcus. (Poynton and Paine, Ainley Walker, Beattie.)

v. Rheumatic fever is due to a virus still unknown. (Pribram, Lenhartz, and others.)

Considering these various possibilities, Bullock rules out the first and second as lacking in evidence in their favour, as compared with the numerous facts against them. Menzer's hypothesis is, however, more difficult to disprove, but the main criticism lies in the frequent absence of streptococci in rheumatic fever; and the question as to how far the throat lesions, on which the evidence is based, are characteristic of acute rheumatism. Against the specific diplococcus of Poynton and his co-workers must be set the work of Menzer and Cole, and especially the difficulty found by competent observers in isolating it from any rheumatic lesion. The numerous negative results in this direction suggest that the microbe is only an occasional complication of the rheumatic process, a view supported by Triloubet, one of the earliest students of the coccus in question. As an alternative view it may be held that rheumatism "is not an entity, and in certain cases can be caused by the micrococcus rheumatica."

In conclusion, Dr. Bullock sums up as follows: "In any case it cannot be held as proved that the micrococcus rheumatica is the cause of rheumatic fever, as it does not fulfil all, or, indeed, any, of Koch's so-called postulates. It is not found in every case of the disease, and the effects which it produces experimentally do not differ essentially from those produced by cocci which have been isolated from cases having nothing to do with rheumatic fever. In spite of the numerous investigations which have been carried out, it seems to me that the etiology of rheumatic fever still belongs to the arcana of pathology, and, although what clinicians call rheumatic fever is probably a specific infective disease, the virus is not known."

This cautious verdict of "not proven" was typical of the general attitude of the medical profession to the specific microbic hypothesis at this time, but a definite advance on the position of 1900 had been made by the wide acceptance of the view of rheumatic fever as a microbic disease. Subsequent progress has not been so rapid, nor so striking in its details; and the views now commonly held differ but little from those of Bullock in 1906. It will, therefore, only be necessary to refer to a few outstanding pronouncements on the subject rather than to detail at length the various and still contradictory results of individual workers.

Certain papers by Connor (xlviii.), of New York, and Dunn (xlix.), of Boston, published in 1907, are of interest as expressing the American attitude towards the disease and the controversies waged around it. Their main conclusions are very similar to those of Bullock, and Connor summarises the matter thus—

i. Acute rheumatism is a specific infectious disease, and is not merely an attenuated pyæmia resulting from the common pyogenic organisms.

ii. The bacillus of Achalme has no etiological relation to acute rheumatism.

iii. Although there is considerable evidence in favour of the view that the disease is caused by a specific diplococcus or streptococcus, positive proof of the specificity and identity of this organism, and of its causal relation to rheumatism, are still lacking.

Dunn (xlix.), on his part, states that, "at present it seems advisable to accept the micrococcus rheumatica, not as the absolute proven specific cause, but as the probable specific cause of rheumatic fever." This author, in addition, gives the results of a careful investigation of 300 cases of rheumatism in childhood, extending over a period of five years. The chief points brought out are worthy of quotation, as, by their close correspondence with the results of observers here, they emphasise the essential similarity of the disease under different climatic and

racial conditions. As a general conclusion, Dunn states that rheumatic fever is by far the most frequent cause of arthritis and endocarditis in children, and that the latter condition is a much more common manifestation of the disease in childhood than in adult life. In regard to the articular cases, the comparative mildness of the symptoms was very noticeable, and the lesion was frequently non-articular. Out of the 300 cases investigated, some variety of heart trouble was found in 281 (93·7 per cent.), and was, not infrequently, the first indication of rheumatism. He further concludes that the most frequent cause of cardiac failure from lack of compensation in rheumatic children is due, not to overstrain, but to a renewed attack of rheumatism. According to Poynton, this is in agreement with observations in this country. Eighty-six of the 300 cases gave a history of chorea, and out of 121 admissions for chorea, 69 gave a history of existing or pre-existent rheumatic fever. Again, 98 of the 300 cases gave a distinct history of sore throat, but no allusion is made to the presence or absence of nodules, an interesting divergence from most workers on the subject. The prognosis was grave: 1 in 5 of the 223 cases of acute infection were fatal; in each case heart disease was the ultimate factor, and only 17 out of the 300 patients were discharged quite well.

In connection with the question of rheumatic fever in children, Poynton (l.), in 1907, gave some examples of the disease at the age of two or three years, a condition which, though rare, merits attention, and he emphasised the difficulty of distinguishing in infants between rheumatic stiff neck and early spinal caries.

Maxwell Telling contributed to the "Practitioner," in May, 1909, a very interesting survey of "The Rheumatic Infection," from its clinical side. He adopts the specific microbic hypothesis as the best basis from which to view the disease, and thinks the clinical evidence is increasingly in its favour. "The more closely," he says, "atypical cases are studied, the more do we tend to the view that rheumatism is a clinical entity, with fairly constant phenomena, and that many of these atypical 'rheu-

matisms' are of a different pathology." From the standpoint of clinical diagnosis, he emphasises the following indications:—

i. The family history.

ii. A particular physical and mental type.

iii. The presence of one or more of the symptoms included in the "rheumatic series," the most important of which are arthritic phenomena, fascial inflammations (including fibrous nodules), cardiac lesions, chorea, and certain skin eruptions.

iv. That the symptom-complex and general course of the disease should conform to a particular type, of which two may clearly be recognised, the rheumatism of childhood and the rheumatism of the adult.

Dr. Telling's observations with regard to family history and the rheumatic diathesis will be considered at greater length in the second part of this essay, and here it will be sufficient to mention that he considers both factors to be of real importance. In regard to the contrast between the rheumatism of children and adults, he quotes the words of Dr. Cheadle,who maintains that "in the rheumatism of childhood, arthritis is at a minimum; endocarditis, pericarditis, subcutaneous nodules, and chorea are at a maximum. As life advances, this rule is gradually reversed, the joint affection grows more prominent, regular, and characteristic, while the other phenomena decline and tend to die out."

Turning, then, to a detailed survey of the manifestations of the "rheumatic series," this writer first comments on the so-called connection of iritis with rheumatic fever, and expresses his emphatic opinion that "the occurrence of iritis is a piece of evidence as conclusive as can be hoped for in case history that the disease under investigation is *not* rheumatic." Dr. Eason, in his lectures at Guy's Hospital, also maintains the greatest scepticism as to whether iritis is *ever* associated with acute rheumatism or heart disease, the probability being that where it appears so associated, either with acute or chronic rheumatism, that it is really gonnorhœal in origin.

Arthritic Phenomena.—In this connection, Telling points out that rheumatism is not essentially a disease of the joints, nor is acute synovitis by any means peculiar to rheumatic fever. It is especially noteworthy, however, that the synovitis of rheumatism leaves the joints as they were before, and he goes so far as to state that "when the joint lesion results in permanent changes, the gravest suspicion attaches to its rheumatic origin." Failure to realise this may mean the overlooking of a case of gonorrhœal arthritis, especially in a woman, and in the diagnosis of this disease he points out the value of salicylate treatment as a diagnostic criterion, failure of reaction to that drug being strongly against rheumatism.

The question of *Rheumatoid Arthritis* is also discussed, and allusion is made to the fact that "cases, which present the anatomical features of rheumatoid arthritis, occasionally appear to have started in a way indistinguishable from rheumatism," and three possible explanations are put forward:—

i. The disease has been rheumatoid arthritis from the first.

ii. An original rheumatism has predisposed the patient to rheumatoid changes.

iii. The disease has become transformed into rheumatoid arthritis.

The last view is somewhat supported by the not infrequent occurrence of heart lesions and fibrous nodules in such cases, but Telling considers there is need for much more careful investigation before anything definite can be stated.

Fibrositis in children, as shown by "growing pains," a limping gait, or torticollis, he considers to be frequently, though not invariably, a rheumatic indication, and in regard to

Nodules, he thinks the evidence is very clear, and their existence a sign of grave prognosis, a large crop being practically equivalent to a death warrant. This opinion will be again referred to in Part II. of this essay.

Chorea is considered at some length in its relation to rheumatism, and its probable direct connection emphasised; but due regard must be paid to the possibility that chorea, like multiple

synovitis, "may not be of constant pathology, but a symptom common to a number of diseases of toxic or infective nature"; for example, the chorea of pregnancy, senile chorea, and that following distemper in dogs. From the point of view of treatment, however, he thinks it wise, especially considering the liability to heart lesions, "to treat every case of chorea as if it *might* be rheumatic," and particularly enforce the necessity of absolute and prolonged rest in bed.

Heart Lesions.—In our practical knowledge of this branch of the subject, Telling points out that we have remained almost at a standstill for many years. "The prevention, recognition, and remedial treatment of rheumatic heart disease is one of the crying needs of modern medicine," and it is a paramount necessity to realise that, especially in children, every care must be taken to watch and guard the heart in rheumatic fever.

Skin Lesions, viz., miliaria, erythema multiforme, erythema nodosum, peliosis rheumatica, and perhaps psoriasis.

The occurrence of the first in rheumatic fever he thinks is undoubtedly merely coincidental.

With regard to erythema nodosum, many uphold its rheumatic nature on the following grounds:—

i. The frequent incidence with or shortly after a tonsillitis.

ii. The very frequent presence of pains in the limbs or of definite joint pains.

iii. The not infrequent occurrence of effusion into one or more joints.

iv. The presence of certain cardiac phenomena.

v. Its occurrence in persons with either a definite or probable rheumatic history.

Whilst admitting all these contentions, Telling does not consider that they afford any *proof* of the rheumatic nature of the disease, but further definite evidence on the last point would be of distinct value. The other evidence, sore throat, synovitis, exanthem, cardiac lesions, are all equally reminiscent of the syndrome often met with in scarlet fever. Sir Stephen Mackenzie, however, strongly supported the rheumatic view of the

disease, but he was opposed by the French school who consider it to be a blood disease.

Peliosis rheumatica is also, in Telling's opinion, not directly connected with rheumatism, and he quotes Litten to the effect that "French and English authors particularly offend in classifying cases of the hæmorrhagic diathesis with joint lesions as 'acute articular rheumatism with atypical course,' thus constructing a new disease picture."

In regard to this general question of the relationship between certain skin lesions and rheumatic fever, it is interesting to note that Byrom Bramwell (lv.) has quite recently published a case in which erythema nodosum was intimately associated with tuberculosis, and he even considers such a connection to be more probable than the commonly supposed rheumatic one, especially as, according to him this skin disease is coincident with a positive von Pirquet reaction. The attitude of the profession with regard to these relationships would thus seem to be one of growing distrust, the tendency being to regard them as mere coincidence.

In the latter part of the year 1908 a lengthy discussion took place at the Hunterian Society on the topic of "Rheumatism" (lii.), and as many different points of view were there put forward, it will be of value to summarise the debate, especially as opinion with regard to the disease has remained practically stationary since then, and thus a general survey may be obtained of the position at the end of the decade 1900—1910.

Dr. Frederick Taylor opened the discussion, and at the outset expressed his intention to adhere strictly to the problem of rheumatic fever alone. He avowed himself convinced that the disease was of an infective nature and due to a micro-organism, but he did not feel that certainty had been reached with regard to any particular microbe as the causal agent. As evidence for the infective hypothesis, apart from the question of a micro-organism, he adduced the following:—

i. The occurrence of occasional endocarditis in cases with no previous rheumatism.

ii. The great frequency of endocarditis in fatal cases.

iii. The striking resemblance between the mode of death in some fatal cases of chorea, and that in the undoubtedly infective diseases—hydrophobia and tetanus.

From the last point he deduced that chorea is undoubtedly toxic, but that the evidence is as yet incomplete as to whether the toxæmia is microbic, or as to the identity of the microbe with that which produces rheumatic fever. He commented further on the opinion prevalent on the Continent that chorea may be a sequel of scarlet fever or measles.

As to "rheumatic" skin lesions, he did not agree that erythema nodosum or multiforme was necessarily a *manifestation* of rheumatism, but admitted their occurence might be some *evidence* in favour of that disease, whilst the same remarks applied with even more force to tonsillitis.

He remarked upon the great rarity in recent years of *hyperpyrexia* as a complication in acute rheumatism, and recalled how, from 1873—1877, there was almost an epidemic of this alarming affection. He questioned, however, whether the change was entirely due to the salicylate treatment, and thought that no satisfactory explanation had as yet been put forward. As to the administration of salicylates in general, he considered they had at first been given in too small and then in too large doses, and recommended as a type, sod. salicyl., gr. xx., 4tis horis. He doubted whether any real advance had been made with regard to the prevention of carditis. At Guy's Hospital in 1888, 76 per cent. of the cases admitted that year showed cardiac lesions, whilst in 1905 the percentage was 70 per cent., a practically negligible improvement.

Dr. Poynton then rose, and put forward his view that "rheumatic fever is a specific disease." After briefly recapitulating the various steps in the advance of this hypothesis, he gave a short summary of his own results in conjunction with Paine. In the course of ten years they had isolated their diplococcus from 40 separate cases, and from such varied sources as the vegetations of rheumatic endocarditis, a rheumatic nodule, the brain

in chorea, the cerebro-spinal fluid, the blood, urine, and tonsils, as well as from rheumatic pericarditis, pleurisy, and arthritis. On the experimental side they had produced by inoculation of the isolated organism typical rheumatic endocarditis and pericarditis, with many graduations from simple to malignant endocarditis. Choreiform movements, rheumatic pleurisy, nodules, broncho-pneumonia, acute cardiac dilatation, arthritis, and perivascular fibrosis had also been so produced in various animals, including monkeys. His *conclusions*, therefore, were:—

i. A diplococcus is a bacterial cause of acute rheumatism.

ii. Rheumatism may be a cause of both simple and malignant endocarditis;

Whilst as an "expression of opinion," he stated that "because no other micro-organism appears to satisfy the necessary postulates, the diplococcus is the only bacterial cause of the disease."

As evidence for these conclusions, he adduced:—

i. The micrococcus can be isolated in pure culture from the cardinal lesions of rheumatism.

ii. It can be cultivated in pure culture.

iii. It can produce by intravenous inoculation similar lesions in animals.

iv. It can be isolated from these lesions in pure culture.

As regards the bacillus of Achalme and Thiroloix, he reported that he had failed to find it, and considered that it probably represented a diplococcus which had become modified outside the body. Dr. Poynton then alluded to the chief objections commonly brought against his work, namely—

i. Skilled bacteriologists have failed to isolate the coccus, though using his technique. To this he could only reply that he undoubtedly *had* found it.

ii. The infection is a terminal one. But he has isolated the organism from a patient with pericarditis who, six years afterwards, was alive and well! Other workers have had similar results.

iii. The experimental results of inoculation are not peculiar, but may be produced by various micrococci.

Against this he urges:—

(*a*) No other micro-organism produces heart disease so frequently.

(*b*) The results were produced by inoculation of a coccus obtained from cardinal lesions of acute rheumatism in pure culture, and this he considers to be a crucial test.

In work with *sera*, however, he admitted to have had no clear success as yet, nor with *opsonins*. In conclusion, he emphasised the difficulties besetting the path of research, in this subject especially:—

i. The minute size of the diplococcus.

ii. The rarity of fatal cases of acute rheumatism.

iii. The rapid decrease in the virulence of the coccus when isolated.

iv. The fact that the coccus does not easily escape into the joint or other exudations; and Beattie has shown that it may be present in human synovial tissue though the exudation is sterile.

v. The absence of any good laboratory test for the microbe.

It may be of interest here to interpose a brief account of Poynton's diplococcus as described by that writer in Osler and Macrae's System of Medicine. He there states it to be allied to streptococcus pyogenes, on the one hand, and to pneumococcus lanceolatus, on the other. In size it is about $0{\cdot}5\mu$ in diameter; it grows in pairs or in short chains, and may or may not possess a capsule. It is partially Gram-fast, and stains readily with aniline dyes. Frequently it is degenerated, and is then pear-shaped. Its acid-producing power is marked, formic acid being obtained in quantity from it.

Dr. Horder continued the discussion, and described his position as one of sympathetic scepticism with regard to the work of Poynton and his allies. He had endeavoured to repeat their results, but unsuccessfully. For example—

i. Observations on the blood during life of 30 cases of acute rheumatism, all well marked, and mostly with endocarditis, had produced *entirely negative* results, and no micro-organism had been isolated.

ii. In post-mortem examinations of the effusions, vegetations, etc., of 16 cases, in 5 cases only had streptococci been isolated, and these were few in number and presented no special features. Moreover, in all these investigations he had closely followed Paine and Poynton's technique.

Turning now to cases of malignant endocarditis, his work had produced strikingly *positive* results. In 33 examinations of the blood during life from separate cases he obtained 28 positive results, in 18 of which streptococci were recognised, many of which might be called diplococci. Some of these cases, moreover, had no rheumatic history. By inoculation of these streptococci into rabbits, he had produced endocarditis, pericarditis, and multiple arthritis, without suppuration. Lastly, by inoculation of the streptococci obtained from the stools and saliva (s. fæcalis and s. salivaria) of a healthy person he had produced an endocarditis in rabbits. On these grounds, he therefore concluded that the "diplococcus rheumaticus" had been obtained by Poynton and Paine from cases of malignant endocarditis, and not of pure rheumatic fever. Furthermore, he pointed out that "the chief micro-organisms present in ulcerative endocarditis, *whether the patient has had rheumatic fever or not,* are microbes which, so far as the most searching tests of differential bacteriology can tell, are identical with the short streptococcus to which the name 'diplococcus rheumatica' has been given." Also, by tracing this coccus back to its source in the healthy human being, isolation and inoculation produce positive results similar to those of Poynton and Paine. In conclusion, he suggested a possible analogy with scarlet fever, where we find two clinical types of disease: the ordinary type, due to an unknown micro-organism; and the malignant type, in which a streptococcus is readily isolated.

Dr. Otto Grünbaum next spoke, and reported negative results in his attempts to grow the specific organism from blood cultures. He was anxious to know in what percentage of cases Dr. Poynton obtained positive results, and also in how many of these the result was obtained 10 or more days before death, and thus eliminating the possibility of a terminal infection. He considered

the production of formic acid was the best evidence for the diplococcus.

Dr. Poynton subsequently replied, and emphatically denied the possibility of a terminal infection, reiterating his evidence with regard to cases which subsequently recovered as quoted above. He is not, however, reported to have given any statistics in reply to Dr. Grünbaum. As to the streptococcus in the fæces and Horder's work with it, he pointed out that from such a source many and varied microbes may be obtained. He also mentioned that he had not been able to use salicylates as a means of differentiation between growths of the diplococcus and other organisms, as the drug has such strong general antiseptic powers on all cultures.

Dr. Leonard Guthrie discussed rheumatism in children. Tonsillitis he considered merely co-incidental, as also erythema nodosum, and, probably, peliosis rheumatica. Nodules were, however, in his opinion, clearly rheumatic; and with regard to them he stated:—

i. They are of varying frequency, and at times appear almost epidemic.

ii. They indicate an active toxæmia, and are always associated with carditis.

iii. Their prognosis is usually, but not invariably, fatal.

As regards treatment, he considered it should be chiefly directed towards the heart, and advocated rest in bed as essential, though not invariably preventing carditis. He queried also if salicylates prevent carditis, for crops of nodules may appear whilst they are being given. He further greatly doubted if the co-administration of sod. bicarb. prevented salicylism. As to chorea, he gave the following statistics:—

In 114 cases:—

Family history of rheumatism	*positive*	in 47·3	per cent.
" " "	*negative*	in 42·1	"
" " "	doubtful	in 9·0	"
Personal history "	*positive*	in 63·0	"
" " "	*negative*	in 32·0	"
" " "	doubtful	in 4·0	"
Carditis was	*present*	in 44	per cent.
" "	*absent*	in 42	"
" "	doubtful	in 4	"

He advocated the view that "chorea is a manifestation of rheumatism in the higher cerebral centres of an emotional individual."

Several other physicians took part in the discussion, but no further communications of striking interest were made.

General Conclusions.

An attempt has thus been made to survey, in approximately chronological sequence, the progress of the work on rheumatic fever during the past ten years. Standing out in bold relief against the background of miscellaneous clinical material, we see the rise, growth, and to a certain extent the fall of the hypothesis of a specific micro-organism as the specific causal agent. The opening years of the decade witnessed a great fertility of experimental bacteriological work, and it appeared probable that ere long some clear demonstration of a specific organism would be presented. This anticipation has, however, been disappointed, and the past few years have failed to maintain the promise of their immediate predecessors in this direction. Progress has been made, nevertheless; for it is now generally admitted that rheumatic fever is probably an infective condition due to some micro-organism or organisms, and this is in itself a distinct advance on the conceptions of the disease prevalent a decade ago, and exemplified in Mitchell Bruce's article of that date. In regard to the more difficult problem of the identification of a specific organism, if, indeed, any such exists, it is obvious that none but expert bacteriologists can express a valuable opinion on so technical and complex a research. Amongst such experts, however, there is much contradictory opinion, and in the presence of this disagreement the inexpert, before pledging himself to any particular hypothesis, must be content to await further developments. At the same time, the increasing isolation of the school of Poynton and Paine from the opinions of other workers, and the manifold criticisms which can obviously be directed against their work, does suggest that subsequent work will support the views of Horder and others who deny the

specificity of the much-debated diplococcus. His analogy between the types of rheumatic fever and those of scarlet fever does appear of considerable validity, and the striking contrast of his results with pure rheumatic endocarditis, as compared with those in the malignant form, will require very clear refutation before the diplococcus can be awarded the specific title with which Poynton endows it. From the outside point of view little more can be said; the case is still *sub judice*.

In other directions, progress, though slight, has certainly been sure. The intimate relationship between chorea and rheumatism has been more firmly established, and treatment based on a recognition of this connection has been of definite value. On the other hand, the importance of tonsillitis, and of the various skin affections as direct manifestations of rheumatism, has somewhat receded into the background; whilst iritis has been finally dethroned from its place in the "rheumatic series."

The greatest cause for disappointment in the study of the disease lies in the almost complete failure to advance in the direction of prevention of rheumatic heart affections. Undoubtedly the crux of the therapeutics of the disease lies here, and, from the standpoint of the ordinary practitioner, and even more so of the patient, this lack of progress is of greater importance than innumerable bacteriological controversies. Something, however, has been done in the increasing emphasis which is being laid upon the importance of early and efficient treatment of the rheumatism of children, and in the realisation that in children the arthritic phenomena are of trifling significance compared with the cardiac. The now almost universal classification of the disease into rheumatic fever in children and in adults respectively is a hopeful sign of the times, and it may, perhaps, with confidence, be regarded as an assurance that in the future the rheumatic child will at least stand a better chance of escaping with an unimpaired heart. The treatment necessary to effect this is only too often rendered nugatory by the social conditions of the children, and the comparative inability of doctors or hospitals to put their precepts into practice. The remedy for

this is largely outside the sphere of medical work, but there are many indications that the child of the future will be in a far better hygienic position than he is to-day.

Questions of general treatment have shown but little advance. Salicylates in one form or another continue to hold the field, as far as drugs are concerned; though they have failed to justify all the hopes founded upon them, especially in their power of preventing carditis. The influence they exert on temperature and pain is nevertheless most marked, and of the greatest value; and the practical extinction of hyperpyrexia, together with the immediate alleviation of the agonies of arthritis, are results of no little value. The drawback of possible salicylism has been, by most people, regarded as counteracted by their combination with alkalis; but in regard to the optimum dosage there is still considerable difference of opinion. Amidst the medley of other remedies, general or local, recommended at one time or another during the decade, none stands out as worthy of mention, sera of all kinds having proved of very doubtful utility.

In regard to diagnosis, chief stress has perhaps been laid on the distinction from rheumatoid and gonorrhœal arthritis. Much work has been done on the former disease, and it is now generally regarded as distinct, and probably due to toxic absorption, many differentiating points from acute rheumatism having been enunciated, though diagnosis is still at times difficult in the early stages. Reaction or non-reaction to salicylates has proved a good general criterion, and in rheumatic fever the cardiac complications and the flitting character of the arthritis have been specially emphasised as distinctive.

In other respects there has been no notable progress, and the problems of climatic influence, heredity, and diathesis have remained but little altered since 1900.

Much, therefore, remains to be done in the elucidation of the etiology, pathology, and treatment of the disease. From the purely clinical standpoint, however, we may accept the working hypothesis of its infective nature, with or without a specific microbe. We may concentrate our attention upon the detection

and prevention of carditis in children, and endeavour to distinguish more certainly between the true rheumatic arthritis and the motley group of other forms of arthritic inflammation.

Realising these results of research, we may assuredly congratulate ourselves upon the attainment of at least one further stage in the difficult and tedious ascent to the summit of medical knowledge from which we hope eventually to view the true realities of the causation of disease.

PART II.

Special and Statistical.

Introduction.—In this part of the essay I propose to bring forward the results of certain personal investigations into the records of the cases of rheumatic fever occurring at Guy's Hospital during the years 1900—1909 inclusive. At the outset, however, it is necessary to regard these records, and consequently any conclusions based upon them, from a critical standpoint. Indeed, some impeachment of the accuracy of the medical and surgical reports at Guy's is a necessity in this research, and with regard to certain points suspicion is justifiable. The method adopted by which each report is written by a ward-clerk, who may or may not be a careful and accurate observer, and who, in any case, lacks full experience, is undoubtedly one of great value to the clerk himself, but, to a large extent, renders exactness of research work into the comparative study of the more delicate shades of diagnosis and treatment almost impossible. Thus, with regard to the existence or non-existence of a particular sign or symptom about which there may be difference of opinion, such as a cardiac murmur, unless it is stated in the report that Dr. So-and-so verified the symptom, we are unable to decide how far the report is to be taken as correct. Especially is it necessary to bear in mind that silence concerning a

sign or symptom does not prove its absence; and unless a direct negative is recorded, the fact must be left in doubt.

Having regard, then, to these obvious difficulties in the study of a series of ten years' reports, I have endeavoured to concentrate my attention on factors which are inevitably recorded in each report, and about which there can be no question; such as the age, sex, date of admission, and final result of discharge or death. Other more doubtful points have been considered, however, and with regard to these a word or two is necessary. I have only admitted as cases of rheumatic fever those which were definitely diagnosed as such, and I have rejected all doubtful cases. In regard to complications, etc., I have followed either the physician's own remarks, as quoted in the report, or the summary of the case made by the Registrar. In short, as far as possible I have only considered points the evidence for which rested on more than the ward-clerk's statement, and was corroborated by the physician or Registrar. Having thus explained my method, I now proceed to the results obtained:—

1. *Total Entries.*—During the ten years, the total admissions for undoubted rheumatic fever numbered 1,053, representing 3·96 per cent. of the total admissions of all cases to the Medical wards. The monthly and yearly variations in the entries are set out in detail and graphically in Figs. 2 and 3.

2. *Mortality.*—42 patients died, either directly during an attack of acute rheumatism or shortly afterwards as the result of its complications, *i.e.*, a proportion of 3·98 per cent. of the total cases. These cases will be subjected to detailed analysis later.

3. *Symptoms and signs.*—

(i.) Cardiac.—

Mitral regurgitation, alone or with other heart lesions, occurred in 43·4 per cent.

Mitral regurgitation and stenosis in 19·3 per cent.

Pure mitral stenosis in 1·5 per cent.

Pericarditis is recorded in 7·7 per cent.

Aortic disease in 8·8 per cent.

"Doubtful bruits" are recorded in 17·6 per cent.

These figures are, however, of only approximate value for the reasons mentioned in the introduction, and I have not attempted to elaborate them with accuracy. The general conclusion may, nevertheless, be drawn that some variety of heart lesion occurred in at least 50 per cent. of the total cases. Church, in Allbutt's "System of Medicine" (i.), analysing 889 hospital cases of his own, found endocarditis in 57·5 per cent., and gives the percentage of pericarditis (in 2,290 cases) at 11·38 per cent.

(ii.) Chorea occurred in 8·7 per cent.

(iii.) Skin lesions (erythema, erythema nodosum and purpura), in 3·9 per cent.

(iv.) Salicylism occurred in 1·7 per cent.

(v.) Nodules occurred in 2·5 per cent., and of these 32 per cent. died in hospital.

(These last two symptoms are considered in detail later.)

(vi.) Hyperpyrexia is recorded definitely in one case.

4. *Sex.*—Out of the 1,053 entries 546 were male and 507 female; in other words, 51·8 per cent. and 48·2 per cent. respectively of the total admissions for the disease. These are the figures for all ages combined, the sex proportions at different ages are discussed later. This slight predominance of male cases on the gross total is in accord with similar investigations at other London hospitals, *vide* Clifford Allbutt (i.)

5. *Age and Sex Proportion at different ages.*—This question has been worked out in connection with the number of the attack, whether first, second, or third. In consequence, a smaller total of cases is given, for only those in which there seemed clear evidence as to the number of the attack have been admitted; attacks beyond the third have not been included, and the series does not comprise the year 1900, as in that year's reports the evidence was somewhat deficient. The total cases nevertheless number 720. a sufficient basis upon which to draw fairly definite conclusions.

(i.) Taking males and females together:—

Age.	1st attack.	2nd attack.	3rd attack.	Total.	Per-centage.
Under 5	9	3	0	12	*2*
5–10	102	35	6	143	*20*
11–20	169	102	41	312	*43*
21–30	76	54	26	156	*22*
31–40	28	23	5	56	*8*
Over 40	12	20	9	41	*5*
Total	396	237	87	720	

(ii.) Taking males alone:—

Age.	1st attack.	2nd attack.	3rd attack.	Total.	Per-centage.
Under 5	5	2	0	7	*2*
5–10	55	22	3	80	*20*
11–20	93	56	22	171	*44*
21–30	37	28	16	81	*21*
31–40	14	12	2	28	*7*
Over 40	5	13	3	21	*5*
Total	209	133	46	388	

(iii.) Taking females alone:—

Age.	1st attack.	2nd attack.	3rd attack.	Total.	Per-centage.
Under 5	4	1	0	5	*2*
5–10	47	13	3	63	*18*
11–20	76	46	19	141	*42*
21–30	39	26	10	75	*23*
31–40	14	11	3	28	*8*
Over 40	7	7	6	20	*6*
Total	187	104	41	332	

On this total of 720 cases the percentage of male and female is—males, 53·9 per cent.; females, 46·1 per cent., showing some difference, though slight, from the percentages on the gross total of 1,053 for the ten years, and emphasising the approximate character of such statistics.

(iv.) Frequency of attacks at different ages, males and females:—

	Per cent. under 5.	5–10.	11–20.	21–30.	31–40.	Over 40.
1st attack	2	26	43	20	7	2
2nd attack	1	15	43	23	10	8
3rd attack	0	7	47	30	6	10
1st, 2nd & 3rd attack	2	20	43	22	8	5

These percentages are shown in the form of curves in Fig. 1 and it is there seen clearly that the age period, 11—20, is the one in which there is the greatest frequency of all attacks, third attacks being, however appreciably most frequent then.

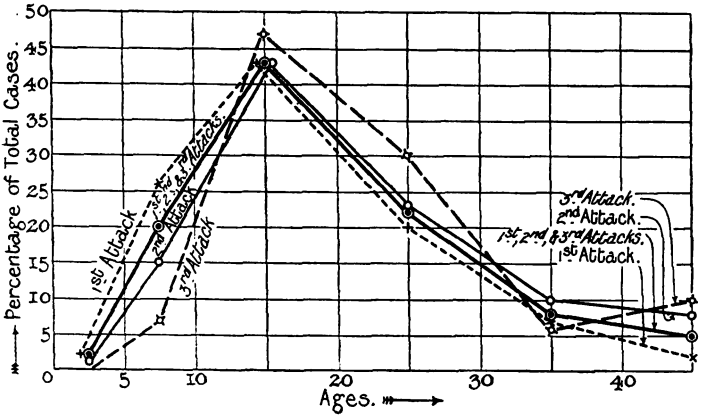

FIG. 1.—Chart to show age incidence in relation to attacks, based on 720 cases.

⊙——— = 1st, 2nd and 3rd attack combined.

×- - - - - - - = 1st attack only.

◯——— = 2nd attack only.

✥- - - - - - - = 3rd attack only.

Males and females combined in each case.

Church, from a consideration of 943 cases of first attacks, gives the following figures:—

Under 10	13·99 %,	compared with	28 % in my cases.
10–19	43·58	"	43 "
20–29	25·66	"	20 "
30–39	13·57	"	7 "
Over 40	2·43	"	2 "

So that the results clearly correspond, and the differences may be partially explained by Church's arrangement of the age periods into 10—19, 20—29, etc., instead of 11—20, 21—30, as in my figures; for I was struck with the large number of cases which occurred at 10 years of age, and their inclusion in one division or the other might account for some of the contrast between 14 per cent., on the one hand, and 28 per cent., on the other. In regard to the general curve of age-incidence, the results are substantially similar. Church deprecates the value of statistics regarding other than first attacks on account of the difficulty in estimating the precise number of subsequent attacks. I think, however, in the statistics given above this difficulty has been reduced to a minimum, and the comparative results seen on contrasting the curves for the first, second, and third attacks respectively are certainly in accordance with what might have been à priori anticipated.

Lastly, regarding the incidence amongst male and female respectively, the following table is of interest:—

	1st attack.		2nd attack.		3rd attack.	
	Male.	Female.	*Male.*	Female.	*Male.*	Female.
Under 5	*71%*	80%	*29%*	20%	*0%*	0%
5–10	*69*	75	*28*	21	*3*	4
11–20	*54*	54	*33*	33	*13*	13
21–30	*46*	52	*35*	35	*19*	13
31–40	*50*	50	*43*	42	*7*	8
Over 40	*24*	35	*62*	35	*14*	30

With regard to the first and last two age-periods, the total numbers on which the percentages are based are insufficient for clear conclusions regarding difference in sex-incidence, and, indeed, the divergencies between the sexes at other ages are not sufficiently definite to warrant any deduction that there is a marked distinction between the occurrence of the disease in the two sexes.

The following were the most notable extremes of age during the ten years:—

Male, aged 63	...	11th attack.	
" " 60	...	2nd "	
" " 55	...	2nd "	
Female " 54	...	1st "	
Two females, aged 3		2nd "	Each with a relapse.

6. *Family History.*—The introductory criticism of the material of research amongst reports applies especially to the question of hereditary influence in the disease, and consequently the subject has been only casually treated. Note has been made of any specific mention of a family history of rheumatic fever in regard to all the fatal cases and several others scattered evenly through the period. In this way, out of 89 cases a definite *positive* result was found in 18 cases, *i.e.*, 20·2 per cent. Many writers consider the hereditary disposition is as much as 70 per cent., and there is little doubt that the proportion found in my cases represents a probable minimum.

7. *Diathesis.*—Here, again, the foregoing fundamental criticisms apply, but the question has been looked into somewhat more carefully. Hutchinson, in "Diseases of Children," describes the "rheumatic child" as follows: "Usually past the second dentition. Dark rather than fair; their hair is dark, their eyes are dark, and they have long dark eyelashes. At the same time they have a peculiarly white skin and a very good complexion; a clear bluish-white sclerotic, and they have often well-formed massive teeth, and particularly large square central upper incisors." They are also described as "neurotic" in type.

Maxwell Telling (lii.), in commenting on this account, agrees substantially with it, and in 18 carefully observed cases reports the presence of this "type" in 15 of them. He thinks, however, that "in most cases I can only get as far as saying, 'This child is *either* rheumatic or strumous.'" He further considers the hair is not infrequently reddish or auburn, and that there is usually a certain delicacy and refinement of feature.

Turning now to the occasional observations by ward-clerks on the appearance of the patients, in 23 out of 89 cases considered, a definite statement as to colour of hair, etc., has been made, and out of these the following results appear:—A definitely *dark type* is noted in 14 cases, 61 per cent.; a definitely *fair type* is

noted in 5 cases, 22 per cent. Amongst these the following descriptions occur:—

Dark hair; clear complexion.
Dark hair; muddy complexion.
Dark and sallow (twice).
Thin black hair; black eyes; long prominent eyelashes.
Sallow; dark brown eyes; eyelashes black and long.
Very white skin; thick auburn hair; grey eyes.
Light brown hair; hazel eyes.
Fair-haired; blue-eyed.

In connection with this question of diathesis, I have made a personal observation of the cases either of rheumatic fever or its consequences present in the medical wards at the end of February, 1911, and the analysis of these results is as follows:—

22 cases examined:—

Dark brown hair, eyes blue to grey, 9 cases brown, 2 „ Black hair, eyes blue to grey, 3 cases dark brown, 2 „ Reddish hair, eyes grey-brown, 2 cases	= "Dark" 18 (82 %)
Light brown hair, eyes grey to blue, 3 cases brown, 1 case	= "Fair" 4 (18 %)
Longish dark black eyelashes in 6 cases	= (27 %)

The predominance is thus clearly in favour of the "dark" type, and especially that of dark-brown hair and bluey-grey eyes. Three cases of chorea were also in the wards, and they might be described thus:—

Very dark brown hair, almost black; long dark eyelashes; dark-brown eyes.
Dark-brown hair, eyes, and eyelashes.
Fair hair; brown eyes.

Here, again, the dark type seems to hold the field, but the number of cases is too few for any real comparison.

8. *Relation between incidence of Rheumatic Fever and Weather Conditions.*—The possibility of any such relationship

has been worked out at length, and the results obtained are diagrammatically shown in Figs. 2 to 15. A brief note on other work on the subject will first be given.

Newsholme (liv.), in the Milroy Lectures of 1895, gave the details of a most complete and exhaustive research into the connection between rheumatic fever and meteorological conditions, both in this country and all over the world. His main conclusions may be summed up as follows :—

(i.) Evidence for rheumatic fever occurring in epidemics:—

(*a*) The very great irregularities in yearly incidence.

(*b*) Two types of "epidemics" occur:—

i. Explosive, which terminate in one to three years.

ii. Protracted, which are more obvious when large areas are taken for examination, and possibly result from a fusion of explosive epidemics.

(*c*) There have been certain years specially favourable for epidemics, *e.g.*, 1855—56, 1859, 1864—65, 1868—71, 1874—76, 1884—85, 1888, 1893 (England).

(*d*) Epidemics are apt to recur at intervals of three, four, or six years.

(ii.) The influence of climate and geography:—

(*a*) Air temperature, only negative evidence obtained.

(*b*) Earth temperature, "great epidemics only occur (London) when the mean earth temperature is very high (50°+)."

(*c*) Humidity, only negative evidence obtained.

(*d*) Rainfall. "A heavy annual rainfall is associated with a low amount of rheumatic fever, and conversely, though in no exact proportion." "Two or three years of excessive or diminished rainfall are certainly associated with a corresponding diminution or excess of rheumatic fever."

(*e*) Ground water. A condition of low ground water is associated with excess of rheumatic fever, and conversely. This factor corresponds with rainfall.

(*f*) Season. Varies in different countries. In Berlin the incidence of the disease is greatest during the first six months of the year, whilst in London the maximum incidence is during October and November.

Thus, Newsholme considered in general that the cause of the disease was some infective agent, probably saprophytic, which became abundant under conditions of low ground water, a condition due proximately to diminished rainfall and assisted by a high earth temperature. A few successive years of excessive rainfall, so to speak, washed the contagion out of the soil, and he contended that excess or prevalence of rheumatic fever is never found with a high level of ground water.

Kleinschmidt (lv.) in 1901 published a careful study of the influence of weather upon acute rheumatism based upon 251 cases extending over 22 years. He found that 64½ per cent. of cases occur during the first six months of the year, the four quarters representing respectively 34½, 33, 16¾, and 18¾ per cent. Cold, or a variable temperature, or a rising or variable barometer, raises the incidence of the fever; wind has no definite effect on it. The disease diminishes with increased humidity.

Church (i.), in Allbutt's "System of Medicine," 1906, considers the question at some length, and publishes several diagrams and tables. He remarks as follows: "The charts constructed by Dr. Garrod from the statistics of Lange in Copenhagen and Gabbett in London, showing the curves during a series of years yielded by first attacks of rheumatic fever, afford no satisfactory evidence that they are influenced by atmospheric or climatic causes. Still more recent investigations by Dr. T. Thompson and Mr. Major Greenwood, junior, into the monthly record of the rainfall at Greenwich and the monthly admissions of rheumatic fever into the London Hospital also show no evidence of any direct connection between the rainfall and the prevalence of the disease."

Church has himself devoted special attention to the incidence of rheumatic fever and its variations with climate in the case

of the British army, but considers that "it is impossible to associate the number of attacks with any peculiarities of climate."

Osler, in his "Text-book of Medicine," 1909, states that in London the maximum incidence of the disease is in September and October, whereas in Montreal and Baltimore the maximum occurs in February, March, and April.

Symes in his book, "The Rheumatic Diseases," 1905, gives the result of the investigation of 193 cases admitted to the Bristol General Hospital, and gives a chart of monthly variations for the years 1893—1902. This chart shows maxima in July and October and a minimum in March, a result which very closely corresponds to that shown in my diagrams.

Bosanquet (lvi.),analysing 450 cases at Charing Cross Hospital between 1890—1897, found a maximum incidence in May and November, but did not think the seasonal curve was well defined.

Such, then, are a few of the published results on the subject, and they are characterised by a considerable lack of clear positive evidence. The general conclusion, indeed, seems to be that there is probably some more or less distinct relationship between climatic conditions and the prevalence of the disease, but that so many varying factors are concerned that it is impossible to make any useful generalisation on the subject.

It may, therefore, seem an unprofitable task to attempt a further investigation of the problem, but it nevertheless has appeared to me worthy of renewed discussion, and I have gone into the problem in some detail, in so far as it is affected by the admissions at Guy's during the past ten years. As regards the method of inquiry, I have ascertained first the monthly entries of undoubted rheumatic fever throughout this period, and have then regarded them from two points of view. First, the *yearly* incidence (expressed in percentage of the total admissions to the medical wards) of the disease has been plotted out as a graph (Fig. 2); and, secondly, the total admissions for

each month for the whole ten years have been similarly represented (Fig. 3). The total yearly and monthly curves have then been individually compared with the average weather conditions throughout the decade. The meteorological statistics have been obtained direct from the Monthly Weather Reports as published by the Meteorological Office, and the station of observation nearest to Guy's Hospital (Brixton or Westminster) has been selected as the source of the figures used. The following climatic conditions have been considered for each separate month:—

i. Rainfall.

ii. Total rainy days.

iii. Rainfall per rainy day, average deduced from i. and ii.

iv. Average humidity.

v. Hours of sunshine.

vi. Mean air temperature.

vii. Prevailing winds.

In addition, note was made of the average barometric height, but the results seemed of little value, and Dr. Newsholme, in his Milroy Lectures, expressly stated that the variations in this factor were so erratic as to be of no practical utility in such an investigation, and with this I agree. Newsholme lays emphasis on the mean earth temperature and the level of the ground water. Unfortunately the Meteorological Office gives no consecutive record of the former factor, and I have been unable to obtain any statistics with regard to the latter. Newsholme, however, considered the rainfall was in sufficiently close relationship to the ground water as to be almost equally valuable for this research.

Each of the above factors has thus been compared both with the yearly and monthly incidence (Figs. 2 to 15), and an attempt has been made to draw deductions from such comparison. I shall now turn to the detailed consideration of these charts.

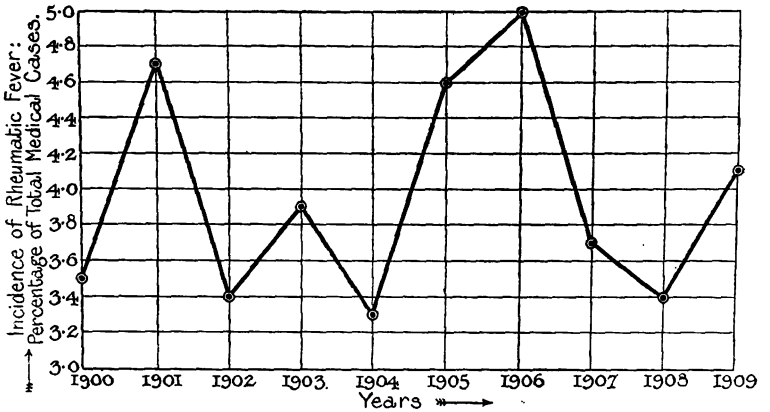

FIG. 2.—Yearly incidence of rheumatic fever at Guy's, 1900–9, expressed in percentage of total yearly admissions.

Year.	Total admissions to Medical Wards.	Total Rheumatic Fever Cases.	Percentage.
1900	2,070	74	*3·5*
1901	2,256	107	*4·7*
1902	2,403	84	*3·4*
1903	2,585	103	*3·9*
1904	2,915	96	*3·3*
1905	2,902	136	*4·6*
1906	2,624	133	*5·0*
1907	2,963	109	*3·7*
1908	2,563	98	*3·4*
1909	2,739	113	*4·1*
Total:	26,020	1,053	Mean: *3·96*

This represents the yearly incidence of the disease, and is expressed in percentages of the total yearly admissions to the medical wards, thus making allowance for temporary variations in the beds available. Two well-marked "peaks" are obvious in the general curve, representing the years 1901 and 1905—6, whilst 1909 would seem to be leading up to a third. (The Reports for 1910, being in the hands of the binders, have not been available for this research.) 1903 was an "average" year for this decade, and the remaining years are distinctly below the mean, but not so markedly as the maximum years are above it. On Newsholme's views there might be said to have been two epidemics and the commencement of a third, the interval between each being three years.

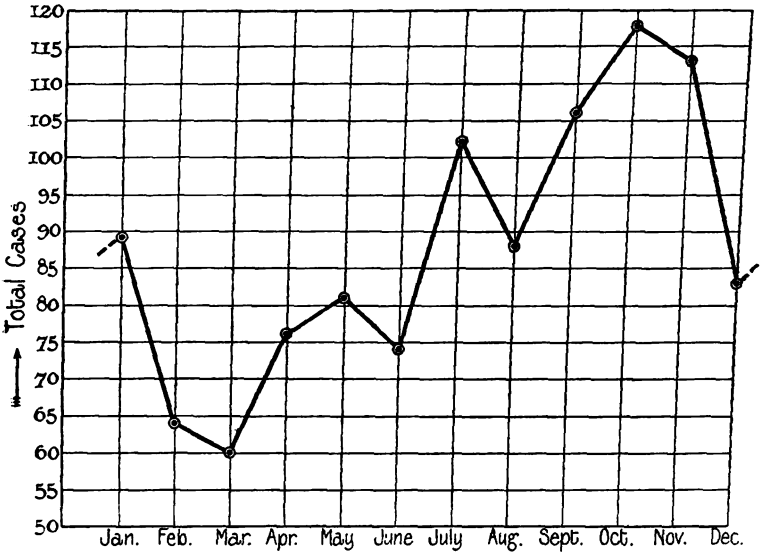

FIG. 3.—Total monthly admissions, 1900–9.

Here the *total* admissions for each month during the decade have been summed up and shown as a curve. It did not seem necessary to express the figures as percentages as in the case of Fig. 2, for, as each point on the curve represents the sum of 10 separate figures, slight variations in the capacity of the hospital in different months are probably sufficiently counteracted. The dates taken have been those of actual admission to the hospital, and there is an obvious objection to this, inasmuch as the onset of the disease does not necessarily correspond with the date of admission. In the great majority of cases, however, only a few days elapsed between the onset and the admission, and the slight additional accuracy which would have been obtained by working out the actual date of onset in each of 1,053 cases did not appear to be worth the large amount of extra labour it would have involved. The large number of cases is, in itself, a considerable guarantee that the curve represents a mean, and that extremes on either side have largely cancelled one another, and the whole research cannot reach such a standard of accuracy as to invalidate conclusions drawn

from this curve on account of this prima facie objection. In general terms, it may be said that if the whole curve were moved about one week (*i.e.*, about one-fourth of a division) to the left, it would be almost exactly accurate. Moreover, in most of the work done previously on this subject, the same basis of estimation has been used, and so these curves can be the more readily compared with them.

Taking now the curve as it stands. In accordance with other similar investigations for London, it shows a very marked rise in the incidence in the second half of the year, a condition almost exactly opposite to that recorded for Berlin and America. Comparison with the charts published by Church for the admissions to the London and St. Bartholomew's Hospitals show a very close correspondence, and the same is true with regard to Symes' chart for Bristol. A further point of interest lies in the fact that my chart almost exactly corresponds with that of notifications of scarlet fever in London, 1890—1904, published in the article on that disease in Allbutt's "System of Medicine" (lvii.), and this striking similarity is perhaps worthy of further study. This point is of additional interest in considering the analogy which Horder draws between the two diseases (*vide* part i., page 26), and suggests the bare possibility of similar micro-organisms producing different diseases according to the human soil in which they grow, *i.e.*, the idiosyncrasy of the patient. Church's charts show the incidence both for first attacks alone and for all attacks, but the difference between them is practically inappreciable, so it is justifiable to conclude that no error of importance is made by considering all attacks together, and this I have done.

We are thus faced with the inference from the facts, an inference supported by evidence from many other sources, that in London the incidence of rheumatic fever steadily declines from January to March, there reaches its minimum, and then ascends till it attains a maximum in October (but with distinct diminutions in June and August respectively). The descent is then slight to November, but a rapid fall then ensues, followed by a

slight rise to January. In other words, the whole year can be accurately divided into halves: during the first moiety (January to June) the disease-incidence is below the mean; and in the second (July to December) it is as much above it. Such a striking variation in incidence, according to the time of year, would seem emphatically to point to the influence of some climatic condition which influences the growth and prevalence of some micro-organism, on the one hand, and the susceptibility of the individual, on the other. It therefore appears worth while again to attempt the task of elucidating such a connection.

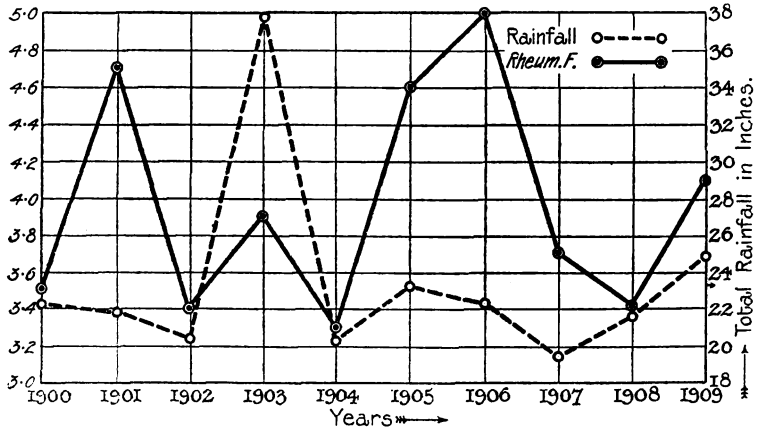

FIG. 4.—Comparison of (1) Yearly incidence of rheumatic fever. and (2) Total annual rainfall.

Yearly Incidence compared with Total Annual Rainfall.—This curve shows that, with one marked exception, the total annual rainfall varied but slightly from year to year. The exception, however, is a very striking one, the year 1903 having a rainfall greatly in excess of any other year, though 1909 shows a distinct rise. Comparing this with the superimposed curve for the incidence of rheumatic fever, it is obvious that no close parallel is visible. The year 1903, with its excess of rain, goes with a slight rise of the incidence, but is followed by a marked and continuous rise in the prevalence after 1904. This is hardly in accord with Newsholme's conjecture that a wet year washes out the disease; for, although there is certainly a diminished

prevalence in 1904, the immediate subsequent rise is striking and persistent. In general, then, these curves show no clear relationship between the rainfall and the prevalence of the disease.

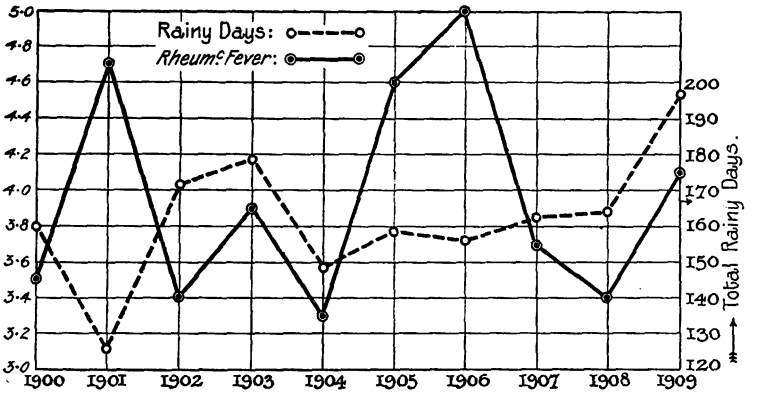

FIG. 5.—Comparison between (1) Yearly incidence of rheumatic fever. and (2) Annual total rainy days.

Yearly Incidence compared with Total Rainy Days per year.—Consideration of the total rainy days gives a better idea of the general wetness of the year than does the total rainfall, inasmuch as it expresses the extent to which the rain is spread out over the year. It is thus noticeable that the year 1903, although possessing a rainfall so greatly above the average, was by no means so conspicuously abnormal in respect to rainy days, being, in fact, closely rivalled in this condition by 1902, and well exceeded by 1909. In other words, 1903 was a year in which the rainfall, though extreme, was concentrated, and the year was not actually much wetter than usual. Here, too, in this curve there appears some slight connection with the prevalence of the disease. From 1902 onwards the two curves show a fairly regular correspondence in their variations, especially in regard to 1909. The maximum years of rainy days (1902 and 1903) are associated, however, with average prevalence of disease, and here again Newsholme's contention as to the eliminating effect of rain does not seem to last for more than a year, and is indeed followed by marked increase shortly afterwards.

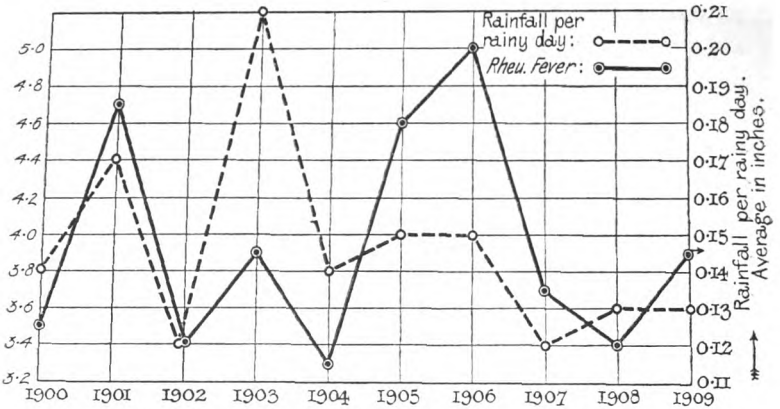

FIG. 6.—Comparison between (1) Yearly incidence of rheumatic fever, and (2) Average rainfall per rainy day.

Yearly Incidence compared with Average Rainfall per Rainy Day.—This curve emphasises the relative concentration of the rainfall each year, and here the general similarity between the disease curve and that of this particular weather factor shows a closer correspondence than in either of the two previous figures. Again the same general remarks apply, and it would appear, superficially at all events, that the concentration of rainfall had some slight direct connection with the prevalence of the disease.

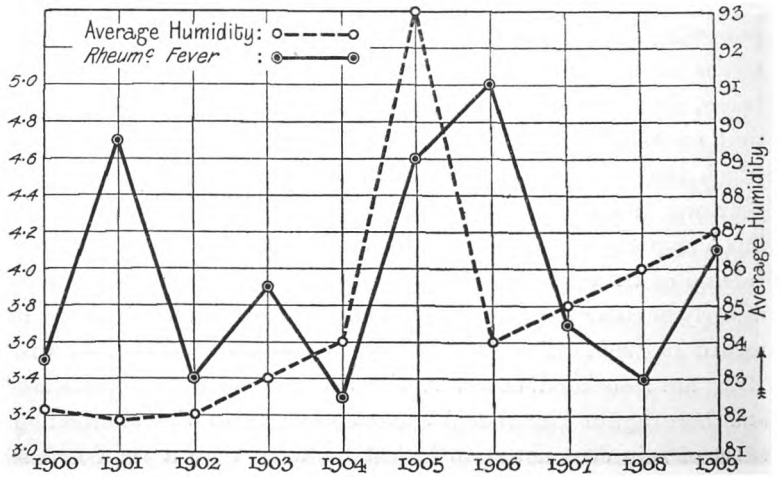

FIG. 7.—Comparison between (I) Yearly incidence of rheumatic fever, and (2) Average humidity each year.

Yearly Incidence compared with Average Annual Humidity.—This curve indicates that consideration of rainfall, rainy days, and rainfall per rainy day is no certain evidence of the extent of average humidity. Thus, 1902 and 1903, years well above the average in the previous curves, are here below the mean; whilst 1905, an average year in regard to these other factors, is markedly above the mean in respect to humidity. With regard to comparison with the disease-prevalence, however, there is no very striking connection, but a very humid year seems in general to correspond with, or to be followed by, an increased incidence of the disease.

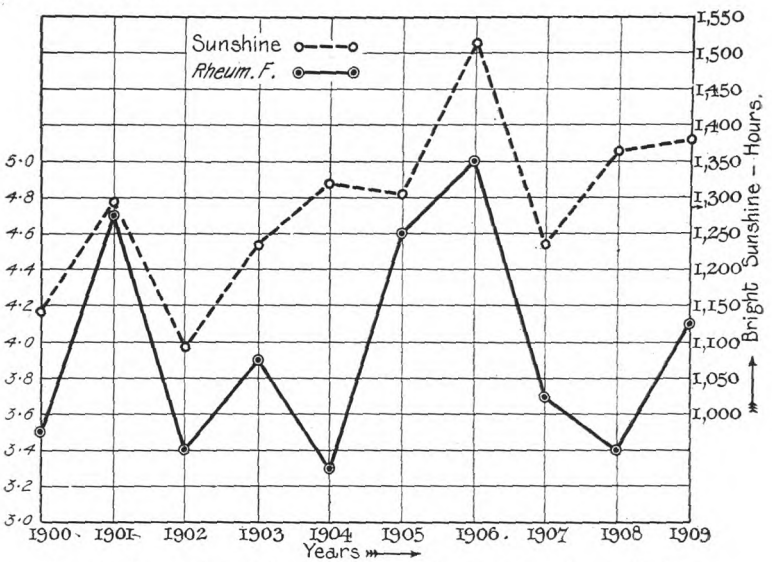

FIG. 8.—Comparison between (1) Yearly incidence of rheumatic fever, and (2) Total annual hours of bright sunshine.

Yearly Incidence compared with Total Hours of Bright Sunshine.—This curve shows the variations in a climatic factor with regard to which I have not found any previous specific reference. It is, moreover, a very striking one, for its variations correspond with marked similarity in both extent and direction with the fluctuations in the rheumatic fever curve. With the exception of 1904 and 1908 the curves closely correspond, and the

deviation in these two years from such correspondence is but slight. It would thus appear as if the extent to which bright sunshine prevailed had some *direct* connection with the incidence of the fever, and we might provisionally suggest that the causal micro-organism was better able to propagate in sunny years.

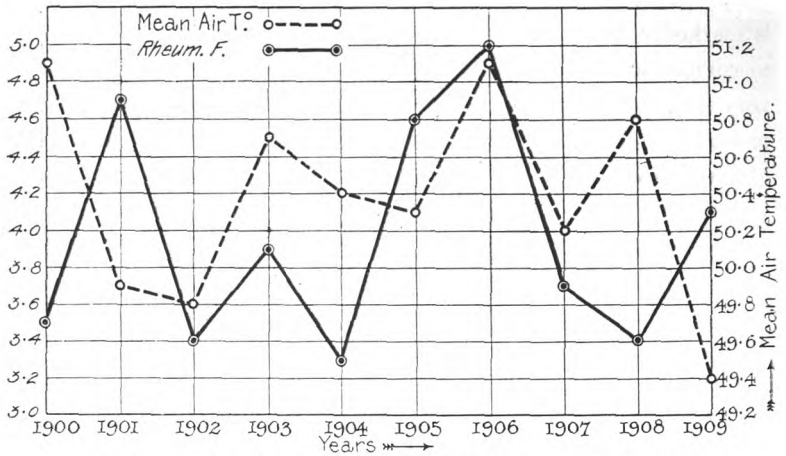

FIG. 9.—Comparison between (1) Yearly incidence of rheumatic fever, and (2) Mean annual air temperature.

Yearly Incidence compared with Annual Mean Air Temperature.—This factor is obviously concerned with the number of hours of bright sunshine, but the two do not exactly correspond; thus, in 1901 the temperature was below, whilst the sunshine was above the average. There does, however, appear a fairly close general resemblance between the disease curve and the temperature curve, and this would seem to be further evidence in favour of the connection between sun and the disease-prevalence being distinctly close.

General Conclusions from the Annual Variations.—This survey has not led to any very definite generalisation, and it appears clear that no single factor is entirely responsible for the prevalence of the disease. A general support, however, is given to the idea that the presence of sun and a high air temperature are directly conducive to the propagation of the disease, and that

these factors are relatively more important in stimulating the occurrence of rheumatic fever than are the factors of rainfall and humidity in decreasing it. The net results are best expressed in the table here appended, where the various factors are considered side by side, and the signs + and — used to indicate the variation from the mean, the thickness of these signs further showing the *degree of variation*, whether small or great.

Year	Rainfall	Rainy Days	Rainfall per Rainy Day	Humidity	Sun	T.°	Rh^c Fever
1900	—	—	—	—	—	+	—
1901	—	—	+	—	Average	—	+
1902	—	+	—	—	—	—	—
1903	+	+	+	—	—	+	Average
1904	—	—	—	—	+	Average	—
1905	Average	—	+	+	+	—	+
1906	—	—	+	—	+	+	+
1907	—	—	—	Average	—	—	—
1908	—	Average	—	+	+	+	—
1909	+	+	—	+	+	—	+

TABLE A.

From this table the following points stand out clearly:—

(i.) 1903, a year with excess of rain, but diminished humidity, and about average sun and temperature, has an average disease-prevalence.

(ii.) The following year, average, on the whole, except as regards a very slight rainfall, is much below the average for disease. Query, therefore, did the rain of 1903 "wash out" the disease?

(iii.) The next two years, however, show a marked and sudden rise in the disease-prevalence, associated with a rising temperature and increasing hours of sunshine. Query, therefore, has the increasing heat and sunshine rapidly counteracted the effect of rain?

(iv.) 1907, a distinctly minus year in rain is also minus in disease, and is followed by a year still more deficient in rheumatic fever. It was, however, also minus with regard to sun and temperature, thus again indicating that these are the more important factors.

(v.) On the whole, the years of + rheumatic fever seem to coincide with, and follow more closely, the years of + sun and temperature, and to a less extent + humidity, than they are related to rainfall.

I shall now turn to a consideration of the *Monthly Incidence* of the disease and its relation to climatic conditions.

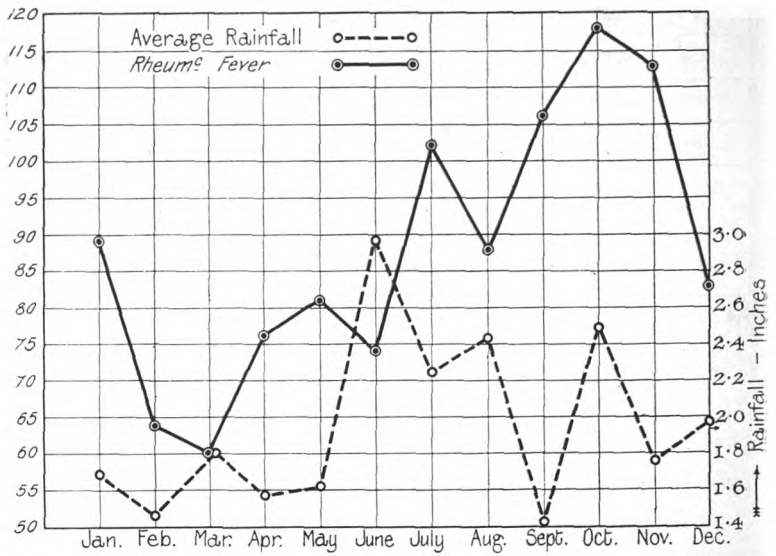

FIG. 10.—Comparison between monthly total cases of rheumatic fever, 1900–9, and average monthly rainfall, 1900–9.

Monthly Incidence compared with Average Rainfall.—No clear connection can be traced between the two curves, though the excess of the disease follows closely upon an excess of rainfall, and is, on the whole, more associated with rainy than dry weather.

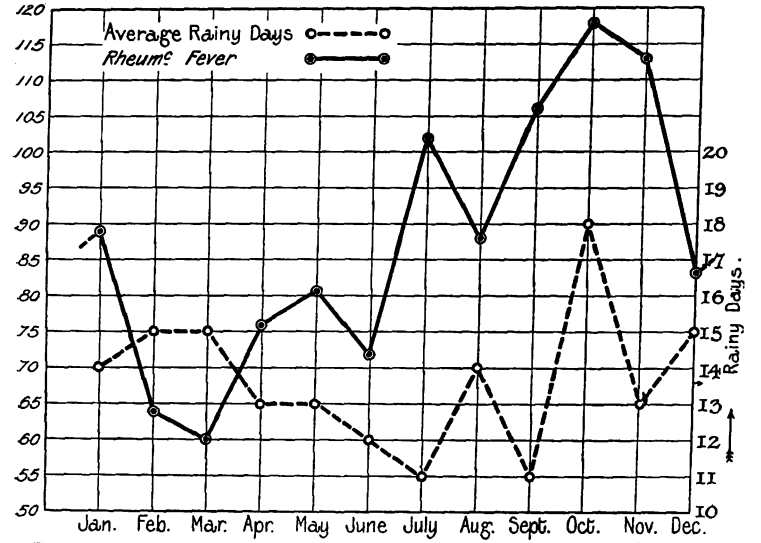

FIG. 11.—Comparison between total monthly cases, 1900–9, and average rainy days per month, 1900–9.

Monthly Incidence compared with Average Rainy Days.—Here a connection seems possible between excess of rainy days and increasing disease-prevalence, the maximum of each curve being reached in October. In general, the two curves correspond rather more definitely than those of Fig. 10.

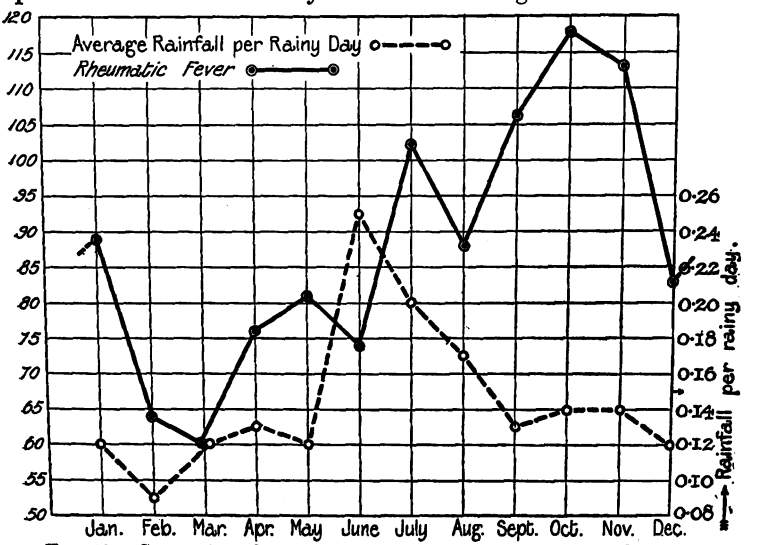

FIG. 12.—Comparison between total monthly cases, 1900–9, and average rainfall per rainy day, 1900–9.

Monthly Incidence compared with Average Rainfall per Rainy Day.—Here a direct connection seems traceable in the first half of the year, but the high disease-prevalence of the latter half is associated with a diminished concentration of rainfall.

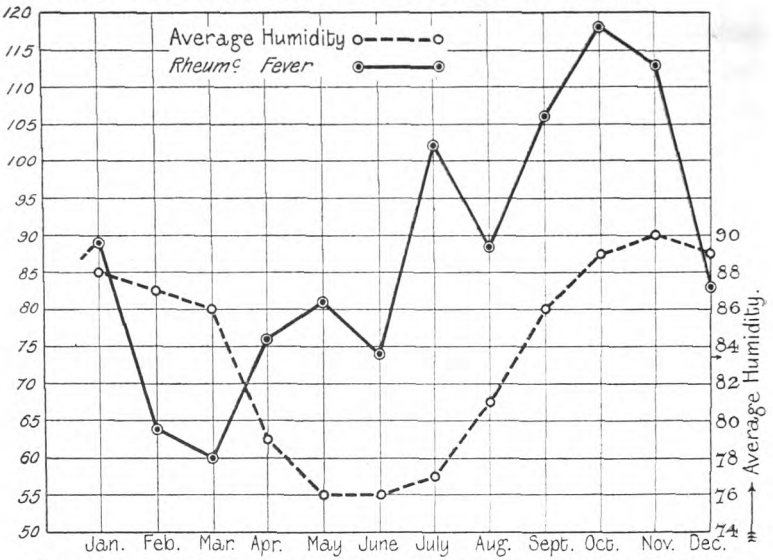

FIG. 13.—Comparison between total monthly cases, 1900–9, and average humidity, 1900–9.

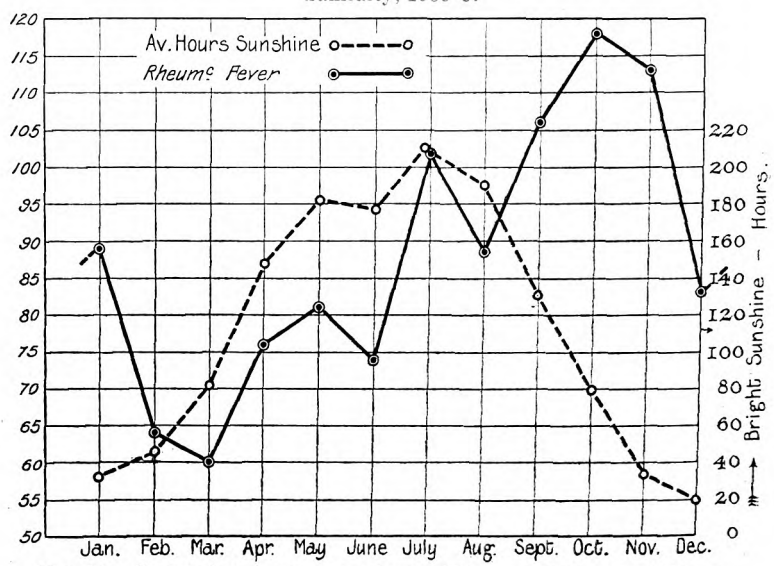

FIG. 14.—Comparison between total monthly cases, 1900–9, and average hours of bright sunshine, 1900–9.

Monthly Incidence compared with Average Humidity.—In this case, with the exception of the months of April, May, and June, the curves show an evidently close approximation, and the disease-prevalence seems to increase in proportion as the average humidity rises, and conversely. The exception noted will be considered later in connection with the question of prevailing winds.

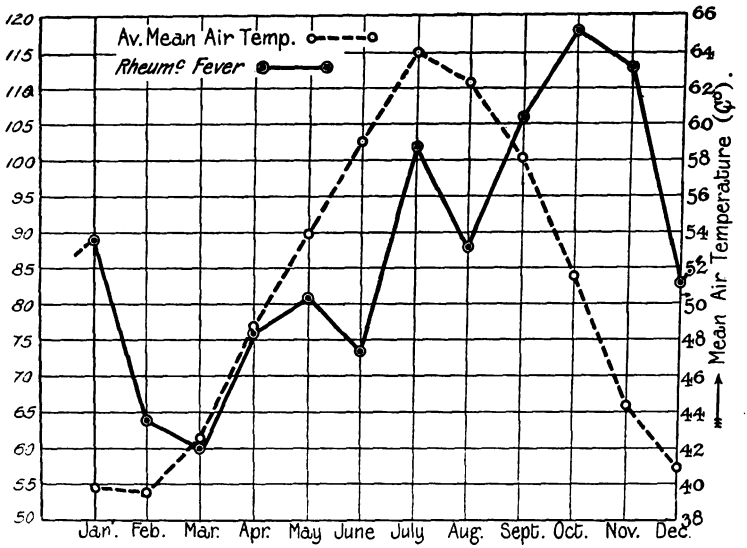

FIG. 15.—Comparison between total monthly cases, 1900–9, and average mean air temperature, 1900–9.

Monthly Incidence compared with Hours of Sunshine.—The correspondence between these curves, whilst not so striking as in the case of annual incidence, is nevertheless of great interest. From February to August the disease curve increases steadily and correspondingly with the sunshine increase. The sunshine curve, however, decreases rapidly after that month, whilst the disease continues to increase in prevalence, but, after November the disease curve falls so rapidly as almost to overtake the diminishing one of sunshine. It would appear, then, that the increasing sunshine steadily accelerated the progress of the disease, and moreover, that its effect in stimulating the causal agent persisted for some time after sunshine itself was declining in amount.

Monthly Incidence compared with Mean Air Temperature.—Here again the same general similarity is seen, though the dip in the disease curve at June is not represented in the temperature curve, though seen in the case of sunshine.

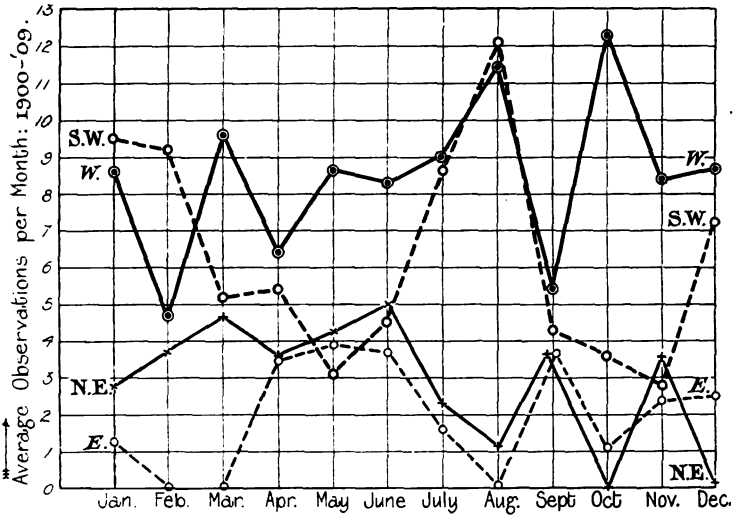

FIG. 16.—Chart to show the prevailing winds each month, based on the average observations, 1900-9.

- ○ - - - - - = South-west wind.
- × ——— = North-east wind.
- ◉ ——— = West wind.
- ○ - - - - - - = East wind.

Influence of Prevailing Winds.—The total observations per month of each wind have been investigated for the whole decade, but out of these complex results only four winds stand out as occurring with sufficient frequency to justify the expectation that they might exert some influence on the disease-prevalence, namely, S.W., W., N.E., and E. winds. These four winds, therefore, have been plotted out in this chart to show their comparative frequency in each month. The curve of rheumatic fever incidence, in order to avoid unnecessary complication, has not been superimposed upon them, but can be readily compared by reference to the immediately preceding figures. The S.W. and

W. winds are thus seen to blow with very steady continuity throughout the year, whilst the north-east wind blows with almost the same regularity, but less frequently. The east wind, however, only appears to any extent in certain months, notably April, May, and June, and thus, as in these months the N.E. wind is also at a maximum, and the west and south-west winds comparatively uncommon, it might be expected that, if winds have any influence on the disease curve, it is in regard to these months that a connection will be seen. It has previously been pointed out that these three months are the ones in which the disease curve fails to correspond directly with that of humidity, and I would therefore suggest that the marked prevalence of E. and N.E. winds at this time may be partly responsible for the discrepancy.

General Conclusions.—The relationship between these various factors and the monthly incidence of the disease are here set out in tabular form in a similar way to that used for the annual variations, plus and minus signs being used with the same significance.

Month	Rainfall	Rainy Days	Rainfall per Rainy Day	Humidity	Sun	T.°	Rhc Fever
Jan.	−	+	−	+	−	−	Average
Feb.	−	+	−	+	−	−	−
Mar.	−	+	−	+	−	−	−
Apr.	−	−	−	−	+	−	−
May	−	−	−	−	+	+	−
June	+	−	+	−	+	+	−
July	+	−	+	−	+	+	+
Aug.	+	Average	+	−	+	+	Average
Sept.	−	−	−	+	+	+	+
Oct.	+	+	−	+	−	+	+
Nov	−	Average	−	+	−	−	+
Dec.	Average	+	−	+	−	−	−

This table serves to emphasise the points already brought out, for it is very noticeable how closely the column of rheumatic fever follows after the columns for sun and temperature, leading apparently to the conclusion that increasing sun and temperature is directly provocative of an increase in the prevalence of the disease. The same applies to the column for humidity, with the exceptions above considered, whilst the columns relating to rainfall show no definite connection whatever, except in so far as the month of maximum rainfall and rainy days corresponds with the greatest prevalence of the fever. The steadily high rainfall of the early summer months seems to have no effect whatever in washing out the disease, a result contradictory to Newsholme's hypothesis.

How, then, may these varied inferences be pieced together, and brought to bear upon the general problem of the etiology of rheumatic fever? From the survey of both the annual and monthly incidence of the disease and its comparison with meteorological conditions, the following are, perhaps, the most prominent conclusions which appear:—

(i.) The factors concerned with rainfall seem to have less direct connection with the disease than do those of sun and air temperature.

(ii.) Increasing sun and air temperature appear directly to stimulate the occurrence of the disease, but the fever continues to increase for some little time after these influences have declined.

(iii.) The period during which sun and temperature decrease, but the disease-prevalence increases, is associated with a maximum humidity and a high rainfall.

(iv.) The curve for humidity bears a close similarity to that of the monthly disease-prevalence, except in regard to certain months during which there is a marked preponderance of easterly winds.

From a consideration of these statements it seems legitimate to deduce that, speaking broadly, the disease-prevalence varies *directly* with the extent to which sunshine, high air temperature,

and humidity are present, but a diminution in humidity may be counteracted by the presence of easterly winds. In other words:—

(i.) In the presence of increasing sun, temperature, and humidity the disease increases.

(ii.) In the absence of sun and temperature, but with high humidity, the disease continues for a while, but rapidly falls as the humidity declines.

(iii.) Easterly winds are conducive, in the presence of rising sun and temperature, to the disease, despite declining humidity.

To sum up.—Sun and temperature, aided by east winds, produce the disease and spread it abroad; humidity maintains it. The etiology of rheumatic fever must be considered from two points of view:—

(i.) Conditions favourable to the growth of the micro-organism.

(ii.) Conditions favourable for the increase of susceptibility of man to the microbe.

In what way do climatic conditions stand towards these two factors in the appearance of the disease? I would suggest, as a possible explanation, that in the very definite rise and fall of the monthly incidence of the disease, we see represented the rise and fall of successive generations of micro-organisms, and I would put forward the following elucidation of the phenomenon. Commencing the year at February and March, when the disease incidence is at its minimum, we find a gradually increasing amount of sun with a heightening temperature, and, in consequence, the hypothetical micro-organism develops with rapidity and attacks those specially susceptible to its effects. As a result, we see the disease curve to rise steeply to May, and its rise is further assisted, I would suggest, by the dry easterly winds of that period. In other words, the microbe, brought out by sun and heat, is aided by the keenness of the wind to lay hold of the highly susceptible individuals whose resisting power is lowered by such climatic conditions. With the steadily increasing sun and temperature, assisted now by increasing humidity, the disease continues to progress, but, with the decline in the two first factors after July, there occurs a slight drop

in the disease incidence. The most favourable conditions for the growth of the microbe are diminishing, and the disease receives a temporary check. Humidity, however, is still increasing, and the rainfall is high, so that in this way, although the growth of the microbe is stayed, the susceptibility of the individual to the already existing micro-organisms is increased by the cold damp weather, and thus, those who had previously escaped the disease, now contract it. The disease curve thus rises steadily to a maximum in October and November. Now, however, humidity declines, sun and temperature are absent, and the supply of susceptible individuals is more or less exhausted. In consequence the incidence of the disease falls rapidly to a minimum; when, with returning sun and heat the cycle once more recommences, taking effect largely upon the new generation of individuals who have now entered the most susceptible age period.

I am fully aware that this is a highly problematical hypothesis, and that I have put it forward with a definiteness which the evidence does not warrant. Nevertheless, by thus outlining my conception clearly, I may, perhaps, have been able at least to draw attention to a possible, if not necessarily probable, explanation of what I regard as the connection between the disease and the climatic conditions.

Curves were also drawn to show the monthly variations in the disease incidence for each separate year of the decade, but they did not appear of sufficient intrinsic value to warrant inclusion here. In general, it appeared to me that in the main they supported my contention, though the limited number of cases in each year, compared with the total considered for the decade, made it possible for extraneous and unknown contingencies to exert a marked influence. It is necessary to study the question broadly, either over a number of years, or with regard to a large number of cases in each year. Only the former method has been available for me, and I have, therefore, based my main conclusions upon consideration of the curves for the whole decade with regard to monthly variations as

giving the truest representation of the facts, and eliminating, to a great extent, unknown and unaccountable influences.

9. *Analysis of Mortality during* 1900—09.—Before coming to the study of the cases at Guy's Hospital, it will be of interest to note a few general statistics culled from the Registrar General's Reports during the period. The deaths are divided into those from rheumatic fever and rheumatism of the heart, and occurred as follows:—

	Total Deaths.	
Year.	Rheumatic Fever.	Rheumatism of Heart.
1900 ...		2787 (not sub-divided).
1901 ...	2170	... 615
1902 ...	2146	... 629
1903 ...	1812	... 570
1904 ...	1788	... 586
1905 ...	2121	... 354
1906 ...	2219	333
1907 ...	2024	... 415
1908 ...	1805	... 363

In 1902 the death-rate was 65 per 1,000,000 living, taking male and female together; in 1903 it was 54, and in 1908, 51 per million. These figures are for rheumatic fever alone.

In 1902 the Registrar reports that the disease has been "rather more fatal to males than to females, except under 15 years of age, during the last two years."

In 1908 he states that during the last 8 years the maximum mortality has been between 10 and 15 years in each sex. From 5 to 25 the female mortality is greater than the male, whilst the reverse is the case at all other ages, but the differences are slight.

At Guy's, 42 patients died during the decade, either directly from an attack of rheumatic fever or shortly after an attack as a result of its complications. They were divided amongst the different years as follows:—

Year.	Patients.	Year.	Patients.
1900	1	1905	4
1901	3	1906	6
1902	4	1907	5
1903	9	1908	2
1904	3	1909	5

	Patients.
Mean.	4·2
Percentage of total	3·98

(i.) *Sex.*—24 of the patients were males, =57·1 per cent.; 18 of the patients were females, =42·9 per cent.

(ii.) *Age and relation to number of attack.*—

(*a*) All attacks:—

Age.	Males.	Females.	Total.	
Under 5	1	1	= 2	= *4·7%*
5–10	9	6	= 15	= *35·7*
11–20	8	9	= 17	= *40·5*
21–30	3	1	= 4	= *9·4*
31–40	3	0	= 3	= *7·2*
Over 40	0	1	= 1	= *2·4*

(*b*) In relation to attacks:—

	Males.	Females.		Average Age.
1st attack	11	10	= 21	9½
2nd "	7	2	= 9	16½
3rd "	3	6	= 9	23½
4th "	2	0	= 2	16
Nth "	1	0	= 1	25

The general result of these figures is that the disease is more fatal in youth (5—20), and that a first attack is more dangerous than subsequent ones, over 50 per cent. of the cases being first attacks, but against this must be placed the greater prevalence of first attacks amongst the total cases of the disease at any period. The numbers are, however, too small to warrant any but the broadest generalisations. The *actual ages* may, however, be of interest, and are therefore given:—

1st attack.—Males: 6, 6, 6, 7, 8, 9, 10, 11, 13, 13, 22. Females: 3, 5, 6, 7, 8, 9, 10, 11, 11, 12.

2nd attack.—Males: 3, 8, 9, 11, 14, 16, 35. Females: 14, 24.

3rd attack.—Males: 15, 32, 35. Females: 12, 13, 15, 17, 19, 43.

4th attack.—Males: 11, 22.

Nth attack.—Males: 25.

(iii.) *Family History.*—Definitely positive in 9 patients (21·4 per cent.).

(iv.) *Diathesis.*—This point has been fully commented upon above. Notes had been made in 16 patients, and out of these, 7 were of a distinctly "dark" type and 4 "fair."

(v.) *Previous Diseases.*—These were naturally very varied, and evidence with regard to them obtained from hospital patients is never very reliable. The following, however, are the main results obtained from an investigation of this point:—"No previous diseases," 12 patients; measles, 11; chorea, 6; whooping cough, 5; tonsillitis, 4.

(vi.) *Diagnosis and Complications.*—In order to set these out in tabular form I have numbered the cases 1 to 42, and have set against each complication or diagnosis the number of the case exhibiting it. In this way the cases can be compared with one another with considerable rapidity. The table is appended below, and in all cases, of course, the diagnosis of rheumatic fever had been made:—

DIAGNOSIS AND COMPLICATIONS, with Number of Case.

1. *Mitral Regurgitation and Stenosis.*— 3, 4, 7, 12, 13, 14, 15, 17, 18, 23, 28, 29, 31, 34, 35, 36, 37.
2. *Mitral Regurgitation.*—1, 2, 5, 6, 8, 9, 19, 20, 21, 22, 24, 25, 26, 32, 39.
3. *Mitral Stenosis.*—38, 40; "commencing" in 5.
4. *Aortic Regurgitation and Stenosis.*—9, 14, 18, 19, 34.
5. *Aortic Regurgitation.*—1, 12, 13, 22, 40.
6. *Aortic Stenosis.*—Nil.
7. *Tricuspid Regurgitation.*—2, 13.
8. *Acute Endocarditis.*—13, 24, 25, 29, 36, 38, 41. *Aortic Endocarditis.*—3, 31. *Mitral Endocarditis.*—33.
9. *Acute Endocarditis of Mitral, Aortic, and Tricuspid Valves.*—15.
10. *Pericarditis.*—*Acute.*—2, 3, 6, 7, 17, 18, 19, 23, 24, 30, 31, 32, 33, 34, 35, 36, 40, 41, 42. *With Effusion.*—1, 9, 13, 25.
11. *Adherent Pericardium.*—11, 12.
12. *Heart Dilated and Hypertrophied.*—3, 9, 11, 12, 14, 15, 17, 19, 24, 28, 29, 35.
13. *Dilated Heart.*—7, 16, 27, 34.
14. *Acute Cardiac Dilatation.*—37, 16 (?).
15. "*Slight Systolic Apical Bruit.*"—10, 16.
16. "*Pulmonary Systolic Bruit.*"—27.
17. "*Heart Apparently Normal.*"—4. (Cf. *Post-mortem Findings.*)
18. *Infective Endocarditis.*—5, 14, 21, 23, 27, 39.
19. *Pulmonary Embolism.*—1.
20. *Pneumonia.*—4 (?), 31 (?), 30, 35, 38.
21. *Pleurisy.*—25, 40.
22. *Follicular Tonsillitis.*—41.
23. *Chorea.*—10, 21, 24, 31, 34, 38.
24. *Bronchitis.*—1, 3, 13, 15, 27, 34.

25. *Albuminuria.*—10, 11, 20, 23, 27, 41.
26. *Hæmaturia and Purpura.*—20, 27, 39.
27. *Anasarca and Ascites.*—9, 23.
28. *Delirium.*—4, 8.
29. *Coma.*—27.
30. *Double Neuro-Retinitis.*—8.
31. *Œdema of Glottis and Acute Pharyngitis.*—20.
32. *Phthisis.*—12. (No signs of this at the autopsy.)
33. *Unilateral Parotitis and Herpes Labialis.*—24.
34. *? Typhus Fever.*—26.
35. *Blood Culture.—Negative.*—9. *Staphylococcus albus.*—12. *Streptococcus pyogenes aureus.*—14.

This table shows conclusively that cardiac lesions are almost universal in these fatal cases, and also emphasises the very frequent occurrence of pericarditis.

(vii.) *Post-Mortem Findings.*—The same method of exhibiting the results of analysis has been adopted here, and is shown also as a table. Case 4 is specially interesting, as, though "nothing apparently abnormal" was recorded as to the heart's condition during life, at death both old and recent mitral and aortic endocarditis, adherent pericardium, and several other lesions were found.

POST-MORTEM FINDINGS.

(No post-mortem held on 11, 17, 20, 25, 26, 34.)

1. *Mitral Endocarditis.*—Recent: 8, 9, 13, 14, 16, 22, 23, 24, 27, 31, 32, 39, 42. Old: 7, 12, 18, 19, 36, 37, 40, 41. Old and Recent: 3, 4, 5, 15, 21, 28, 29, 30, 33, 35.
2. *Aortic Endocarditis.*—Recent: 1, 3, 9, 12, 13, 14, 15, 16, 22, 23, 24, 28, 31, 33, 38, 39, 42. Old: 11, 19, 40. Old and Recent: 4, 30, 35.
3. *Pulmonary Endocarditis.*—24.
4. *Tricuspid Endocarditis.*—Recent: 15, 29, 33. Old: 4, 29.
5. *Myocarditis.*—3, 24. *Fatty Heart.*—13.
6. *Dilated and Hypertrophied Heart.*—2, 4, 7, 8, 12, 13, 15, 29, 42. Right side much dilated: 3. Left side much dilated: 16, 21, 22. *Hypertrophied Heart.*—18, 19, 33, 37. Left ventricle dilated: 23.
7. *Pericardial Effusion.*—5, 10, 13, 18, 24, 29, 30, 40, 41.
8. *Pericarditis.*—5, 21, 24, 30, 32, 33.
9. *Adherent Pericardium.*—1, 2, 4, 9, 12, 19, 22, 31, 35, 36, 38, 40, 42.
10. *Infarction.*—8, 14, 23, 24, 27, 36, 38, 39.
11. *Thrombosis of Mesenteric Vein.*—32.
12. *Pleurisy.*—4, 35, 41. *With Effusion.*—19.
13. *Meningitis.*—10.
14. *Bacteriological Cultures* gave—Streptococcus longus, 10; staphylococcus aureus, 21; bacillus coli communis, 39.

(viii.) *Protocols of a few specially interesting cases.*—

CASE 4 (Cl., 387).—Female, aged 43 years; married. *Admitted* July 7th, 1901. P.H.: Rheumatic fever at 14 and 33 respectively, but no chorea, and, she said, no cardiac symptoms. Husband also suffered from the disease. No other illnesses of importance. H.P.D.: Five days' history of fever and joint pains. C.O.A.: Well nourished. ? Pleurisy. Slight albuminuria. *Heart apparently normal.* Progress: Pyrexia intermittent. *July* 10th: Sudden delirium. Many crepitations and rhonchi. ? Pneumonia. Sank rapidly. Needling gave no result. *Died*, July 13th, six days after admission. *Autopsy.*—Recent double pleurisy. No pneumonia. Acute mitral and aortic endocarditis and stenosis. Adherent pericardium. Tricuspid valve very thick. Heart dilated and hypertrophied with lung firmly adherent to it.

CASE 8 (Cl., 468).—Female, aged 17 years; fish-worker. *Admitted* July 22nd, 1902. P.H.: Rheumatic fever 7 years and 16 weeks ago, "rheumatic type." F.H.: Negative. P.D.: Measles. H.P.D.: Fourteen days' diarrhœa and vomiting. ? Enteritis from fruit. C.O.A.: Palpitation. Râles and rhonchi all over. Trace of albuminuria. Abdominal pain and distension. Spleen enlarged and tender. Mitral regurgitation. Progress: One or two acute cardiac seizures. Irregular pyrexia. Leucocytes, 11,000; reds, 3,900,000. Increasing anæmia. Persistent diarrhœa and cough, with general pains. Double neuro-retinitis. Anti-streptococcic serum used, but no effect. *Died*, October 26th, after violent delirium. *Autopsy.*—Infarcts in spleen and kidney. Vegetations on mitral valve. Aorta normal. Heart dilated and hypertrophied. "The blood, post-mortem, gave a growth of streptococci which appeared identical with the rheumatic coccus."

CASE 10 (W., 130).—Male, aged 8 years. *Admitted* March 30th, 1903. P.H.: ? Any previous rheumatic fever. Father had had disease three times. "Fair, pale." Measles. Chorea. H.P.D.: Three weeks' sore throat, and later, joint pains. Mother said he was always getting wet through and chilled. C.O.A.: Joint pains and chorea. Slight erythema on both knees. Slight apical systolic bruit. Progress: April 2nd: No swelling or pain in joints. April 6th: Temperature normal. April 10th: Drowsy; temperature 101·2°. April 11th: Restless; temperature 104·8°. Albuminuria. *Died* later. *Autopsy.*—Early localised purulent cortical *leptomeningitis. Streptococcus longus* isolated from pus. Old pleurisy. Fluid in pericardium. Valves healthy. ? Nephritis.

CASE 20 (W., 137).—Male, aged 22 years; labourer. *Admitted* March 4th, 1905. P.H.: Negative. H.P.D.: Three months ago swelling of left ankle. Lately increasing flitting pains in joints. C.O.A.: Diagnosed, "acute rheumatism with mitral regurgitation." *Discharged* March 19th. Pains gone; heart unaltered. (There had been once a transient albuminuria and an isolated pyrexia (101·8°) on March 16th.) *Re-admitted* March 27th, 1905. Renewed pains. April 2nd: Purpura all over. April 3rd: Commencing œdema of glottis. Blood and albumen in urine. Hæmoptysis. April 4th: Throat better; Finger joints painful. April 6th:

Throat much worse. April 8th: Throat very bad. Aphonia. Increased purpura, with a patch on tip of tongue. April 9th: *Died.* No post-mortem was held, but the throat was found to be in a condition of "acute pharyngitis, with ulceration of the pharynx."

CASE 21 (1905, P., 4).—Female, aged 9 years. *Admitted* December 29th, 1904. P.H.: ? Negative. Measles and sore throat. Mother and sister rheumatic. H.P.D.: Four days' joint pains and sweating. C.O.A.: Mitral regurgitation. Varying mid-diastolic bruit. Progress: February 20th, 1905: Chorea. Pyrexia. ? Infective endocarditis. Dyspnœa. *Died* February 24th. *Autopsy.*—Old pericarditis. Left ventricle dilated. Recent endocarditis of thickened mitral valve. *Note by Registrar.*—"Staphylococcus aureus was found in the blood, and a similar case has been in another ward. Sore throats have been very prevalent lately."

CASE 26 (T., 376).—Male, aged 22 years; worker at tannery; formerly in army. *Admitted* October 8th, 1906. P.H.: Rheumatic fever in 1901 (heart affected); 1903 and 1905 (with mitral regurgitation). "Florid." H.P.D.: Pain in knees and shoulder coming on after a boxing match on October 7th. Headache. C.O.A.: Mitral regurgitation. Progress: October 12th: Worse; much sweating. Irritable. October 13th: Very irritable. Red spots round knees. October 15th: Spots all over. ? Typhus fever. October 16th: *Typhus fever* diagnosed. Sent to fever hospital. *Died* October 19th of "malignant endocarditis," according to post-mortem report from fever hospital.

10. *Analysis of cases in which "nodules" occurred.*—According to most authorities, the presence of nodules is associated with severe heart lesions, and indicates a grave prognosis. During the decade at Guy's, 25 cases of such are recorded, 8 of which died, *i.e.*, 32 per cent., and all of which presented heart disease in one form or another. 17 of these cases were admitted with rheumatic fever, and these may be analysed thus, the numbers referring to the individual case number:—

1. *Acute Rheumatism.*—First Attack: 3,* 4, 5,* 6,* 10,* 12, 19. Second Attack: 1, 8,* 11, 17, 23,* 25. Third Attack: 2, 7, 9, 18.
2. *Mitral Stenosis and Regurgitation.*—1, 2, 4, 6,* 7, 9, 10,* 11, 12, 18, 23,* 25.
3. *Mitral Regurgitation.*—3,* 8,* 17, 19.
4. *Pulmonary Regurgitation.*—17. *Infarction.*—8.*
5. *Acute Endocarditis.—Mitral.*—6* 10,* 11. *Mitral and Aortic.*—5,* 23.*
6. *Pericarditis.*—4, 5,* 6,* 9, 11, 12, 25. *With Effusion.*—3.*
7. *Adherent Pericardium.*—8,* 17.
8. *Dilated and Hypertrophied Heart.*—6,* 10,* 12, 17, 25.
9. *Chorea.*—1, 3,* 4, 19, 25.
10. *Lobar Pneumonia.*—3,* 6.*

Fatal cases are marked thus *

The remaining 8 cases were as follows:—

CASE 13.—Male, aged 18 years. *Acute rheumatoid arthritis.* Mitral stenosis and regurgitation. Dilated and hypertrophied heart. Multiple subcutaneous nodules. *Relieved.* The above was the diagnosis made by Dr. Pitt, under whom the case was admitted, but Dr. Hale White suggested that it might be a case of rheumatoid arthritis combined with acute rheumatic fever, and both he and Dr. Fawcett specially commented on the rarity of the case. (Reference—1905, Pitt, No. 152.)

CASE 14.—Female, aged 9 years. *Chorea.* Acute endocarditis. ? Pericarditis. Mitral stenosis and Regurgitation. Dilated and hypertrophied heart. She had had rheumatic fever three times; her father suffered from the disease, and she was of a dark type. *Relieved.*

CASE 15.*—Male, aged 18 years. *Aortic regurgitation.* Mitral stenosis and regurgitation. Hypertrophied and dilated heart. ? Adherent pericardium. He had had acute rheumatism twice at least. He was re-admitted after this on two occasions, and *died* during the second.

CASE 20.—Male, aged 13 years. *Chorea.* Mitral stenosis and regurgitation. Erythema nodosum. *Relieved.* Rheumatic fever a year previously.

CASE 21.—Female, aged 6 years. *Chorea.* Mitral regurgitation. Hypertrophied and dilated heart. Pericarditis. Pertussis. *Relieved.* Rheumatic fever four months previously.

CASE 22.—Male, aged 10 years. *Chorea.* Mitral stenosis and regurgitation. Aortic regurgitation. Acute pericarditis, with effusion. Adherent pericardium. ? Malignant endocarditis. *Relieved.* ? Rheumatic fever a month previously.

CASE 24.*—Female, aged 6 years. *Acute endocarditis.* Pericarditis. Mitral regurgitation and stenosis. *Died.* In the previous year she had scarlet fever, followed by rheumatic fever.

CASE 16.—This was a male, aged 67 years, who was admitted with granular kidney; enlarged liver and spleen; enlarged heart; chronic bronchitis and emphysema; anasarca and œdema. He gave no history of rheumatism, and had lived much of his life in India. He was discharged relieved. The *nodules* present were multiple and subcutaneous.

Age and Sex.—Excluding the above Case 16 as being very aberrant, the ages were as follows :—

Male.—6,* 7,* 9, 10,* 10, 13, 14,* 14, 18,* 18, 20, 21.
=12 cases. Average age, $13\frac{1}{4}$.

Female.—6,* 6, 6, 9,* 9, 10, 11,* 11, 12, 13, 14, 19.
=12 cases. Average age, $10\frac{1}{2}$.

The distribution between the sexes is thus exactly equal, and the average age for the two sexes combined is 12 years. It is noticeable that the nodules seem especially a manifestation of

Fatal cases are marked thus *

young subjects, and possibly their absence above about the age of 22 is connected with the heavy mortality and acute heart lesions associated with them resulting in the early decease of those exhibiting them.

This analysis thus affords considerable confirmatory evidence to the belief that nodules are a sign of grave prognostic value, and intimately associated with severe cardiac lesions.

11. *Salicylism.*—There were in all only 17 cases of this during the decade—1·6 per cent. of the total cases. I have analysed each case with considerable care, but, owing largely to the frequent vagueness of the reports in the matter of treatment, there is little of positive value to record as the result of the investigation, and I shall not elaborate the subject to any extent. The main results are as follows:—

(1) Salicylism occurs much more frequently in *adulis* than in children or young people. The actual ages of the patients were the following:—

Male.—6, 15, 20, 25, 26, 32, 33, 36, 39, 42.
Average age, 27·4 years.

Female.—9, 21, 28, 30, 31, 33, 38.
Average age, 27·1 years.

Thus, with one exception in each sex, every case was over 15. and the majority about 30 years old. This is the more remarkable considering the greater frequency of the disease in children. Children are, of course, given proportionately smaller doses of salicylates, but this would not account for the almost equal freedom from salicylism of the age period 15—25. It would, however, be unwise to make too much of results based on so few cases, but the age incidence is, nevertheless, striking and worthy of comment.

(ii.) The symptoms produced by the drug were typically:—Deafness, "especially at night"; tinnitus; headache, dizziness; "wandering talk," "light-headed"; hallucinations; erythema; delirium.

(iii.) These symptoms usually came on within 1 to 3 days of the administration of the drug. which was, in nearly every case.

1 oz. of mist. sod. salicyl. (containing xx grs. of sod. salicyl.) 4tis horis.

(iv.) The symptoms usually rapidly ceased on discontinuing the salicylate, though the pyrexia and joint pains frequently returned in consequence.

(v.) In 4 cases *aspirin* was substituted for sod. salicyl., and in each case the salicylism seems to have cleared up, whilst the joint pains and pyrexia did not recur.

(vi.) In one case the administration of boracic acid, xx grs. (in cachets) with mist. pot. cit. 1 oz. 4tis horis, rapidly removed the symptoms which were persisting even after the cessation of salicylates.

(vii.) The influence of the addition of *sod. bicarb.* to the salicylates varied, and apparently had little effect, unless given in at least xx gr. doses every 4 hours. In one case aspirin succeeded in reducing the symptoms where sod. bicarb. had failed.

(viii.) The occurrence of salicylism was specially noticeable in 1907 and 1908. The numbers each year were :—

1900	—	1905	—
1901	—	1906	2
1902	3	1907	5
1903	1	1908	5
1904	1	1909	—

12. *Conclusion.*—My analysis of the cases of rheumatic fever during the past decade ends here. A few points only have been investigated with thoroughness, and the conclusions to be drawn from them have not been strikingly novel, though they have afforded additional evidence for the accuracy of much previous work. There are many other problems which press upon the attention, notably the real relationship of rheumatic fever with chorea, but my scheme has been to limit the inquiry to a few definite points with regard to which the evidence could be obtained with certainty, and criticism of the *facts* recorded reduced to a minimum.

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NOTE.—This Essay was submitted and approved as a Thesis for the M.B. Degree of Cambridge University.

TUBERCULOUS STRICTURE OF THE ILEO-CÆCAL VALVE, WITH A SUCCESSFUL EXCISION OF THE CÆCUM AND ASCENDING COLON.

By

HERBERT FRENCH, M.A., M.D., F.R.C.P.,

R. P. ROWLANDS, M.S., F.R.C.S., and E. P. POULTON,

M.A., M.B., M.R.C.P.

E. H., aged 30, a torpedo-fitter, was sent up by Dr. W. Kidd, of Blackheath, and was admitted into Guy's Hospital on August 11th, 1910, under the care of Dr. Fawcett, and later of Dr. French. He complained of abdominal pain after meals. The family history was satisfactory.

The patient had suffered from "influenza colds" since he was 20 years old, and these had been followed by a discharge from the nose, which often passed into the nasopharynx. The colds usually came on in the winter time. He had been accustomed to wake up in the morning with a dry mouth. Two years ago he coughed up some blood, but tubercle bacilli were not discovered in the sputum on examination, and it was at this time that the attacks of abdominal pain began. They occurred intermittently, sometimes several weeks elapsing between the attacks. The pains were noticed about four or five hours after a meal,

and the patient complained that they were most severe when the meal had been heavy, and had contained a lot of vegetables, of which he was very fond.

The pains were colicky in nature; they lasted a short time each, and they were repeated. He stated that they started in the right iliac fossa, and spread from there over the abdomen. At the same time he frequently observed the formation of a lump in the right iliac fossa. The pains did not occur during starvation, and the patient used to find that he obtained relief on making himself sick. He had, however, spontaneously vomited on one occasion only. He had been inclined to constipation for the last two years, and he had been obliged to use medicine and enemata on this account.

He usually had a good appetite and enjoyed hearty meals, although he disliked their after-effects. He complained of being rather wasted, and stated that he could not put on flesh in spite of his healthy appetite. On several occasions the patient had been confined to bed with attacks of "appendicitis," a definite swelling in the right iliac fossa and a raised temperature being noted. He was admitted at the end of such an attack.

On admission his weight was 8 st. 6 lbs. He was an intelligent man who was able to give a very clear account of his illness. His pulse was 64; temperature 96·6°F.; and respirations 24. His chest showed signs of phthisis at the right apex, where there was some impairment of note on percussion, especially noticeable at the apex of the right lower lobe, together with whispering pectoriloquy below the right clavicle. No râles were heard.

Skiagram (Fig. I.) showed a well-defined blotchy impairment at the apex of the right lower lobe, especially behind. The diaphragm moved poorly on both sides in front, but better when viewed from behind. Some rigidity was present on the right side of the abdomen, and a lump as big as a walnut could be felt in the right iliac fossa, and there was tenderness at this spot. A big meal containing plenty of vegetables was administered, and subsequently visible peristalsis was observed starting low down near

Tuberculous Stricture of the Ileo-Cæcal Valve, with a Successful Excision of the Cæcum and Ascending Colon.

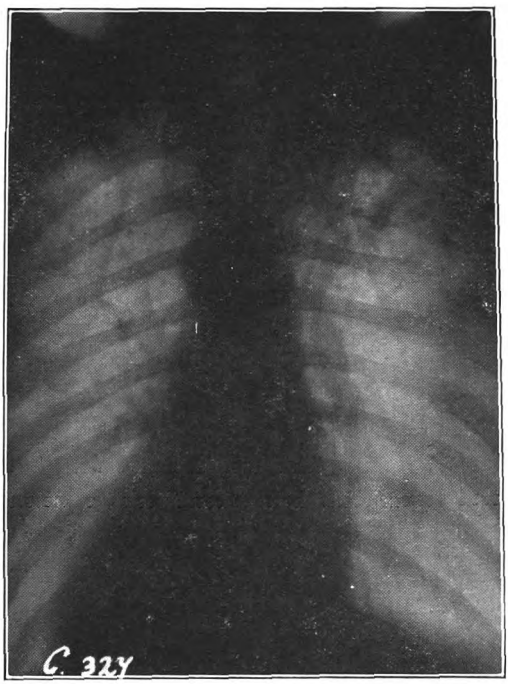

FIG. I.—Skiagram of the chest showing phthisical opacities of both upper lobes. (By Dr. A. C. Jordan).

the middle line and travelling into the right iliac fossa, and disappearing below and to the right of the umbilicus. A bismuth meal was given to the patient one day at 6 a.m., and the diagram shows the presence of the meal at the lower end of the ileum after 9 hours (Fig. II.). The bismuth was still present

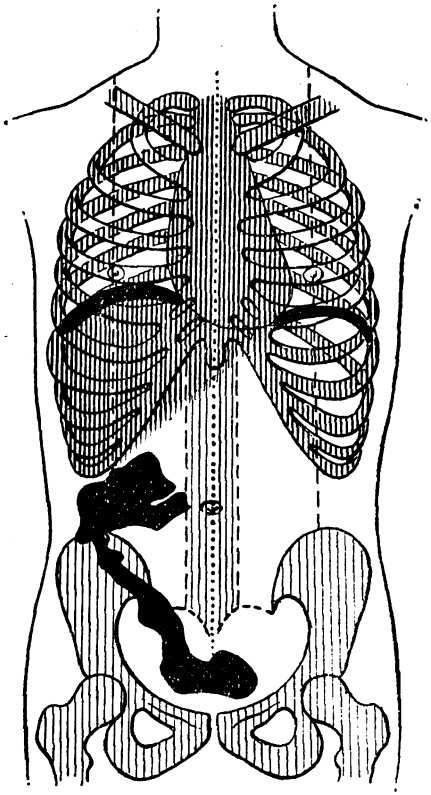

FIG. II.—Skiagram of bismuth in lower part of ileum and cæcum nine hours after its administration by the mouth. (By Dr. A. C. Jordan.)

in the ileum in large amount after 10 hours had elapsed. After 32 hours most of the bismuth was in the transverse colon, but some had already reached the rectum (Fig. III.).

On another occasion the bowel was cleared out and air was injected into the colon per anum. The X-rays showed that most of the air remained in the rectum (where the tube is seen doubled on itself). The air, however, penetrated as far as the hepatic flexure, and the whole of the large intestine can be seen transparent to the rays up to this point. The opacity at the right iliac fossa, however, shows that the air had not entered the cæcum.

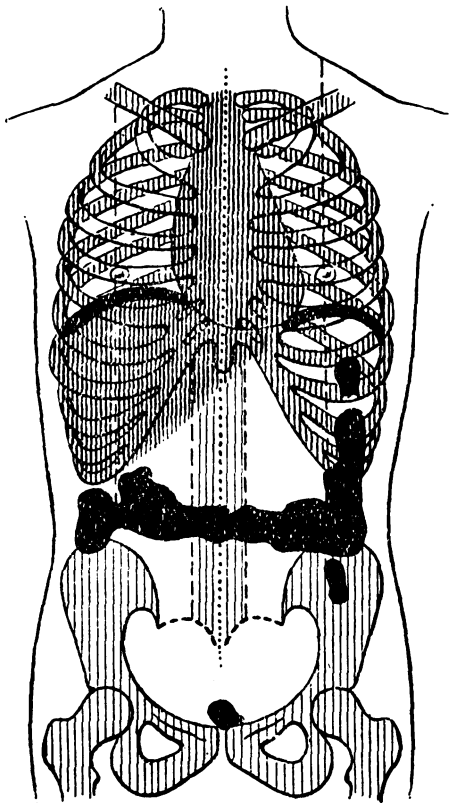

FIG. III.—Skiagram of bismuth in colon 32 hours after its administration by the mouth. (By Dr. A. C. Jordan).

On rectal examination something abnormal could be felt on the right side of the recto-vesical pouch. This was thought to be a diseased appendix.

Tuberculous Stricture of the Ileo-Cæcal Valve, with a Successful Excision of the Cæcum and Ascending Colon.

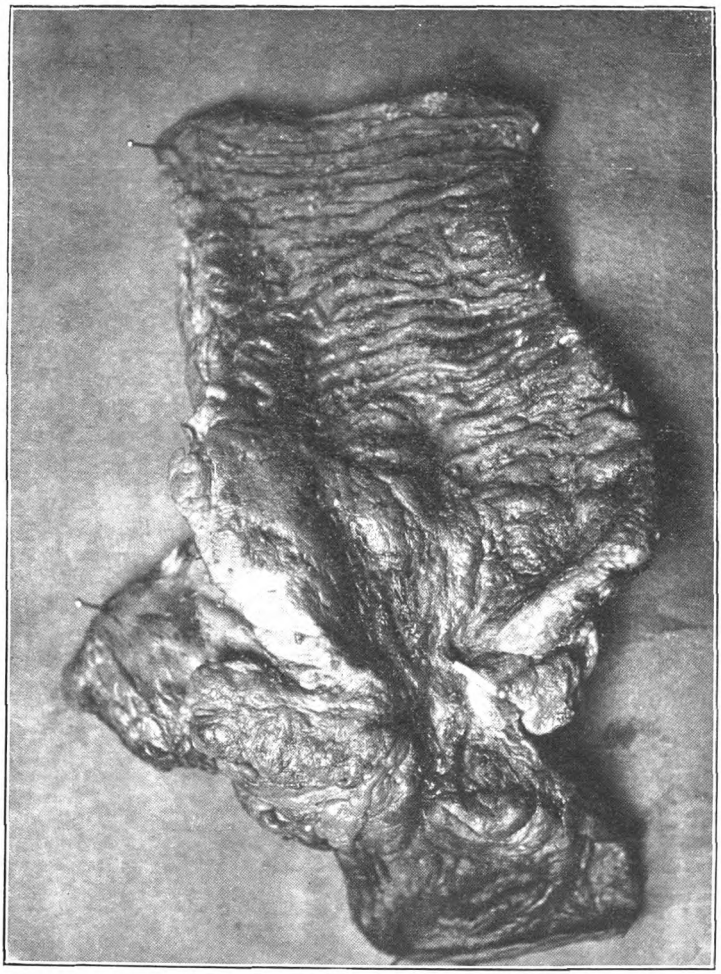

FIG. IV.—Photograph of the tuberculous ileum, cæcum and ileo-cæcal valve, removed by operation.

Operation.—At a consultation in the ward it was decided to operate. When the patient was under the anæsthetic on the 19th a swelling and peristalsis appeared in the right iliac region far inwards, and a distinct movable swelling was felt. The abdomen was opened by displacing inwards the lower part of the right rectus, and the cæcum was felt to be enlarged, and the lower end of the ileum was greatly dilated and hypertrophied. The appendix was greatly distended and yellow and intimately bound to the cæcum. The mass was brought out of the wound. There was a firm congested thickening at the lower end of the ileum as it entered into the cæcum. The peritoneal coat of the lower end of the ileum and cæcum was inflamed, and there were a good many minute tubercles to be seen upon it, but there were none upon other parts of the intestine. Many glands in the meso-colon were considerably enlarged. It was decided to remove the swelling in preference to doing an anastomosis between the ileum and the colon. Six inches of the ileum, the cæcum, and the ascending colon, together with the appendix and the enlarged glands in the meso-colon were removed *en masse*. The ends of the ileum and ascending colon were tied and inverted. Then a lateral anastomosis was made between the ileum three inches above the blinded extremity, and the first part of the transverse colon. The abdomen was completely closed in layers. The operation lasted one hour and a half. The patient was not collapsed at the end of it, and he made an uninterrupted recovery. The bowels were opened naturally four days after the operation. On discharge from the hospital on September 13th his weight was 8 st. 8 lbs. The specimen removed shows:—

(i.) *Macroscopically.*—Ulceration and infiltration of the cæcum, the ileo-cæcal valve, and the lower end of the ileum, with thickening of the walls, and stenosis at or near the valve. The cæcum was greatly contracted in size. The ileum was greatly dilated and hypertrophied. Tubercles were evident on the peritoneum of the ileum. Contracting ulceration was observed for $2\frac{1}{2}$ inches all round the bowel at the valve, and extending into the cæcum and ileum. The strictured opening of the appendix was in the

floor of the ulcer at the point where the stenosis was greatest. The appendix was thickened, infiltrated with tuberculous disease, coiled, and very adherent to the cæcum. Its lumen was almost occluded in places.

(ii.) *Microscopically.*—Sections showed the presence of typical tuberculous giant cell systems in the wall of the bowel at the stricture and also in one of the enlarged lymphatic glands.

The patient came up for re-examination on May 19th, 1911. He said he had felt much improved in health since the operation, and did not now feel any discomfort after food. His weight at this time was 9 st. $2\frac{1}{2}$ lbs. He had thus gained $10\frac{1}{2}$ lbs. since the operation. The condition of his lungs as shown by a skiagram and by physical signs was found to be unchanged.

We wish to express our thanks to Dr. A. C. Jordan, Medical Radiographer to the Hospital, for his co-operation in the various X-ray examinations recorded in this paper.

Pigmentation of the Buccal Mucous Membranes in Pernicious Anæmia.

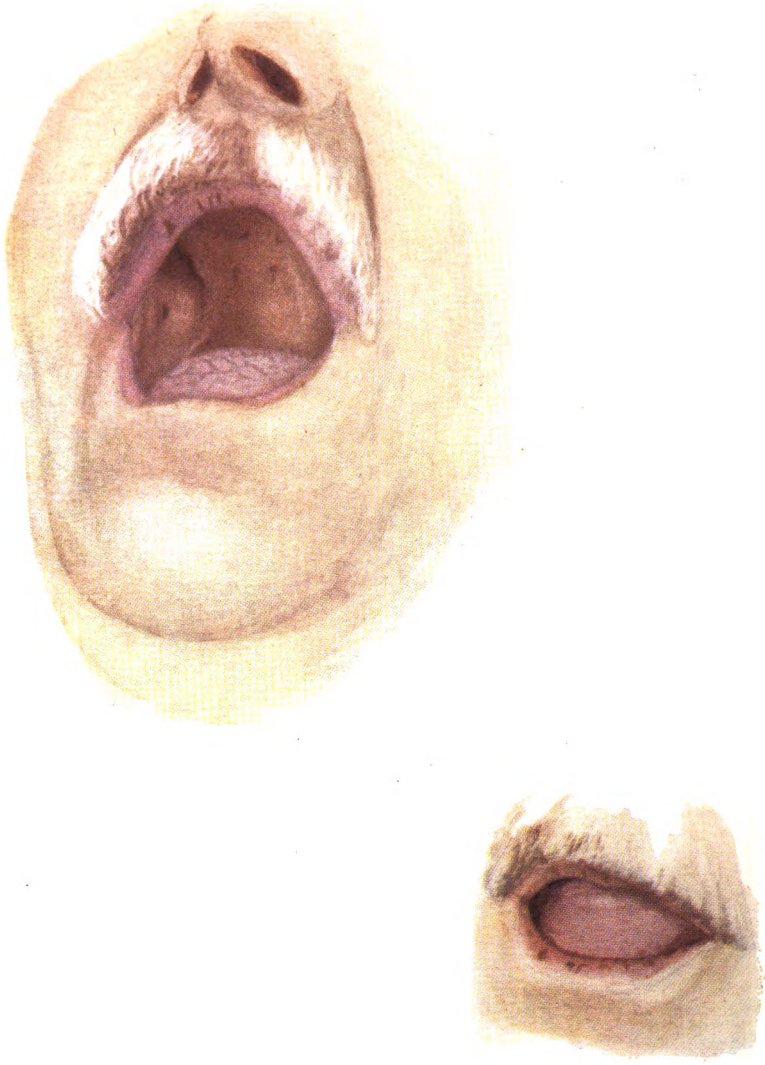

FIG. I.—Pigmentation in the mouth in Pernicious Anæmia.

PIGMENTATION OF THE BUCCAL MUCOUS MEMBRANES IN PERNICIOUS ANÆMIA.

By

HERBERT FRENCH, M.D.

It is interesting from an historical point of view that Addison discovered the disease known as Addison's disease when he was investigating cases of severe anæmia of the type now generally spoken of as pernicious anæmia, but sometimes referred to as Addison's anæmia in contra-distinction to Addison's disease. Until recently it has been held that amongst other points of distinction between these two diseases the presence of buccal pigmentation points to Addison's disease. Dr. Hale White was the first to record a case of pernicious anæmia in which there was extensive buccal pigmentation precisely similar to that usually seen in Addison's disease. In his case, however, arsenic had been administered before the buccal pigmentation was noticed, and it could not be said definitely that this pigmentation was solely due to the pernicious anæmia and not to the arsenical treatment. There have been one or two similar cases recorded since.

The illustration accompanying these notes, Fig. I., represents, I believe, the first recorded instance in which buccal pigmentation in pernicious anæmia was clearly established before any arsenic had been used in the treatment of the disease.

The patient was a man, aged 62, under the care of Dr. T. Warner Lacey, of Woolwich. He had been perfectly active and

well until three years before his death, when he was laid up in bed for over three weeks with severe diarrhœa, associated with red blotches on his skin, the condition being spoken of by himself as "dysentery with blood poisoning from eating oysters." It is difficult to say whether this had anything to do with his final illness, for he seemed to recover completely and to remain in perfect health until 16 months before he died. The terminal illness began with progressive loss of strength all over, but particularly in his legs; there was little or no wasting, but the patient became so asthenic that he was unable to walk any distance, and at the same time both he himself and his friends had noticed that "his colour had been going from his face." He also had subjective sensations in his fingers, which he described as being as though he "had lost the use of their tips." He was a stoutish man who, when seen four months before he died, was able to dress himself slowly and sit up in an easy chair, but he was so readily fatigued that he could not walk about in his garden as he had been wont to do. He was quite clear intellectually, but he was unable to exert himself physically. There were few days upon which he was not sick, sometimes he had diarrhœa, sometimes constipation, but, upon the whole, the constipation was more marked than the diarrhœa. The only objective signs were, first, his typical lemon-yellow complexion, and, secondly, the marked pigmentation of the red part of his lips, the inside of his cheeks, his gums, and hard and soft palate, all of which exhibited scattered spots of pigment, of which the illustration gives some idea. He exhibited no very obvious pigmentation of the trunk or limbs, and although the changes in the buccal mucosa at first raised a suspicion of Addison's disease, the lemon-yellow colour of the skin, not only of the face, but of the whole body, was highly suggestive of pernicious anæmia, and the condition of the blood was characteristic of this malady. At this time there were 1,560,000 red corpuscles per c.mm., or 31 per cent. of normal; the white corpuscles numbered 4,680 per c.mm.; the hæmoglobin measured 40 per cent. by Haldane's method; and the colour index was 1·333.

The differential leucocyte count presented a slight relative increase in the small lymphocytes. Poikilocytosis and megalocytosis were both well marked. The patient weighed 13 stone.

Arsenic was administered, together with drachm doses of hæmoglobin three times a day. Vomiting ceased and the patient recovered sufficient strength to be able to walk about in his garden, but three months later he relapsed, and again felt that he had no life in him, though he was not wasted. He became "sick and bilious" as before, and his legs and feet "felt like cold meat." The red corpuscles now measured 1,110,000 per c.mm., or 22 per cent.; the hæmoglobin, by Haldane's method, 39 per cent.; the colour index was 1·7; and the white corpuscles numbered 3,750 per c.mm.

The patient did not rally a second time, but sank steadily and died a few weeks later, sixteen months from the beginning of his asthenic symptoms.

It may be mentioned in this connection that pigmentation of the buccal mucous membranes is not limited to cases of Addison's disease and pernicious anæmia, for it is found in a certain proportion of patients suffering from ordinary phthisis without any gross disease of the suprarenal capsules being found post-mortem; and it is also present in some patients who have inherited blood from one or other of the dark races.

A CASE OF ACUTE INFLAMMATION OF THE GENICULATE GANGLION.

By

F. W. MORTON PALMER, M.A., M.D., B.C.

The following case seems worthy of report, both because of the rarity of the condition and also because of a physical sign with which that condition is very rarely associated.

In October, 1907, W. J., a tailor, aged 51 years, had a week's bad neuralgia, which he ascribed to having "caught cold standing under an archway." On October 21st, when I saw him, he had well-marked facial paralysis, with herpes of the ear and soft palate—all on the right side. His temperature was 100·2°; his pulse was 110. He was completely deaf on that side, and had lost all sense of taste with the anterior half of the right side of his tongue. Facial paralysis was complete and of the usual infranuclear type. He could neither close his right eye nor wrinkle the right half of his forehead. He pursed his lips towards the left side, and could not prevent his food collecting on the right side of his mouth. There was no paresis of the palate, and the uvula was not deflected.

Herpes Zoster affected the ear in a well-defined manner: the vesicles, which had the usual erythematous base, were distributed as in the accompanying Diagram I. They were almost entirely confined to the concha, though there were two on the adjoining part of the antihelix, one large and two small vesicles in the fossa of the antihelix, and two on the posterior wall of the meatus. In the mouth there were twenty-three vesicles,

which were distributed principally over the right half of the soft palate as in Diagram II. There were one or two on the anterior pillar of the fauces, and a few spread over the posterior

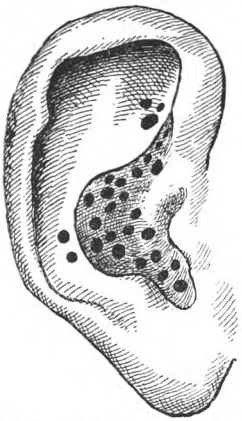

FIG. I.—Distribution of Herpetic Vesicle on the Ear.

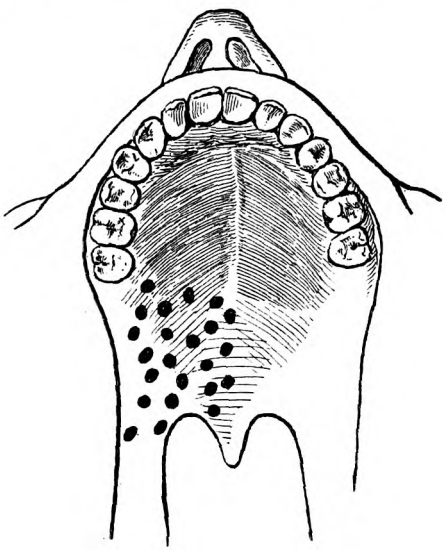

FIG. II.—Distribution of Herpetic Vesicles on Palate.

edge of the hard palate as far forward as the last molar tooth. They did not cross the middle line, and there were none on uvula or tonsil. There was no tenderness of ear or palate.

He was completely deaf on the right side, being unable to hear a watch, even when in contact with the mastoid process, though he said that previously his hearing on that side had been very good. There was no otorrhœa, and he said there never had been any discharge. Subsequent examination revealed a normal membrane with complete absence of bone conduction of sound.

Loss of taste was very definite over the anterior half of the tongue on the right side. He could not tell the difference between solutions of sugar, salt, or strychnine if they were applied on cotton wool pledgets to the protruded tongue anywhere over that area; the rest of his tongue was very sensitive to these different flavours.

The pain soon cleared up, and there has been no subsequent neuralgia, such as so often follows zona, especially when it attacks the head. The vesicles on the ear dried up and left no scars, those on the palate were converted into small ulcers, which quickly healed; but the deafness and palsy still persist, even after four years. He is still (August, 1911) as deaf as he was at the onset, and has no bone conduction for the tuning fork. The paralysis is slightly better, but is still most marked, and this in spite of massage and prolonged treatment. He cannot completely close the right eye, and consequently suffers from epiphora. There are no wrinkles round eye or nose—a contrast to the plentiful supply he has on the left side—and, when he tries to whistle, the lip sags down on the paralysed side. Sense of taste is still absent over the same area of his tongue.

Herpes Zoster of the external auricle is comparatively rare and not infrequently combined with facial paralysis (i.), but I have been unable to find any record of a case in which these symptoms were associated with palatal herpes. Among 100 cases of zona recorded by Dr. Pye-Smith (ii.) there were only four in which the auricle was involved, and in none of these was there any facial paralysis. The cause of these cases has been obscure till recent years; it was supposed that the neuritis, first affecting the branches of the sensory fifth, had spread to those of the motor seventh nerve (iii.). But the researches of Head and

Campbell have shown us that herpes is due to an inflammation of the root ganglion, and that any neuritis which may be present in the nerve trunks is slight and secondary.

A glance at Diagram I. will show that in this case the herpetic vesicles were confined to a small part of the distribution of the auriculo-temporal nerve, which supplies the upper two-thirds of the pinna, the concha, and the external meatus. Ramsay Hunt has shown (iv.) that herpes with this distribution is the external sign of an inflammation of the geniculate ganglion, and is often associated with paralysis of the seventh nerve. The auriculo-temporal nerve courses up from the ear, divides to allow the passage of the middle meningeal artery, and then joins the inferior maxillary branch of the gasserian ganglion. Cushing, however, has shown that division of the branches of that ganglion does not produce anæsthesia of the auricle, and so the sensory fibres from the ear cannot run up to the gasserian ganglion. Extirpation of the second and third cervical ganglia produced anæsthesia over the area of distribution of the great auricular nerve on the external surface of the pinna, the lobule and the lower part of the helix, but did not affect sensation on the concha or meatus. So the axons in the afferent fibres affected in this case must take some other course to reach the ganglion in which their cells lie, and we can probably find this course, as Ramsay Hunt points out, by examining the connections of the auriculo-temporal before it joins the inferior maxillary nerve. These connections are two: it communicates with the seventh nerve behind the neck of the condyle of the jaw, and also with the otic ganglion by filaments given off at the commencement of the nerve, which ganglion in turn communicates with the facial nerve through the small superficial petrosal.

At the bottom of the internal auditory meatus the auditory nerve and the geniculate ganglion are in close proximity, so that any lesion involving the latter would be almost certain to involve the former, as we know often occurs in fracture of the petrous bone, when paralysis of the seventh is always associated with paralysis of the eighth nerve.

In the case above recorded we have deafness caused by a lesion of the auditory nerve, as shown by the absence of bone conduction for sound, facial paralysis, and paralysis of the nerves of taste of the anterior half of the tongue, which pass along the chorda tympani to the geniculate ganglion. Their nerve cells are situated in the gasserian ganglion, but the neurons pass through the geniculate, and so would be involved in any inflammation of that ganglion, which is certainly the lesion present in this case, as it alone can cause all the signs discussed hitherto.

This case, however, presents another physical sign, which is almost inexplicable, unless we assume the presence of two causative lesions. Herpes Zoster affecting the soft palate is extremely rare. Head, in his article in Clifford Allbutt, does not mention it, though he says the hard palate may be the seat of herpetic eruptions, which are, however, of the febrile type. Semon and Watson Williams, however, in another volume of the same System of Medicine (v.) give a very good coloured plate of a case, and say, "the eruption follows the course of a sensory nerve, and is probably a local Herpes Zoster." In my case, the herpes was certainly a true Zoster, and not of the febrile type, for it was strictly unilateral, and not associated with any other herpetic lesion on the lips or elsewhere in the mouth.

The nerve supply of the soft palate may be divided into three groups:—

1. Motor nerves supplying the palatal muscles, of which the course and ultimate destination are still subjects for discussion by anatomists. They do not concern us in this case.

2. Those fibres carrying ordinary tactile sensation, which undoubtedly pass up by the small and accessory posterior palatine nerves to Meckel's ganglion. This ganglion has as its main sensory root the spheno-palatine nerves from the gasserian ganglion, but, in addition, it is given some sensory fibres from the great superficial petrosal nerve which comes from the geniculate ganglion. Cushing has shown (vi.) that division of the gasserian ganglion renders the soft palate completely anæsthetic,

but does not affect the faucial pillars or the tonsil, neither does it affect the special sensation of the palate. Accordingly, the nerve cells whose fibres carry tactile sensation from the soft palate must lie in the gasserian ganglion for the most part.

3. Those fibres carrying sensations of taste:—
   a. By the pharyngeal plexus to the glossopharyngeal nerve, and so direct to the brain.
   b. Possibly a few fibres to the geniculate ganglion, via the great superficial petrosal (vii.).

Thus, to explain the presence of the herpes on the soft palate in this case we must assume either that inflammation existed in the gasserian ganglion as well as in the geniculate, or else that in this man many of the nerve cells were situated in the latter instead of the former ganglion, and that the geniculate was the only ganglion affected. With regard to the former explanation we find that two posterior root ganglia are occasionally involved in herpes (viii.), especially if adjacent, and embryologically the gasserian and geniculate ganglions may be regarded as adjacent, for the sixth nerve is purely motor and has no ganglion on its trunk. If the latter explanation be adopted, it may point to the possibility of the herpetic vesicles following the distribution of the nerves of taste and not of ordinary sensation—a possibility for which I can find no other evidence.

I think we must conclude that this man suffered from severe inflammatory changes in his right geniculate ganglion, associated with slight inflammation in his gasserian ganglion on the same side.

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THE OPERATIVE TREATMENT OF EXOPHTHALMIC GOITRE.

By

L. BROMLEY, M.B., B.C.

In a paper which is to deal with a certain line of treatment in a particular disease, it is necessary that an exact definition of the disease should be given. For this purpose a definite group of symptoms and signs must be found whereby the disease may be recognised. These symptoms and signs may then be said to be characteristic of the disorder. Further, in discussions as to treatment, the pathology must be fully understood, and as it is only by numerous post-mortem examinations that a decision can be made as to the situation of the lesion which is responsible for the disease, the morbid anatomy and histology must be studied. Discussion concerning surgical treatment without the full knowledge of these facts would be useless.

Having come to some decision as to the nature and position of the lesion in the body, two lines of treatment are open: the more conservative, or medical; and the more radical, or surgical. Before there is justification for adopting the second line of treatment, results which have been obtained from the medical treatment must be carefully considered; a definite idea must be formed of the prospects of a patient who is suffering from the disease, his chance of life, his mode of life, and, from a practical point of view, the circumstances of the patient.

From these premises, consideration must be given to the possibilities of surgical treatment, the various operative methods which have been adopted at different times, and the results obtained from these methods. Finally, the results of surgical treatment are contrasted with those of medical treatment, and some conclusions can be drawn as to the advisability of operative interference. This paper is, therefore, divided into six headings, as follows:—

1. Definition of the disease, with the characteristic symptoms and signs.
2. Pathology, morbid anatomy, and histology of the disease.
3. Results obtained from medical treatment.
4. Methods of surgical treatment, and the results.
5. Comparison between the results of medical and surgical treatment.
6. Conclusions.

SECTION I.

Definition of the Disease, with the Characteristic Symptoms and Signs.

Exophthalmic goitre is the name given to a constitutional disease which is associated with a certain group of symptoms. The most essential of these symptoms are:—

1. Thyroid enlargement.
2. Rapid action of the heart.
3. Protrusion of the eye balls.
4. Palpitation.
5. Tremors of the extremities.

Numerous other symptoms and signs are associated, for example:—

Irritable and excitable nervous system.

Loss of flesh.

Increased action of the skin.
Flushing.
Anæmia.
Derangement of the catamenial function.
Diarrhœa.

There is a close connection between some of the chief symptoms and the more immediate effects of terror. It has been suggested that the disease is the result of derangement of the emotional nervous system followed by a perverted condition of the thyroid gland which intensifies the symptoms.

Thyroid enlargement is usually gradual, and it may not be the first symptom which attracts the patient's attention: sometimes it attains a large size in a short space of time. As in a normal thyroid, the enlargement is usually more in the right side, very rarely the left lobe is the larger, and still more rarely is the enlargement unilateral. The swelling is soft and uniform; sometimes it is irregular, firm, and hard. This usually occurs in cases where an ordinary goitre has existed before the onset of symptoms of Graves' disease. The swelling may pulsate, and there is often a systolic thrill. The swelling may temporarily increase after excitement, or over-fatigue, or during the catamenial period. In some cases it is first noticed at puberty. There is no relation between the size of the goitre and the intensity of the symptoms.

Exophthalmos.—This varies in amount; it may sometimes be unilateral. There are certain signs in connection with exophthalmos peculiar, as a rule, to Graves' disease. These are:—

Von Gräfe's sign, in which there is lagging of the upper lid when the patient looks down.

Stellwag's sign.—There is diminished frequency and incompleteness of winking.

Mobius' sign. — Insufficient power of convergence for near objects.

The vessels of the optic disc are sometimes dilated and tortuous.

Disturbances of Circulation.—There is increased rapidity of the heart's action, for example:—

Mild cases	...	...	90—110 beats per minute.
Ordinary cases	...	...	110—130 „ „
Severe cases	...	...	130—160 „ „

Cases in which bradycardia has occurred have been reported, but they must be extremely rare. The rate of the heart is liable to variations according to exciting causes.

Other features in connection with the circulatory disturbances are:—Palpitations, and in unfavourable cases there is considerable irregularity of the heart. There is often accompanying cardiac hypertrophy or dilatation; there are usually functional cardiac murmurs. The blood pressure is insignificant; it is liable to variations, and there is nothing constant which is peculiar to Graves' disease.

Tremor affects the whole extremity, that is, it is a communicated tremor.

Emaciation is rapid in unfavourable cases, and it is related to an increased metabolism; there is an enormously increased consumption of oxygen and output of carbon dioxide.

Nervous System.—The patient suffering from Graves' disease is a person of many moods, and not infrequently this psychical element of the disorder is the first to attract the attention of relatives. Unexplained melancholy and still more unaccountable excitement, restlessness, or irritability are phases of mental unrest which profoundly alter the character of the individual, inevitably producing errors of judgment and disorders of conduct. Still later there may be delusions, hallucinations, ideas of persecution, and occasionally there is acute mania—this latter type of case is usually fatal. Graves' disease is thus associated with a fairly constant group of symptoms; one may be considerably more prominent than another, and some may be entirely absent. However, those which may be called the cardinal symptoms are:—

Enlargement of thyroid.
Rapid heart.
Tremor.
Exophthalmos

SECTION II.

Pathology, Morbid Anatomy, and Histology of Graves' Disease.

The pathology of exophthalmic goitre has been the subject of much discussion for many years. Three main theories have been put forward:—

1. A disease of the central nervous system.
2. A disease of the cervical sympathetic.
3. A disease of the thyroid gland.

The view that the disease has its origin in the central nervous system is supported by the fact that the disease is apt to begin after a profound emotion.

Dr. Raymond Crawfurd, in King's College Hospital Reports, vol. iii., 1897, writes an article—"Graves' Disease: an Emotional Disorder."

The disease is almost confined to the years of sexual activity. It has been observed that shock and emotion have been soon after followed by some enlargement of the thyroid. Furthermore, the symptoms, as previously noticed, bear a striking resemblance to the effects of terror.

The view that the symptoms are produced by a lesion of the cervical sympathetic has its origin in the fact that degenerative changes have been described, by more than one observer, in the cervical sympathetic trunk, but these are possibly due to pressure in cases of extreme enlargement of the gland. Mannheim—Der Morbus Gravesii. (Berlin, 1894.) Operations have accordingly been performed on this nerve trunk and ganglia, as we shall see later, with some good results; but there seems no other evidence that this view is correct.

Lastly, there is the theory that the disease lies within the thyroid gland. This theory was, in its earliest days, supported by

Mobius, Greenfield, and Murray. How far this thyroid disease is dependent on some unknown disease of the higher centres is unknown. The view held is that there is probably an alteration in the internal secretion of the gland, both in quantity and quality, the abnormal secretion acting on the heart, nervous system, and nutrition of the body. There are several facts in favour of this view ; these are based on physiological experiments

Myxœdema is a disease of the thyroid gland, and the symptoms are due to a deficiency in the internal secretion of the gland. When one compares the symptoms in myxœdema with those in Graves' disease, one is struck with the remarkable contrast between the two. The main symptoms may be tabulated:—

Myxœdema.	*Exophthalmic Goitre.*
Weight increases.	Weight diminishes.
Patients intolerant of cold.	Patients intolerant of heat.
Skin is dry, swollen.	Skin is moist, shrunken.
Subnormal temperature.	Temperature above normal.
Slow, placid, deliberate.	Quick, irritable, impulsive.
Heart's action quiet and slow.	Heart rapid.

Therapeutics of the disease demonstrate the probability that the sufferer from Graves' disease has an intoxication of thyroid secretion; the administration of thyroid extract to a patient suffering from Graves' disease will exaggerate the symptoms enormously. In animals, the administration of thyroid preparations produces:—

1. Increase in the rate of the heart.
2. Loss of body weight.
3. Diaphoresis and cutaneous vasodilatation.

All these are symptoms of Graves' disease. No exophthalmos has ever been produced in man by the administration of thyroid extract, but it has been brought about by Mr. Edmunds in experiments on dogs and monkeys.

Murray says that thyroid extract produces an artificial Graves' disease. However, it is necessary to differentiate between a

physiological and a pathological hyperthyreosis; the former may occur at such times as puberty in the healthy, and increased secretion is necessary at that time; pathological hyperthyreosis, on the other hand, is a perverted action of thyroid secretion, practically becoming a toxæmia. There is further proof of the thyreogenous origin of Graves' disease in that partial excision of the gland cures the disease. Kocher, B.M.A., July, 1910.

Further experiments go to show that complete excision of the thyroid gives rise to myxœdema. Therefore, one may justly conclude that the symptoms are produced by a hyperactivity of the gland. The changes in the body which are found at the post-mortem examination of a patient who has died from Graves' disease confirm the view of thyroid disease. There is most usually considerable emaciation. The exophthalmos is sometimes accompanied by an increased amount of fat in the orbits; this condition remains unexplained. In the neck there is increased connective tissue, and the cervical and bronchial glands are enlarged. There is sometimes swelling of the lymphatic structures of the intestines. Swelling of lymph glands in the neighbourhood of the thyroid is constant in the severe forms of Graves' disease.—Kocher. The spleen is occasionally enlarged. The heart may be normal, it may be dilated, or hypertrophied; valvular disease from independent old endocarditis is sometimes found. The lungs are free frem disease, except where complications have occurred; pneumonia is the most common of these. In the nervous system no naked-eye changes can be detected.

The Thyroid Gland.—There is an uniform enlargement. Formerly, vascularity of the gland was said to be a distinguishing feature, but this is denied; any increase of vascularity is superficial. Professor Greenfield says that in his cases there was no increase in vascularity, but rather a diminution in the gland itself. Mr. Edmunds states that remarkable hypertrophy of the blood vessels is sometimes found. Mr. Paul says vascularity is decidedly greater than in other forms of goitre. There is no doubt that the veins over the capsule are numerous and dilated. The nutrient arteries are large, tortuous, and dilated.

Microscopic appearances of the thyroid gland in Graves' disease are characteristic, and they show the gland in state of increased secretory activity. There is increase of the secreting structure, the vesicles are branched, or stallate; the lining membrane is involuted, thus forming papillary projections. Further, the secreting structure is altered, the epithelium, which is normally cubical, has become columnar; colloid material normally present in the vesicles has disappeared and is replaced by a mucoid substance which stains badly. There is marked resemblance between the appearance of the goitre and that of a salivary gland. The goitre bears the same relation to the normal thyroid that the mammary gland during lactation bears to the resting gland.—Prof. Greenfield. Thus, confimation is given to the view that the thyroid gland takes on an increased functional activity, the reason of which is obscure.

There is a frequent, if not constant, persistence and enlargement of the thymus gland; it consists of two flat, triangular shaped fleshy lobes behind the manubrium sterni lying anteriorly to the upper part of the pericardial sac and the origin of the great vessels. The microscopical structure of the thymus is unaltered.

It has been stated that every case in which there is a thymus persisting into adult life is one of potential, or latent Graves' disease. Changes in the sympathetic nerves have been described, but they are not peculiar to Graves' disease. Recent work in the pathology of the disease has brought to light several interesting and diagnostic features, chief amongst which are the blood changes. This work was mentioned by Kocher in his paper before the British Medical Association in July, 1910, on the subject of the surgical treatment of Graves' disease. There is a marked diminution of polynuclear cells in the blood, the normal 5,000 are reduced to 1,260 per cubic millimetre; and there is a relative increase of the small mononuclear (lymphocytes), namely, 20 per cent., the normal up to 50 per cent.

Dr. Turin, Clinical Assistant to Professor Kocher, produced lymphomatosis by the injection of thyroidine; and also, in in-

dividuals who had no atrophy, or aphasia of the thyroid, he produced lymphomatosis by the administration of potassium iodide. These phenomena are in marked contrast to the leucocytosis which obtains in myxœdema. The coagulation index of the blood is altered. This was worked out by Miss Lidsky under the direction of Dr. Kottman. There is slower coagulation in Graves' disease. In animals, slower coagulation was produced experimentally by thyroidine. Kocher states that after operation complete cure shows the blood normal, and this is a most valuable test for the efficacy of operative interference.

There is a certain amount of hyperthyreosis associated with ordinary goitre, and a line of distinction cannot always be drawn between simple goitre and the more serious affection so called exophthalmic goitre. It is well known that symptoms of the latter may follow the appearance of simple goitre after an interval of many years. Louis B. Wilson, of Rochester, in his paper read before the Pittsburg Academy of Medicine on February 9th, 1909, makes the remark that exophthalmic goitre and simple goitre are closely related, and they may change from one to the other. At the discussion of the symposium upon Surgery of the Thyroid Gland, Dr. Lichty says that he has occasionally noticed the change of simple goitre into exophthalmic goitre particularly liable to occur at the time of the menopause, or after severe strain. Two cases of this kind recovered. Surgery, Gynæc. and Obstetrics, vol. viii., 1909.

All the facts discovered so far as to the pathology of exophthalmic goitre tend to show that it is a disease of the thyroid gland, which is brought to a state of extreme activity more than physiological, and results in a thyroid intoxication or thyroidism. The general effect of the increased internal secretion is that of a toxin circulating in the blood, and the toxin exerts its specific action on the tissues of the body; thus, there is weakening and destruction of heart-muscle, and effect on the kidneys, and general asthenia. As Kocher expresses it, there is a "diarrhœa" of the thyroid secretion.

SECTION III.

The Results obtained from Medical Treatment.

The methods of medical treatment which have been employed may be summarised as follows:—

1. Rest.
2. Hypienic, altitude, etc.
3. Drugs.
4. Serum.

No attempt will be made to discuss the merits of the individual methods; they will be classed together as medical treatment, and the prognosis will be considered. Dr. Hale White published a paper in the Quarterly Journal of Medicine, October, 1910, on "The Outlook of Sufferers from Exophthalmic Goitre," and I am much indebted to Dr. Hale White for his kindness in allowing me to quote extensively from the figures given in his paper.

Dr. Hale White collected a number of cases which had been inpatients of Guy's Hospital between 1888 and 1907 (inclusive), and he traced them up to 1910, and a most valuable series of figures was obtained. Dr. Hale White further gives details of a number of cases which occurred in private practice between 1894 and 1909 (inclusive). This section deals with the cases that were medically treated, and those which were operated upon will be left for later consideration. Altogether, 161 patients were treated medically in Guy's Hospital (1888—1907 inclusive); of these, 18 died in hospital, 49 can be traced, and 94 cannot be traced (1910); of the 49 cases that have been traced, 8 are now dead. The rate of mortality of a disease is the comparison between the number of actual deaths and the number of deaths that would have occurred among the same body of lives if the mortality had followed that of a standard mortality table. Thus, actual deaths in 49 cases, 8; according to standard

mortality, 5. However, the standard mortality varies with the age, and it was found that of the 8 deaths, there were none after the age of 45 years, and only one occurred under 30 years, while the age at death in two cases is unknown.

At this period of life the standard mortality is given at 3, and thus the comparison is, 5 actual deaths; 3 expected deaths. On comparison of these figures with those obtained in the private practice of Dr. Hale White between 1894 and 1909, inclusive, we find the mortality rate somewhat less. Fifty-three cases were treated, and 7 are now dead (1910). Thus, actual number of deaths in 53 cases, 7; according to standard mortality table, 3; of these 53 cases, there was 1 death over 45 years, and 2 deaths under 30 years, and age of 1 unknown; therefore, actual deaths, 3; expected deaths, 2.

These figures show that at any rate the mortality in Graves' disease is heavier than is expected according to a well-known healthy standard table. Adding the two classes of cases together :—

Hospital cases ...	...	49 ;	deaths	...	8
Private cases ...	...	53 ;	„	...	7
		102			15

Expected deaths, 8.

Most of the deaths occurred at an age when the expected deaths are few, and twice that number is not a great number. These patients were mostly very ill; the hospital patients were sufficiently ill to be admitted to the ward, while the private cases had sought a second opinion. To these statistics must be added 18 deaths which occurred in the hospital, thus:—

Hospital cases ...	...	49 ;	deaths	...	8
„ „ ...	...	18 ;	„	...	18
„ „ ...	...	67 ;	„	...	26

But, at the same time, 94 cases were discharged from the hospital, and these have not been traced. If we assume that the mortality among the 94 was at the same rate as among

the 49 which have been traced, in which case 15 would now be dead; therefore:—

Cases	...	... 67 ;	deaths	... 26
,,	...	... 94 ;	,,	... 15
,,	...	... 161 ;	,,	... 41

According to this there is greater mortality amongst the poorer class.

Further history of hospital cases discharged. As regards the progress that has been made by the 49 cases that were discharged from the hospital all have been traced. Subtracting 8 deaths, and one other case that is known to be alive, but the condition is not stated, there are 40 cases, details of which are as follows:—

Dr. Hale White arranged them into three groups:—

1. Those that have done well	26
2. Those that are moderately well, or better ...	12
3. Those that are not well	2
	40

Prognosis appears rather better on consideration of the private cases. These number 55 (2 have been added to the previous list). In the 55 cases there were 7 deaths, and little is known of one case, so that 47 cases are traced, as before:—

1. Those that have done well	35
2. Those that are moderately well, or better ...	9
3. Those that are not well	3
	47

Dr. Hale White mentions that of the second class most of the patients had some disease besides, or did not rest; and of the third group, one refused treatment, one refused to continue treatment and relapsed, and one had no special treatment. Tabulating the results:—

		Done well.	Better.	Not better.
Hospital patients ...	40	26	12	2
Private patients ...	47	35	9	3
	87	61	21	5

It is noticed that private cases have done better than hospital patients, to which must be added the fact that the mortality rate of the hospital patient is the higher. In conclusion, Dr. Hale White says that judging from these cases exophthalmic goitre appears likely to get well even if no operation is performed, a conclusion borne out by clinical experience, for we do not often see elderly women suffering from it, and the mortality from it is not severe enough to account for this.

The prognosis in Graves' disease under medical treatment is by no means wholly bad; speedy death is the exception rather than the rule. Dr. Hector Mackenzie gives the following figures in conjunction with Ord, and also figures of the results of the cases under Dr. Williamson:—

Result of 57 cases.	Ord and Mackenzie.	Williamson.	Total.
Fatal termination	8	6	14
Recovery complete ...	5	5	10
Recovery almost complete...	9	2	11
Improvement considerable	9	4	13
Improvement slight ...	1	3	4
In statu quo	1	3	4
Alive, but condition unknown	0	1	1
	33	24	57

Buschan found that in 900 cases, 105 were fatal; in 25 per cent. of these death was due to the disease.

Taking part in the discussion at the British Medical Association Meeting in July, 1910, Dr. Mackenzie made the statement that among hospital patients 36 per cent. recover completely, while not more than 25 per cent. of cases terminate fatally.

In private cases the results are better. There is always the possibility of a relapse occurring in exophthalmic goitre. Sir W. Gowers reports a case in which three relapses occurred at intervals of seven years. Another case reported had symptoms of hyperthyreosis six times in six years.—Trousseau. Dr. Hug-

gard, of Davos, had a case of several relapses, and eventually myxœdema was developed.

It is possible that relapses are simply exacerbations of the disease. Myxœdema has followed in a very few cases; occasionally the two conditions are combined. Finally, as regards prognosis it must be remembered that there is a great tendency towards the occurrence of intercurrent disease which may prove fatal, and, indeed, one-half of the fatal cases have their termination in this way; the most usual complications are pneumonia, bronchitis, cardiac disease, and renal disease.

Conclusions may now be drawn, from the statistics, concerning the danger to life in this disease, and the prospect of recovery. Summarising the previous figures in Dr. Hale White's series, it is found that they agree with the findings of Dr. Mackenzie, and less than 25 per cent. of the cases terminate fatally.

Hospital patients	...	49 ;	deaths	...	8
Private „	...	53 ;	„	...	7
Hospital „	...	18 ;	„	...	18
„ „	...	94 ;	„	...	15
Total patients	...	214 ;	deaths	...	48

These figures do not represent the number of patients who are killed by exophthalmic goitre; even among the 18 who died in hospital, 5 at least died from super-added disease, or complications. These were:—

1. Rheumatic fever.
2. Cerebral softening following on thrombosis of the middle cerebral artery.
3. Diabetes, and old endocarditis.
4. Mania, and later death from pneumonia.
5. Ascending nephritis.

The termination of the other hospital cases has not been traced. Dr. Hale White was able to trace the cause of death in

his 7 cases, out of 55 private patients. He gives the causes as follows:—

1. Phthisis, 1 case.
2. Pleural effusion, 1 case.
3. Heart disease, 1 case.
4. Alcoholism, 1 case.
5. Diarrhœa, 1 case.
6. Diabetes, 2 cases.

He makes special mention of the absence of cerebral symptoms in this group. Thus, it is seen that actual deaths from the disease are not so many as would appear from the figures; and in repeating Buschan's statistics of 900 cases, in which there were 105 deaths, of which only 25 per cent. were due to the disease, one probably obtains a fair estimate of the danger to life.

The next important point as regards prognosis is the chance that the patient has of becoming completely cured by medical treatment. In Dr. Hale White's series of hospital cases, 40 cases who did not die, and could be traced, 26 did well, and 12 were better. That is to say, 65 per cent. were cured, and 90 per cent. were improved. Results are even better in the private patients: 47 cases, 35 did well, and 9 were better; that is, 75 per cent. were cured, and 93·6 per cent. were improved. Altogether, in 87 cases only 5 were not improved, and, as was stated above, 3 at least of these did not undergo proper treatment.

A summary of Dr. Mackenzie's statistics shows 42 cases in which 34 are considerably improved, or 81 per cent. almost quite well. From the point of view of the patient, having satisfied him that there is a good prospect for life, and a very fair chance of complete, or almost complete, recovery, one is bound to consider the duration of the disease.

It will be necessary for the wage earner to submit to that line of treatment which will be most likely to restore him to health in the shortest time; this point will be referred to in the discussion of the surgical treatment.

SECTION IV.

Methods of Surgical Treatment, and the Results.

Various methods of surgical treatment have been practised in the past. The more important of these may be classified into:—

1. Operations upon the cervical sympathetic nerve.
2. Operations upon distal parts of the body.
3. Exothyropexy.
4. Operations upon the thyroid gland itself.
5. Operations upon the thyroid vessels.

1. *Operations upon the Cervical Sympathetic.*—These operations were performed by those who attached importance to the theory that Graves' disease was the result of some lesion of the cervical sympathetic. This view was suggested by the marked changes in the eye. It was further said that the enlargement of the thyroid and exophthalmos were due to increased vascularity in the gland and orbit.

Jessop showed that instillation of cocaine into the eye of an animal produced exophthalmos and enlargement of the palpebræ fissure. Jessop and Edmunds showed that previous division of the cervical sympathetic prevented this. However, this ivew of the pathology is totally unsupported by reliable post-mortem evidence, no characteristic changes have been detected in the nerve or ganglia. The interesting feature is that some apparently good results have followed operative treatment of this kind, although the operation is not without risk to life. The following operations have been performed on the cervical sympathetic:—

(*a*) Simple section of the nerve (Jaboulay's operation, or sympathicotomy).

(*b*) Partial resection. The superior cervical ganglia is resected, alone or together with the nerve trunk.

(*c*) Complete and bilateral resection of the whole nerve and all its ganglia.

Jaboulay was the first to apply the principle of the sympathetic origin in the treatment. The first operation was performed in February, 1896, in which the nerve was simply cut. Jaboulay's example was followed by other surgeons, and in August, 1896, Jonnesco of Bucharest excised the superior cervical ganglia and part of the main nerve trunk. Later, the whole of the cervical sympathetic, including its ganglia on both sides of the neck, were removed.

The results of the operations are recorded by Boisson in his "Etude critique des interventions sur le sympathetique cervical dans la maladie de Basedow." Paris, Henri Jouve, 1898. Boisson collected 27 cases of operation on the sympathetic nerve, including up to July, 1898. Of the 27 cases, 4 prove nothing, and 8 are atypical (cas frustes), which leaves a total of 15 cases, the results of which are:—

Cures	2
Marked improvement	6
Slight improvement	3
Failure	1
Deaths	3

Of the 8 atypical cases:—

Cure	1
Marked improvement	2
Slight improvement	4
Failure	1

In another series of cases the results were as follows:—

13 partial sympathectomies, with 3 cures and 1 death.

7 total sympathectomies, with 2 deaths.

Two cases of cure reported in Boisson's thesis are detailed as below. They occurred in the practice of Jonnesco, cases xi. and xii., pp. 148—154.

1. A widow, aged 30. Bilateral resection of cervical sympathetic, the inferior ganglia were left, 1896. The patient was

discharged after 10 days; no marked change had occurred, pulse, 120. After one month the size of the neck had diminished from 37 c. in. to 35 c. in. Fifteen months later the patient had no symptoms, and the pulse kept between 74 and 80 per minute.

2. A girl, aged 16 years. The pulse rate before operation was 110—120 per minute. The whole cervical sympathetic, with the exception of the inferior ganglia, was resected, on both sides. The patient was discharged after 19 days, the pulse rate remaining at 110—120 per minute. The exophthalmos diminished at once. Fifteen months later there were no symptoms, and the pulse rate was 90 per minute.

Details are also given of 3 fatal cases occurring in the practice of Jaboulay, Faure, and Pengniez, respectively.

1. A woman, aged 30 years. Three cm. of cervical sympathetic were resected on each side of the neck; on one side the superior ganglion was removed, on the other it was not. After the operation the pulse was 120 per minute, and the temperature 104·5°. The exophthalmos diminished; later the pulse was 90—105 per minute, and the temperature 101°.

This patient died on the twelfth day. Post-mortem examination showed congestion at the base of the right lung.

2. A woman of 24 years. The whole of the right cervical sympathetic and superior and inferior ganglia had been removed, and an incision had been made on the left side, when the patient suddenly died. Post-mortem examination threw no light on the cause of death; it was possibly due to the chloroform administered as the anæsthetic.

3. A woman of 20 years. Two operations were performed with an interval between them of 23 days. The first operation consisted in removal of the whole cervical sympathetic of the left side, and at the later operation the right side was similarly treated. After the first operation, the exophthalmos diminished on that side; the pulse remained at 144 per minute. After the second operation, the pulse was reduced to 128 per minute. The patient left the hospital with apparent slight improvement. The

day after she went out from the hospital she became feeble, with precordial pain. She had pain in the head and eyes, vomiting, and she became emaciated. Exophthalmos became extreme, and blindness set in, with ultimate ulceration of the left eye ball. The patient died in coma on the fiftieth day after the operation.

Boisson remarks that on looking into the cases which are called "improved," the facts are not convincing; most improvement has appeared in the atypical cases—the formes frustes. As a whole, the results of these cases are not satisfactory. At the outset, the treatment seems unjustifiable from the pathological evidence, and the reported cures, or cases that have improved, are not sufficiently numerous to justify the risk of death subsequent in these operations. The danger of blindness is an important consideration.

2. *Operations on Distant Parts of the Body.*—The chief interest in this group lies in the fact that a great many cases are considerably improved by some kind of operative interference. Boisson has collected 73 cases of Graves' disease in which improvement has followed operations on a distant part; for example, operations in the nasal fossæ, genito-urinary organs, abdomen, etc.

3. *Exothyropexy* is an operation which has become out of date, chiefly on account of the large scar which is formed, and, in addition, on account of the very doubtful benefits resulting from the operation.

4 and 5. Operations upon the thyroid gland itself, or upon the vessels now come under consideration; and it is from these operations that statistics of the value of operation in Graves' disease as a line of treatment are obtained. Upon the thyroid gland the following operations have been performed:—

(1) Injection of irritant substance into the gland tissue, *e.g.*, perchloride of iron, iodine. This procedure can be dismissed at once, it is based on a wrong pathology; in the thyroid of Graves' disease there are no vesicles to obliterate, and, further, the operation is associated with considerable danger.

(2) Similarly, a second method of surgical treatment, that of division of the isthmus may be performed to allow free drainage of the colloid; this in Graves' disease is absent. Division of the isthmus may become an imperative operation in cases in which dyspnœa is a feature from tracheal pressure by a goitre.

(3) Extirpation of a portion of the thyroid gland.

(4) Extirpation of whole gland; this is dangerous owing to liability of onset of myxœdema.

In the operation of partial excision of the gland, the larger lobe and the isthmus are usually removed. Finally, the last operative measure is that of ligature of the vessels of the gland. More usually the superior thyroid arteries and veins are ligatured on both sides. Kocher advises a step further in which both superior thyroid vessels are ligatured and one inferior thyroid vessel. These operations on the vessels may, where considered necessary, be followed later by partial thyroidectomy. Mayo is strongly in favour of this method of treatment. He says, when referring to the importance of selecting operative treatment to suit each individual case, "With regard to those patients seen in the early stage of the disease in whom thyroidectomy is not justifiable, ligation of the superior thyroid arteries and veins on both sides seems to bring about a rapid cure." This does away with the risk of hypothyroidism. He goes on to say that this operation may be followed later by excision, if necessary. In the following considerations of the results obtained by surgical interference in Graves' disease, it is taken for granted that in each case partial thyroidectomy was performed, with the exception of some cases in which ligation of the vessels was the treatment. In most of these cases this will be specially mentioned.

The results of those cases of Graves' disease which have undergone operative treatment, either by thyroidectomy, or by ligation, must now be considered. In tracing the cases which have been operated upon in the surgical wards of Guy's Hospital during eleven years, 1899—1909, inclusive, a collection of 6 cases

is made. I propose to give details of these cases taken from the Surgical Reports of Guy's Hospital.

Case 1.—Female, aged 19 years; a house parlour maid living at Surbiton. This patient was admitted on December 23rd, 1906, suffering from an enlarged thyroid.

Pulse, 100 per minute.
Temperature, 98°.
Respiration, 34 per minute.

There was no family history of goitre, and no history of previous illness. The goitre had been noticed for four months before admission, and it was said to be rapidly increasing in size. The patient went to see the doctor because she was "run down." Physical examination showed a smooth, bilateral swelling of the thyroid, with slight enlargement of the isthmus, the goitre was larger on the right side than on the left. Carotid pulsation was felt behind the tumour. The patient experienced difficulty in swallowing; she had exophthalmos and tremor. There had been amenorrhœa for four or five months. On January 7th, 1907, diarrhœa became a prominent symptom. Tachycardia was marked, and the patient retched, but did not vomit. She suffered from pain round the eyes, and the tremor was more noticeable. On January 29th, 1907, an operation was performed—the right lobe and isthmus were removed. Cocaine was used as a local anæsthetic, but it was found necessary to administer a small amount of general anæsthetic; chloroform was employed. In this case the wound was drained by a tube. The following day the pulse remained consistently rapid, and the temperature kept subnormal, respirations were extremely rapid; the condition was obviously very bad. January 31st—

Pulse, 160.
Temperature, subnormal.

Later—Pulse, 168.
Respiration, 52.

February 1st, at 2.30 a.m., the patient died, the temperature immediately before death reaching 103°. At the post-mortem examination the thymus was found to be enlarged, weighing

48 grms. The lower lobes of both lungs were full of bronchopneumonia. The heart weighed 238 grms.; there was hypertrophy of the right ventricle; the mitral valves were thickened. The liver was fatty.

Case 2.—Female, aged 23 years, admitted to the hospital on February 20th, 1907. This patient was a single woman, living at Herne Hill. The patient had noticed three months before that her neck was full. At that time there was no inconvenience, but since then there had been a gradual increase. The patient had a large thyroid, rather larger on the right side; and lately she had had some breathlessness. The pulse rate was 120—130 per minute; the temperature was normal; she had tremors. There was an inclination to diarrhœa. In the report there is no mention of exophthalmos. Discomfort and palpitations were the subjective symptoms, and she decided to be operated upon. March 15th, 1907: The right lobe was removed at the isthmus, and tube drainage was employed. April 4th: The patient was better; pulse was 86. April 7th: The patient was discharged well.

Case 3.—Female, aged 23 years; living at Bushey. This patient was admitted on April 5th, 1907. She had first noticed swelling of her neck nine months before, and this had increased rapidly. She had undergone medical treatment, which had reduced the swelling somewhat. On admission to the hospital the patient looked well; she complained of loss of appetite.

Pulse, 112 per minute.
Temperature, 99·2°.
Respiration, 32 per minute.

The swelling was more marked on the left side of the neck; it was fairly firm and tender. The carotid arteries were pushed back by the tumour. The patient was nervous and excitable, and she suffered from tremors. Again, in this case, there is no mention of exophthalmos. April 15th: The patient was given a general anæsthetic, and the left lobe of the gland was excised; the wound was closed, no drainage tube being provided. April 22nd: The pulse was variable, between 64 and 96.

Tremors were only slightly marked. April 28th: The patient was discharged, very much relieved.

Case 4.—Female, aged 29 years; living at Walworth. This patient was admitted on September 3rd, 1907. She was a married woman with two healthy children, and there was no family history of goitre. It is stated that her husband's cousin had a similar swelling. The patient had had no previous illnesses, but she had always complained of bad sight. First, fulness in the neck was noticed in March, 1906; the swelling soon increased in size, and then caused some difficulty in breathing and swallowing. The swelling grew larger until about six weeks before admission, since when it had decreased slightly. For one year the patient had been very nervous, and had suffered from palpitations. The eyes had become more prominent since the appearance of the swelling in the neck. She had always sweated a good deal. The condition on admission: The patient was nervous, with a flushed face and moist skin. There were well marked tremors. The swelling was a bilateral goitre, with enlargement of the isthmus, soft and throbbing all over. Exophthalmos was present, but the lids moved normally. The pulse rate is not given. There was tachycardia, with irregularity. September 10th: The first operation was performed, consisting in ligature of the superior thyroid vessels on both sides of the neck. Local anæsthetic—encaine and adrenalin—was employed, but in the theatre recourse was had to chloroform. The wounds were closed. October 3rd: The patient had improved after the operation, though she now had diarrhœa, and was depressed. On this date the patient was prepared for the second operation of ligature of the inferior thyroid artery. An attempt was made to administer local anæsthetic, but the patient was too distressed to allow proper administration. In the theatre, chloroform was given lightly on a skinner's mask. The patient moved with the incision; later, retched and vomited; she changed colour, and the pupils dilated, and the patient died on the table. Post-mortem examination showed a persistent thymus gland, weighing 90 grms.; fatty infiltration of the heart.

Case 5.—Female, aged 43 years; living at Foot's Cray. She was admitted on August 2nd, 1908. The patient was a married woman, with two healthy children; there was no family history of goitre. She had pneumonia and pleurisy five years previously. The swelling of the neck was noticed fourteen months ago, since then it has gradually increased in size; there is a slight sense of suffocation, and some pain in the swelling itself. There had been heart palpitation and pain behind the ears for some time; she had had headaches for five years. Previous medical treatment had been employed for about six weeks, with some improvement. On admission:

Pulse, 112.
Temperature, 98·4°.
Respiration, 20.

She was thin, nervous, and had tremors. Von Gräf's sign was positive, and there was exophthalmos. The tumour consisted of both lobes and the isthmus. This patient was operated upon under chloroform and ether. Both superior thyroid arteries were ligatured; the wound was closed. The patient was discharged on September 4th with the wound healed. No notes are added as to the condition of the patient.

Case 6.—Female, aged 24 years. She was an in-patient during 1909. The goitre appeared directly after diphtheria, which had occurred six years before. The patient had been unable to work for six years owing to difficulty in breathing. The patient had the typical signs, such as tremor, and exophthalmos, with lagging of the lids. The patient was operated upon, under ether, after the previous administration of morphia and atropine. The right lobe was removed; a good deal of hæmorrhage occurred. It is not noted whether drainage was employed. The patient was discharged one month after admission.

A summary of these cases shows 6 cases operated upon (4 excisions and 2 ligations), of which a general anæsthetic was administered in 5 cases. In Case 2 there is no mention of anæsthetic, local or general. The results in this group are:—

2 deaths.

2 much relieved by the time they were discharged from the hospital.

2 whose condition is not mentioned on their discharge from the hospital, which took place one month after their admission.

All these cases possessed the typical signs of Graves' disease. Cases 2 and 3 have no mention of exophthalmos, but the other symptoms and signs are sufficiently well marked to enable the diagnosis to be made.

Cases 1 and 4, the fatal cases, show moderately severe symptoms, including all those typical of Graves' disease, and, in addition, diarrhœa is noted in both of these cases. Slight diarrhœa is mentioned in Case 2, but in no other. The peculiarly fatal sign about Case 4 is the tachycardia (the actual rate is not mentioned) and the irregularity of the heart. Two of the cases which were successfully operated upon appear in Dr. Hale White's series of cases published in the Quarterly Journal of Medicine previously referred to when dealing with the results of medical treatment in this disease.

Thus, we are able to trace Case 2 (this case was last heard of after three years). The patient was better on discharge; now she is "perfectly well since the operation."

Case 3 was last heard of after three years. Result: Better on discharge. Now she still suffers from attacks of palpitation, but they are much less. She has greater self-control. She feels the cold more than before the operation. Since the operation she has been subject to attacks of giddiness and lassitude for the first twelve months almost daily, but they are getting less. She has been in the doctor's hands, suffering from a slight attack of anæmia.

The data obtained from these cases is too little to enable me to come to any conclusion as to the benefit of operative treatment, but the results do not appear to be encouraging. For convenience in reference, the symptoms, treatment, and results of these cases are tabulated:—

SIX CASES OF OPERATION IN THE SURGICAL WARDS OF GUY'S HOSPITAL.

SYMPTOMS.	Case 1.	Case 2.	Case 3.	Case 4.	Case 5.	Case 6
Enlarged thyroid	Yes	Yes	Yes	Yes	Yes	Yes
Pulse rate	100	120–130	112	Tachycardia irregular	112	—
Exophthalmos	Yes	Not mentioned	Not mentioned	Yes	Yes	Yes
Tremor	Yes	Yes	Yes	Yes	Yes	Yes
Palpitation	—	Yes	—	—	Yes	—
Sweating	—	—	—	Yes	—	—
Nervousness	—	—	Yes	Yes	Yes	—
Dyspnœa	—	Yes	—	Yes	Some	Cause of stopping work
Dysphagia	Yes	—	—	Yes	—	—
Diarrhœa	Yes	Slight	—	Yes	—	—
Rate of growth of thyroid ...	Rapid	Gradual	Rapid	Gradual	—	—
Length of history	4 months	3 months	9 months	18 months	14 months	6 years
Treatment:—						
Anæsthetic	Chloroform	Not mentioned	General	(1) Chloroform (2) "	Chloroform and ether	Ether
Operation	Removal of right lobe and isthmus	Removal of right lobe	Removal of left lobe	(1) Ligature of superior thyroid artery (2) Incision. Inferior thyroid artery ligatured	Ligature of superior thyroid artery	Removal of right lobe
Result	Death after 36 heurs	Perfect recovery	Relieved, although not perfectly well now	Death on operating table	Discharged from Hospital after 1 month. Condition not known	Same as 5

On returning to Dr. Hale White's findings amongst the patients treated in Guy's Hospital between 1888 and 1907 (inclusive), it is found that altogether 8 patients were operated upon, 3 of these died in the hospital as the immediate result of operation. Two of these cases who died have already been described, namely, Case 1 and Case 4. The third death occurred in a female patient, aged 30 years, who had been ill for twelve months with the ordinary symptoms, most of which were well marked. The special symptoms were exophthalmos, and she desired operation, as this condition prevented her from following her occupation as a barmaid. She was given a general anæsthetic, A.C.E., and the right lobe was removed. The next day she was extremely excitable. Temperature, 103°; and she died. Post-mortem examination showed nothing to explain death. Of the remaining 5 cases, 2 have already been traced—cases 2 and 3.

Dr. Hale White's details of the other cases are as follows:—

A.—Female, aged 32 years. She had had symptoms for six years. She was a very mild case in all respects. She was last heard of after $7\frac{3}{4}$ years. In 1905 she went to King's College Hospital, and was operated upon; she says she has been better since.

B.—Female, aged 19 years. Symptoms noticed for four years. An average case; last heard of after 6 years. She writes to say that her health has been fairly good, and she has felt better since the operation. At the operation the right lobe of the thyroid was removed.

C.—Female, aged 53 years. Symptoms present for ten years. She was an average case; pulse, 138. She was last heard of after 8 years. She writes that she has received great benefit from the operation, but that her health is very bad at times. At the operation the right lobe and the isthmus were removed.

The cases treated by operation at Guy's Hospital between the years 1888 and 1909 give a total of 10; 3 died as the immediate

result of operation, and 5 have been traced. These may be grouped as before into:—

1. Those that have done well 1
2. Those that have done moderately well or are better 3
3. Those that are not so well 1

In Dr. Hale White's series of patients in private practice, three were operated upon; one was a severe case which had the left lobe removed, and was better for a time, then the right lobe enlarged enormously, and again all the symptoms of exophthalmic goitre appeared in a severe degree. A second case was of an average type, which got better after removal of the right lobe. Sixteen years after the operation, the report was, "Distinctly better, no exophthalmos, some tachycardia, and palpitation. Still odd mentally." The third case was a severe one, and died upon the operating table.

Addition of these cases to the hospital cases gives the following:—

10 hospital cases	3 deaths
3 private ,,	1 death
13 cases	4 deaths

These deaths are the immediate outcome of the operation. Tabulating as before:—

1. Those that have done well 1
2. Those that have done moderately well or are better 4
3. Those that are not so well 2

It was previously demonstrated that the total mortality might be gauged at about 48 deaths in 214 cases, or 1 in 4·5, in cases treated medically, and a comparison with these operation results of 4 deaths in 13 cases shows a high mortality. Further, it must be remembered that several of the 48 deaths of the medically treated series were patients so ill that operative interference would have been impossible; also the mortality of cases operated on is a mortality of the operation, as death occurs very shortly after operation.

Probably Professor Kocher has done more operations upon the thyroid in Graves' disease than most surgeons, and his statistics show a far smaller mortality than those already studied. As regards the method of operation, Kocher says that ligature of the artery causes some amelioration, ligature of two arteries causes a greater effect, while ligature of three, out of four, arteries produces a good result. Excision of the lobe with ligature of the superior thyroid artery of the other side yields greater benefit.

In severe cases there is much more post-operative reaction than in ordinary or in malignant goitre; there is a tendency towards a sudden rise of temperature and increased rapidity of the heart; the heart may suddenly fail and death occur without warning.

Speaking at the British Medical Association Meeting in London, July, 1910, Kocher gave the following statistics:—

Amongst 4,394 operations for goitre, 469 were for Graves' disease; the total mortality in this group was 3·4 per cent. Moreover, the mortality figure has dropped progressively with increasing experience: of the last 72 cases but 1 has died. Kocher's figures four years before this in 176 cases showed a mortality of 5 per cent. In the fourth thousand of the goitre operations, of which 155 cases were of the exophthalmic variety, there was a mortality of 2·5 per cent.

The results obtained in Mayo's cases are given in the American Surgery, Gynæcology, and Obstetrics, vol. viii., 1909. Mayo says that in about two-thirds of the cases seen by the surgeon, the operation for removal of the larger lobe and isthmus can be undertaken without undue risk. In at least a quarter of the cases the condition is so extreme from continued toxic condition, or from acute exacerbation, that ligation of the vessels is advisable as a preliminary; in a few of these there is great relief. Later, thyroidectomy is done with much less risk. These may be called the graduated operations for hyperthyroidism.

In December, 1908, Mayo read a paper before the Southern Surgical and Gynæcological Society entitled "A consideration of the Mortality on 1,000 Operations for Goitre." Speaking of

exophthalmic goitre, he said a quarter of those suffering from the disease get well without treatment. Mayo gives the following most interesting results. In the early surgical work, fifteen years ago, only the most desperate cases were treated, and results showing a mortality of 25 per cent. in the first 16 cases were considered up to the average. One of these deaths occurred on the table.

The next group of cases were operated on at a more favourable moment, and the patients were more carefully prepared, with the result that in 40 cases there were three deaths.

During the last two years, 6 cases were sent from a distance, and they all died a medical death between the fourth and ninth day after arrival, their inoperable condition being recognised because of former experience. Post-mortem examination of all these cases which died a medical or surgical death showed:—

Degeneration of heart muscle.
Fatty liver.
Soft spleen.
Chronic nephritis.
Enlarged thymus.

One of the medical deaths (death on the fifth day) had no palpable thyroid, but post-mortem it was found enlarged, weighing 3 oz.

Further statistics show 405 cases of marked hyperthyroidism operated upon with 19 deaths; three-quarters of these were treated by extirpation of one lobe (usually the larger right lobe) and the isthmus. Sometimes part of the left lobe was also removed. Of the remaining cases, one-fifth were mild cases, and they were treated by ligature of arteries and veins at both upper poles; the remainder were the worst possible type of case, and the operation of ligature was performed as a preliminary measure.

The results are as follows:—

97 cases of hyperthyroidism treated by double ligature of the superior thyroid arteries and veins. 1 death.

14 cases who had previous excision of one lobe and isthmus with recurrence of symptoms were treated by ligature of remaining superior thyroid artery and vein.

295 cases of removal of more or less of the gland. 18 deaths.

7 of these deaths occurred in the first 40 operations.

1 death occurred on the table from shock.

15 deaths occurred from hyperthyroidism, nearly all within 20 hours of the operation.

2 deaths occurred from embolism:—

(1) Pulmonary.

(2) Cerebral.

The most usual cause of death is hyperthyroidism, while primary or delayed hæmorrhage is a frequent cause.

Berry, in his book, Diseases of the Thyroid Gland, 1901, quotes the statistics of several operators. Operations performed by Sorgo, 1884—1896, for exophthalmic goitre totalled 174: the result is not known in 2 of these cases, but in 172 operations—

27 were much improved, 15·2 per cent.

62 distinctly improved, 36 per cent.

48 cured, 27·9 per cent.

11 not improved, or made worse, 6·4 per cent.

24 died soon after operation, 13·9 per cent.

Lord Lister in 1877 removed the bulk of the thyroid in case which threatened suffocation; the patient was alive in 1887.

Allen Starr, 1896, gives the following results. 190 operations:—

74 entirely cured.

45 improved.

45 results doubtful.

3 no improvement.

23 immediate deaths.

Rehn, 291 thyroidectomies:—

165 cured.

77 improved.

37 deaths.

The death rate is just over 12 per cent., but for severe cases it was 22 per cent.

Oppenheimer, 68 cases:—

18 cured.
26 benefited.
9 deaths.

(5 died immediately; 4 died within 24 hours).

Kocher, 106 cases:—

62 cured, 58·5 per cent.
9 greatly improved, 8·5 per cent.
17, or 16, improved, 16 per cent.
9 not traced, 8·5 per cent.
9 died, 8·5 per cent.

Freidheim, of Hamburg, 20 cases of thyroidectomy:—

14 lasting cure.
5 improvement only.

More recent statistics were given at the Meeting of the British Medical Association, 1910. Dr. Mackenzie gave the results of operation at St. Thomas's Hospital. 13 cases:—

5 fatal.
3 in statu quo.
5 were improved.

Dr. Bruce, of Toronto, had operated upon 22 cases:—

20 were successful.
1 died of pneumonia.
1 died immediately. This case was operated upon in an acute stage.

He had collected results of 1,000 cases operated upon, which showed a mortality of 4 per cent. Of the 1,000 cases:—

16 per cent. were absolute cures.
85 per cent. were able to resume normal life.

Mr. Armour had 1 death in 20 cases. He reserved simple ligature for acute cases, looking upon it as a temporary measure.

Mr. Williams collected, altogether, the results in 1,055 cases of Graves' disease operated upon with a mortality of 4 per cent.

Professor Garré, in the *New York Medical Journal*, March 21st, 1908, reports on 35 cases in which the following operations were performed:—

30 partial excisions.
8 ligature of vessels.
2 resection of sympathetic enucleation of intra-glandular nodules.

Nearly all these cases were operated upon under ether; some under local anæsthetic. There was an immediate diminution in pulse rate. After five years:—

Exophthalmos gone, one-third.
Exophthalmos persistent, one-fourth.
Exophthalmos present in some degree, rest.
Tachycardia persistent, 4 cases.
Tachycardia, pulse below 92, two-thirds.
Tachycardia, pulse not below 100, one-third.

The general condition in 50 per cent. was excellent.

SECTION V.

A Comparison between the Results of Medical and Surgical Treatment.

Firstly, it should be noticed that the mortality in Graves' disease under medical treatment, though not large, would appear to have remained at about the same rate for some years, whereas the more recent work among the surgeons in this disease shows a decreasing mortality as the result of their treatment. Each later series of cases appears to give improved results; this is shown in the statistics of Kocher and Mayo. The cases which

occurred in Guy's Hospital do not show any improvement as regards mortality by operative treatment:—

Medically treated.	*Surgically treated.*
161 cases, 41 deaths. Of those that lived, 40 have been traced.	10 operations, 3 deaths. Of those that lived, 5 have been traced.
26 did well.	1 did well.
12 are better.	3 are better.
2 not well.	1 not well.

Dr. Hale White's private cases:—

Medically treated.	*Surgically treated.*
55 cases, 7 deaths. Of those that lived, 47 have been traced.	3 cases, 1 death. Of the 2 living,
35 did well.	1 is better.
9 are better.	1 is not well.
3 not well.	

Dr. Mackenzie, in Clifford Allbutt's System of Medicine, 1908, traced 57 cases medically treated, with 14 deaths; and again in July, 1910, he said that 36 per cent. of hospital patients recover completely, while not more than 25 per cent. terminate fatally.

Kocher, as the result of a large series of operations, puts the mortality at 3·4 per cent., and in more recent work at 2·5 per cent.

Mayo says that 25 per cent. of those suffering from the disease get well without treatment, and, as the result of operative treatment, there is a progressive diminution in the mortality owing to a more careful selection of cases and improved technique. The general inference from the majority of other observers is that the mortality is rather less than 4 per cent. in selected cases as the immediate result of operation.

The question of the relative improvement in the condition of the patients as the result of medical or surgical treatment is not easy to decide. Statistics rather tend to show that complete cure is confined to about 33 per cent. of the cases after operation, but the data on this subject are not sufficient.

SECTION VI.

Conclusions.

It is clear that operations on the thyroid in patients suffering from Graves' disease are associated with considerable risk to life, and the question to be decided is whether the operation is a justifiable one. Pathological evidence suggests that thyroidectomy, or ligature of the vessels, is a rational operation in cases of exophthalmic goitre, but it is only practical evidence which can be the real criterion.

There can be no doubt that experience plays a most important part. There is direct evidence of a decreasing mortality following operation of later years, owing to improved methods, and the knowledge gained by previous cases as to which are more favourable for operation. This knowledge is the most important factor in deciding on the treatment; where the cases are most carefully selected there seems little danger to life. Professor Kocher is a staunch advocator of the operative treatment. Speaking at the British Medical Association, London, July, 1910, he says: "We must not, then, wait and risk the prolonged poisoning of the system, which will produce organic changes in heart muscle, the kidneys, liver and brain. We must treat the diseased organ itself, and diminish its activity by diminishng the quantity of the secreting cells. We must exclude, by cutting the superior pedicle, the nerve influence, and produce partial atrophy by ligature of the vessels, or perform partial excision in sufficient quantity to reduce the secretion to the normal degree. I can prove that this is practically possible without damaging our patients in any way or risking their life. Therefore, surgical treatment is the only sure and quick way to come to a real cure, but it must be kept in mind that it should be done only after most careful consideration."

He also says, "A physician who delayed operation in the early stages was accepting a grave responsibility."

Dr. Mackenzie, at the same meeting, says that medical treatment is becoming increasingly successful, and in time some antidote to the causative toxin will be discovered.

Status lymphaticus really underlies many cases of exophthalmic goitre; it is this condition of lymphatism which contributes so largely to the immediate risk to life from operation in exophthalmic goitre. He states that "as yet I do not know any case where this quickly fatal result has occurred and an enlarged thymus has not been found." Later, "I have seen no cases that I should consider cured by operation." Dr. Mackenzie cannot believe that Professor Kocher gets the same class of case to operate on.

On the other hand, Crile says: "I have seen no case that was not benefited by operation, and I know of few classes of cases that experience such deep and fundamental relief as cases of acute toxic Graves' disease successfully operated upon." In cases left to the later stages, he says: "after the ship has gone to the rock, one has to deal with the wreckage."

Kocher in an address to the American Medical Association, states: "We have not seen a single case in which the patient had not been benefited by the thyroid operation."

Mobius, in his original work on the operative treatment, came to the conclusion that the result was probably a comparatively rapid improvement, but that the operation was not without danger.

Hartley was of opinion that, as there was so good a chance of recovery under medical treatment in the milder forms, the risk of operation should not be taken.

In the acute and more severe forms the risk of death from operation is so high that it renders this measure doubtfully justifiable. Of course, there are times when operation is called for, such cases as those associated with respiratory obstruction. It would appear that the general concensus of opinion is becoming inclined to the view that operation is justifiable in certain well-chosen cases.

It now remains to briefly point out the contra-indications—the main factor in producing fatal results is the mental shock;

the prolonged toxæmia causes an alteration in the cerebral cortex, cerebellum, and medulla. Patients in whom the mental attitude is disturbed are extremely likely to take an anæsthetic badly. Cases of irregular heart are very dangerous from the point of view of operation—there is considerable risk of heart failure. Operation should not be attempted in cases where albuminuria and nephritis are present. Perhaps one of the greatest risks is the association of status lymphaticus with Graves' disease; this may develop early in the disease. Glycosuria should be a contra-indication.

Finally, the question of anæsthesia must be considered. These cases are notoriously bad from the anæsthetist's point of view, and the case for surgical interference would seem to become much stronger if general anæsthesia can be avoided. Local anæsthesia is much employed, but in the normal type of case, marked by a good deal of nervousness, this method may not be satisfactory, unless special efforts are made to reassure the patient and occupy his attention during the operation.

It is safe to say that general anæsthesia may be employed in a case which is considered a suitable one for operation, having paid due regard to the contra-indications. There is some difference of opinion as to the merits of chloroform and ether in these cases. Both anæsthetics have been given, and mixtures also; the most generally accepted method, however, is the administration of ether after a previous injection of morphia and atrophine. Dr. Crile, of Cleveland, has brought forward a most excellent method which is to obviate the mental excitement so often the cause of post-operative death. The patient is put to sleep without her knowledge. Every day for several days before the operation the patient is given inhalations of essential oils, and on the morning of the operation ether, or chloroform, is substituted (Dr. Crile prefers ether) without the patient's knowledge, and she goes under without trouble, thus the excitement is obviated and mentality as a factor is eliminated.

Chloretone is a drug recommended by Dr. Fergusson. It may be administered within two hours of the operation.

Mr. Berry, in his paper read before the Surgical Section of the Royal Society of Medicine in November, 1907, concludes as follows:—"The advisability of the removal of the goitre in true Graves' disease is, in my opinion, still an open question. The risk of operation in true Graves' disease is undoubtedly very serious, the ultimate benefits, so far as I can learn, are by no means certain or lasting. Those who appear to have had fairly satisfactory results from the removal of goitre in cases of Graves' disease are apparently very careful in the selection of cases they submit to operation."

The difficulty in coming to a conclusion on a subject presenting so many points in favour of both lines of treatment is great. Those cases which are early and amenable to medical treatment are claimed as the ideal cases for surgical interference. Again ,that class of case which provides the greatest risk in surgical treatment responds least to medical treatment. The facts of a decreasing mortality in operation cases as worked out by Kocher and Mayo satisfies one that surgical treatment should not be abandoned. More years of experience may reduce this present mortality considerably. It would appear that it is a matter very much for the patient to decide: in mild cases one can promise a good chance of recovery under medical treatment, while the attractions held out by operation are possibly quicker recovery, a point which is of importance to the worker, and probably as good a chance of recovery. On the other hand, it must not be forgotten that death from operation is immediate, and this from the point of view of the patient is very serious.

In later stages of the disease the question as to operation must still be left open. The records obtained do not show sufficiently the amount of improvement that is to be expected as the result of performing the operation. Up to the present time no surgeon has ever published a series of cases showing the subsequent mortality of cases operated on, as compared with the mortality of healthy females of the same ages.

In conclusion, it may be said that operative treatment, in carefully selected cases, by an experienced operator, is a justifiable proceeding.

AN INVESTIGATION OF THE PRESSURE EXERTED BY COLLECTIONS OF SEPTIC PUS.

By

K. H. DIGBY, F.R.C.S., M.B., B.S., F. E. POLLARD, F.C.S., F.I.C., and W. H. CATTO, M.B., B.S.

It is usual to recognise five chief local signs of inflammation—heat, pain, redness, swelling, and impairment of function. This list, however, omits one sign which, from a pathological point of view, is at least equal in importance to any one of the classical five. This sign is tension.

When suppuration supervenes the signs of inflammation become more prominent, and this is true of the tension which often increases. Suppuration may be defined as liquefaction in and of the tissues in response to irritation. The resulting fluid collection is pus. Tension, which is a frequent property of inflammation, commonly accompanies pus formation, has much influence upon the course of suppuration, and no little bearing upon treatment.

It cannot be claimed that tension is pathognomonic of inflammation or suppuration. Pressure is sometimes exerted by a new growth, and retained secretions manifest considerable tension. And, on the other hand, chronic abscesses may show little or no tension. But the same kind of criticism can be made with equal truth about any of the other signs of inflammation.

No clinician would deny the existence of tension in most acute suppurations. Some of the facts proving its presence may here be mentioned.

In one set of cases suppuration occurs in some part possessing more or less elastic boundaries. Acute suppuration will always produce distension of such a part. Thus, the skin will be raised and stretched over a subcutaneous abscess. The synovial membrane of a suppurating joint will be tightly distended and the joint forced to assume the position of maximum capacity. In the case of pericardium, pleura, or peritoneum, the adjacent visceral and parietal layers become widely separated. In suppurative cholecystitis, the gall-bladder will bulge below the costal margin, and suppuration in the Fallopian tube will produce a large retort-shaped tumour. In the case of a suppurating lymphatic gland, the fibro-muscular capsule will be greatly stretched.

In another class of cases, suppuration is proceeding within some more or less rigid compartment of the body. Acute suppuration is here seen to produce characteristic pressure effects. An abscess within the cranium produces paralysis and coma as surely as will an extradural effusion of blood pumped out at arterial pressure from a lacerated middle meningeal artery. Displacement and compression of viscera accompany suppuration in the thorax, and, to a less extent, in the abdomen. Suppuration in the medulla at one end of the diaphysis of a long bone will so raise the pressure in the rigid tube of bone as to arrest the blood supply and cause necrosis of the whole diaphysis. It cannot, however, be assumed that the pressure of the pus comes to equal that in the nutrient artery, for a much lower pressure could produce necrosis by occlusion of the capillaries. A prostatic abscess, confined by the unyielding pelvic fascia, presses upon the urethra causing retention of urine.

There is, then, abundant direct proof of the pressure exerted by acute septic pus. A full recognition of the existence of this pressure leads to a comprehension of many of the phenomena

in septic infections. Its significance may be considered in connection with (1) the spread of suppuration; (2) the toxæmia; (3) the pain; (4) the question of treatment.

(1) *The spread of Suppuration.*—Septic organisms in the tissues may spread locally by direct multiplication. It is unlikely that they are aided to any extent by such motility as they may possess. They chiefly extend their influence by the movements of the tissue fluids in which they are growing. These currents, favoured by all movements of or interference with the part, may lead to widespread cellulitis. If the organisms invade a lymphatic channel, their conveyance along the lymph stream is indicated by lymphangitis and lymphadenitis. If the organisms invade a blood vessel, their distribution throughout the circulation may lead to septicæmia. Hence, the most important element in the treatment of an acute septic infection is immobilisation of the affected part. So, too, it becomes clear in, say, a case of septic finger, how valuable sometimes may be the application of a proximal elastic band in retarding lymphatic and venous circulation, not only in checking toxic absorption, but also in delaying dissemination of the organisms.

If suppuration supervenes, the pus shows considerable burrowing power. It will strip the dura mater off the interior of the calvarium, raise wide areas of periosteum, and track anywhere in the direction of least resistance. It seems fair to ascribe this burrowing tendency entirely to the pressure of the pus, for it is at once checked by the relief of tension afforded by a free incision without complete evacuation of the infected material.

There are, of course, other factors as well which determine the spread of suppuration. That gravity has some influence is seen in deep submaxillary cellulitis (Ludwig's angina), and in cases of general peritonitis where subphrenic and pelvic collections of pus are so often to be found. Direct liquefaction of the abscess wall enables the slow spread of suppuration through tough structures, such as deep fascia or skin. Lastly, suppuration round a vein may lead to liquefaction of clot, with sudden

dissemination of infected particles of thrombus, clinically manifested by a rigor and followed by pyæmia.

(2) *The Toxæmia.*—It is a common clinical observation that septic intoxication is more rapid and of a greater degree when infection happens in a confined part of the body than when it occurs in looser tissues. A good example is found in the staphylococcus pyogenes aureus. Staphylococcal cellulitis is less serious and less acute than staphylococcal osteomyelitis; though the greater severity of the latter is probably due in part also to the increased risk of septicæmia resulting from the uncollapsible character of the veins in bone. Not only is toxic absorption greater from an abscess where tension is considerable, but, conversely, toxic symptoms will disappear at once on relief of tension. In many cases of single circumscribed abscesses pyrexia is found to have gone after incision as soon as the patient is sufficiently round from the anæsthetic for the temperature to be taken. The following case illustrating the effect upon the temperature of relief of tension is given, because its bearing is clear and unambiguous.

George B., æt. 53 (see Sir Cooper Perry's Medical Reports, 1910, No. 475), was admitted on November 6th, with a history of pain in the chest for the preceding six weeks. Two days before admission the chest had been tapped; a clear fluid had been drawn off and injected under the skin. On admission, an empyema was diagnosed, but it was thought safer to perform a preliminary aspiration before resecting a rib. At 5 p.m. on November 7th about two pints or less of foul-smelling pus were removed, the pus spurting out by itself with each expiration. At six o'clock the temperature was down, and it kept low throughout the thirty hours between the aspiration and the subsequent resection of a rib. The fall can hardly be ascribed to shock, for no anæsthetic was given, and only a moderate quantity of pus was removed slowly. By no means all the septic material was evacuated, so that the fall in temperature can only have been due to the relief of tension (Fig. I.).

Further evidence in this direction is given by the not uncommon experience of the rapid rise of temperature which follows the too tight packing of gauze into the mouth of an infected sinus. Indeed, in some cases it seems that the tem-

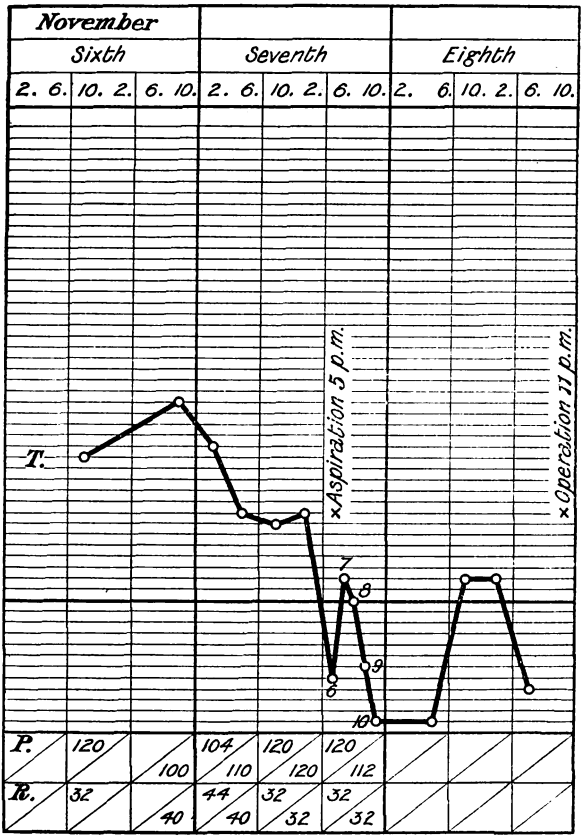

FIG. I.

perature can be raised and lowered with the certainty of a laboratory experiment by simply "corking" or "uncorking" the mouth of the sinus.

(3) *The Pain.*—Pain in inflammation has, probably, more than one cause. It is likely that the toxins stimulate the nerve

endings by chemical action. Ritter* suggests that a hypertonic condition of the inflammatory exudate is the effective agent. This author is opposed to the common-place view that pain is the result of the pressure in inflammation. He points out that anæsthesia and not pain is produced by the subcutaneous infiltration of solutions which are hypotonic. Perhaps the answer to this is that the pressure in these cases is upon the nerve fibres—thus interfering with conduction—rather than upon the nerve endings. However this may be, the association between pain and tension in inflammatory processes is frequently observed. One may find a patient sleepless with the pain of a whitlow, yet later the same patient comparatively comfortable with a subsequent abscess containing many times the quantity of pus due to the same organism in the axilla. And there can be no doubt of the greater severity of pain from a boil in the ear or on the tip of the nose than from one upon the arm. Moreover, whilst external pressure intensifies the pain, the incision of a tense abscess is followed by its prompt cessation.

(4) *Treatment.*—As soon as pus forms—and sometimes before—it is necessary to make a free incision, thus lowering the tension. In this way the local spread of suppuration, the toxæmia, and the pain will all be checked. As the pus contains pyogenic organisms many of these will be removed. Scraping the interior or squeezing the part involves the danger of spreading infection by damaging the protecting abscess wall. The remaining organisms are killed or removed by the serous discharge which takes place. Hypertonic solutions† have been used to encourage this serous discharge. They are probably very injurious to the tissue cells.

The impossibility of the immediate sterilisation of the cavity and walls of the abscess makes drainage necessary. Otherwise, pus will re-accumulate under pressure, often with surprising

* Ritter. Archiv. für Klin. Chirurg., 1902, vol. 2, page 68.

† Wright. "Studies on Immunisation." (Constable & Co., London.) pp. 280 and 464.

rapidity. It would seem, therefore, only safe to sew up an acute abscess, where (if anywhere) one can be certain that one is closing a sterilised cavity, or when (if ever) one can be reasonably certain that the residual infection will be overcome by the natural protective reactions of the body before the tension is again raised. In a cold abscess there is no risk of increased tension. Drainage accordingly becomes unnecessary. It is indeed dangerous with our present imperfect ways of maintaining post-operative asepsis, and the terrible results of mixed infection.

Having dealt with some of the manifestations of the pressure of purulent collections, it remains to find out the factors at work in producing that pressure. Pus consists of a solid and a fluid part. The solid part includes tissue débris, organisms, and immigrated leucocytes. Chemiotaxis accounts for the presence of the latter, but their congregation cannot determine the pressure, for usually there is a certain amount of fluid between and around them. The problem, then, is to account for the collection of the liquor puris under pressure.

A review of the biological processes within an abscess suggests a possible explanation. There is an excessive breaking down of protoplasmic materials, relatively few large molecules, disintegrating into relatively many small ones. There is an exaggeration of katabolic action. Katabolism everywhere in the body tends to raise the osmotic pressure of tissue solutions by increasing their molecular concentration. The harmfulness of tissue waste-products may be partly due to their hypertonicity. One may regard the kidneys (which excrete urine having three times the molecular concentration of blood-serum) as being engaged in maintaining the isotonicity and normal concentration of the body fluids. Further, the proteolytic ferment, present in pus, which is produced both by the organisms and by the leucocytes, digests the proteid. This theoretically, should increase the osmotic pressure. Finally, the growth of the micro-organisms might be expected to act in the same direction.

In following this clue, some method of measuring osmotic pressure had to be employed. Direct measurement was impossible for want of a perfect semi-permeable membrane. The osmotic pressure varies directly with the molecular concentration of a solution; but so also do other properties of a solution, such as the depression of the freezing-point and the electrical conductivity. These latter can be measured accurately, and so the osmotic pressure can be deduced. A physiological method based on the fact that the volume of red corpuscles varies in different strengths of solutions has also been used by physiologists.

With regard to the present research, reference is made to the cryoscopic results of others, but the only fresh determinations have been made by estimating the electrical conductivity. In doing this, advantage was taken of the Conductivity Tube devised by Mr. W. P. Digby and Mr. C. V. Biggs. As the method is novel, a brief description taken from a paper by Mr. S. Evershed* is given :—

"The complete apparatus is shown in Fig. 2, where G is a bent glass tube to contain the solution under test, and A and B are the electrodes for passing the electric current through the water. The electrodes are connected by wires to a direct-reading conductivity meter M, and a continuous-current hand-driven dynamo E; so that by turning the handle W of the dynamo, a current traverses the meter and the water in the conductivity tube G. The pointer of the meter is deflected, and comes to rest at some point upon the scale which directly indicates the conductivity of the water in the tube. The test is completed as soon as the pointer has come to rest, that is to say, in two or three seconds.

The tube G is made long enough, and the electrodes are given sufficient surface, to make the electric resistance in the parts of the current-path immediately surrounding the electrodes negligibly small compared with that of the length of water in the tube. Hence, gas bubbles may accumulate on the electrodes without making any observable difference in the measured conductivity. Moreover, gas bubbles liberated from the electrodes rise upwards and escape freely at the upper ends of the tube; they can never diminish the conductivity by travelling downwards into the path of the electric current. The electrodes are short hollow cylinders of platinum, so that they present a large surface, from every part of which gas bubbles are free to escape upwards.

After paying so much attention to the evolution of gas and providing for its ready escape, it is just as well to add that in practice the amount of gas formed on the electrodes in the course of a single test is very

* The Dionic Water Tester. Evershed and Vignoles, London, 1910.

small and generally invisible. Whatever there may be as the result of one test, it is all washed away when fresh water is poured through the tube preparatory to another test.

Although the current used is very small, never exceeding ·004 amperes under normal conditions, and the time during which it flows is very short, two or three seconds only, there is more than enough time to establish the maximum polarisation of the electrodes: so that unless some means were adopted to eliminate it, the error due to back-electromotive force would be considerable. Tnis difficulty is removed by taking the electromotive force into account when calibrating the scale of the conductivity meter. Evidently, any back-electromotive force will make the conductivity of the water in the tube appear to be less than it really is; and what is done is to mark the divisions on the scale so that they represent the true conductivity of the water. To do this it is necessary

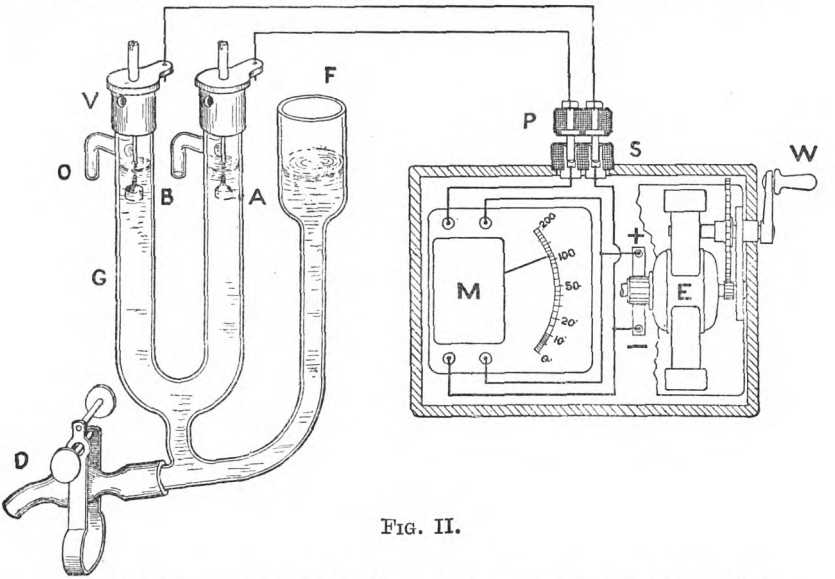

FIG. II.

to take a fair average value for the back-electromotive force of polarisation. With bright platinum electrodes in a dilute salt solution the back-electromotive force is about two volts, and this is the value allowed for in marking the scale. The dynamo generates a constant pressure of 100 volts, so that any variations in back-electromotive force above or below two volts are negligibly small by comparison, and do not produce any observable error. To maintain the necessary constancy of pressure the dynamo is fitted with the constant-speed clutch which I introduced several years ago for insulation testing purposes. The effect of this device is to keep the pressure constant at 100 volts within one-quarter of a volt, when the dynamo handle is driven at any speed above that at which the clutch is adjusted to slip.

Conductivity (specific conductance) is the reciprocal of specific resistance, and the most convenient unit . . . is the reciprocal of one megohm."

The method is rapid, and also extremely accurate. The following is a diagram of results obtained by testing standard solutions of sodium chloride. The circles with dots represent the readings actually taken. If these circles be connected, it will be seen that the resulting line is a straight one.

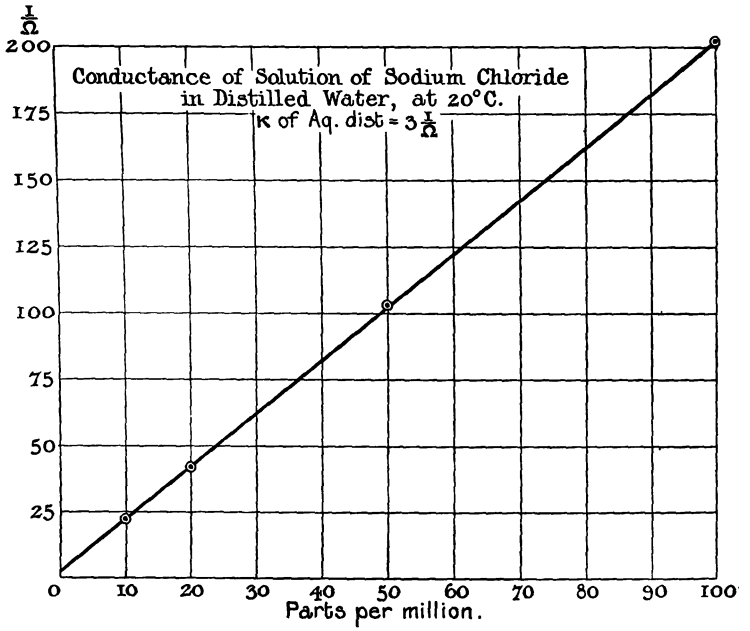

FIG. III.

The extreme sensitiveness of the apparatus is shown in the following table:—

TABLE A.

Conductance in reciprocal megohms of sodium chloride solution in aq. dist. (Ω=4).

Parts per million.	Specific conductance.
1	6·7
2	10·6
4	15·4
6	19·6
8	23·5

Parts per million.	Specific conductance.
10	28·6
20	47·6
30	69·0
40	87·0
50	110·1
60	131·5
80	169·5
100	210·0
200	385·0
300	556·0
400	714·0
500	870·0
600	1052·0
800	1250·0
1000	1538·0

Three points in practice have to be borne in mind. In the first place, the temperature must be taken for each experiment, and the reading multiplied by the factor $\frac{100}{56+2\cdot2}$ T (where T is the temperature) will give the electrical conductivity at 20° C.* In the second place, the most concordant results are obtained in weak solutions. In the third place, the distilled water used for dilution must be exceptionally pure, and its conductivity must be determined in every experiment to be sure that it does not contain more than a trace of impurity.

By the conductivity method it has been possible to prove that the processes within an abscess must tend to raise the electrical conductivity, and therefore to increase the osmotic pressure. This is well shown in the following series of experiments. Pus contains a proteolytic ferment, and proteolysis raises the osmotic pressure as shown by the increased electrical conductivity, thus:—

Experiment 1.—Dilute solution of egg white in tap water was divided into two parts (A and B) to each of which 1 cc. of Fairchild's trypsin was added. A was kept at 0°C., B was

* Eversheld, idem.

incubated for 16 hours at 37°C. Both were then similarly diluted with the same distilled water, and tested at the same temperature, 21·5°C. Electrical conductivity of A=9·8 reciprocal megohms and B=10·9.

In another experiment, the effect of trypsin on actual serum was investigated. The serum was sterilised in this and in subsequent experiments by keeping at a temperature just below its coagulation point for three days.

Experiment 2.—1 cc. of sterile trypsin with 10 cc. of sterilised liquid sheep's serum was incubated at 37° C. for five days, and the conductivity determined at the end of that period. An exactly similar mixture was made and tested immediately. In each case the temperature during the determination was 24°C., and the dilution the same (0·33 cc. in 55 cc.). Conductivity of fresh mixture=108 reciprocal megohms; conductivity of incubated mixture=120 reciprocal megohms.

Pus also contains bacteria. The subjoined series of experiments prove that bacteria growing in liquid serum raise its electrical conductivity.* In every instance to each of two equal volumes of sterilised liquid sheep's serum was added a similar loopful of the same growth of the micro-organism. One was kept in an ice chamber, the other incubated at 37°C., for a period, and then (after centrifuging) the electrical conductivities of both were determined at the same laboratory temperature. Identical dilution (0·33 cc. in 55 cc.) was used in every case. The distilled water was a good sample, 55 cc. giving readings of 0·23 to 0·30. The serums were kept in rubber-capped tubes to prevent evaporation.

Experiment 3.—The conductivity of the serum after 48 hours' growth of staphylococcus aureus was found to have been raised from 105 to 111.

* According to O. C. Gruner (Studies in Puncture Fluids, pp. 147 and 148), Zangmeister had already shown that bacteria increased the molecular concentration of solutions in which they were growing.

Experiment 4.—The conductivity of the serum after 48 hours' growth of streptococcus was found to have been raised from 105 to 112.

Experiment 5.—The conductivity of the serum after 14 days' growth of staphylococcus albus was found to have been raised from 104 to 130. (A previous experiment with another strain of staphylococcus albus showed no rise in 24 hours.)

Experiment 6.—The conductivity of the serum after 14 days' growth of bacillus pyocyaneus was found to have been raised from 105 to 158.

Experiment 7.—The conductivity of the serum (10 cc.) after 14 days' growth of bacillus coli communis was found to have been raised from 105 to 120. Further experiments with various mixed growths gave similar results. The effect of bacterial growth in the presence of a proteolytic ferment, such as is found in pus, was also investigated.

Experiment 8.—The conductivity of the serum after 5 days' growth of bacillus coli communis in the presence of 0·5 cc. of trypsin was found to have been raised from 108 to 129.

Experiment 9.—The conductivity of the serum after 56 hours' growth of bacillus mesentericus in the presence of trypsin was found to have been raised from 111 to 188.

From experiments 2, 7, and 8 it would seem that organisms, plus proteolytic ferment, produce the greatest rise in conductivity. It was possible, however, to imitate more closely the processes in an isolated abscess.

Experiment 10.—Pus was aspirated from an empyema (from the case referred to in connection with Fig. I.). This, with the usual dilution, gave an electrical conductivity of 86. A portion of the pus collected was incubated at 37°C. for a fortnight. At the end of this time a pure growth of pneumococcus was cultivated from the pus, the electrical conductivity of which had risen to 110, the precautions already mentioned being employed here as in the other experiments.

The final step was to prove that pus serum actually had a higher osmotic pressure than blood serum. Ritter,* by means of cryoscopy—he does not give details of his methods—had already claimed to have shown that this was commonly the case in septic collections. Gruner's† figures point in the same direction, but Gruner says that v. Rzenthomski has attributed the greater depression of the freezing point to the presence of pus cells. All these results are clearly not above suspicion. In investigating the matter by means of determinations of the electrical conductivity, the following procedure has been adopted:—

A sample of pus was collected by means of a dry, clean, sterilised syringe before the abscess was incised. The pus was immediately centrifuged for from thirty to sixty minutes by means of a very powerful centrifuging machine worked by electric motor. As this failed to produce sufficient separation of the pus serum in the majority of cases, only a few pus determinations could be completed. (It may here be said that every completed experiment has been recorded in this paper with the single exception of a sample of pus of unknown origin which gave a low reading.) When pus serum could be obtained, it was pipetted off and kept in a rubber-capped test-tube in an ice box till its electrical conductivity could be determined. All the apparatus employed was scrupulously cleaned, rinsed with distilled water, and dried. The same degree of dilution was employed in every case, *i.e.*, 0·33 cc. in 55 cc. of distilled water. The latter was of especial purity and was tested before each experiment to ensure its constancy. The room temperature during the experiment was invariably taken, and the necessary correction for variations applied. For the most part, the samples were collected and centrifuged by one of us and tested by another, who was unaware at the time of the source of the sample.

The electrical conductivities of blood serums and other body fluids have been determined for the sake of controls. The

* Ritter. Archiv. für Klin. Chirurg., 1902, vol. 2, page 68.

† O. C. Gruner. "Studies in Puncture Fluids."

subjoined table gives the results obtained. These are expressed both as the electrical conductivity of the diluted sample in reciprocal megohms, and also in terms of equivalent values of sodium chloride percentages (deduced from the results in Table A).

TABLE B.—SEROUS FLUIDS.

Source of Fluid.	Nature of Case.	Reference to Reports.	Electrical Conductivities at 20° C.	Concentration as expressed in NaCl percentages
Blood serums—				
Blood serum	Venesection for post-operative uræmia	Clinical, Oct. 28, 1910	96	0·733
Blood serum	Venesection for bronchitis and failing heart	Pitt, Apl. 27, 1911	94	0·719
Blood serum	Venesection for failing heart	Med. Reps., Apl. 27, 1911	98	0·747
Passive effusions, etc.—				
Hydrocele fluid	Hydrocele following varicocele operation	Lane, 393, 1910	95	0·726
Hydrocele fluid	Hydrocele	Lane, 241, 1910	97	0·740
Hydrocele fluid	Hydrocele	Out-patients	93	0·712
Hydrocele fluid	Hydrocele	Out-patients	97	0·740
Hydrocele fluid	Hydrocele following varicocele operation	Dunn, 506, 1910	95	0·726
Ascitic fluid	Chronic "peritonitis." No albuminuria	Hale White, 343, 1910	99	0·754
Ascitic fluid	Chronic "peritonitis." Albuminuria. 33rd time of tapping	Hale White, 353, 1910	102	0·775
Cerebro-spinal fluid	2½ ounces removed by trocar in case of supposed cerebral tumour	Med. Reps. Copson, 1911	105	0·796
Cerebro-spinal fluid	Removed for diagnosis in mastoid case. Fluid clear	—	94	0·719
Hydatid fluid	Removed by trocar from a living hydatid cyst in the liver	Dunn, 481, 1910	103	0·782

It will be seen that these non-inflammatory body fluids do not vary to a great extent in their molecular concentration. If the hydatid fluid be excluded, the concentration equals, on an average, that of a ·739 per cent. sodium chloride solution.

Next will be considered the molecular concentrations of inflammatory fluids. The results (Table C) are found to be widely divergent, and at first sight some of them are unexpected.

TABLE C.—Inflammatory Fluids.

Source of Fluid.	Nature of Case.	Reference to Reports.	Electrical Conductivities at 20° C.	Concentration as expressed in NaCl percentages
Pyomas—				
Inguinal abscess	—	Rowlands, 188, 1910	138	1·049
Mammary abscess	Staphylococcus aureus	Steward, 129, 1910	112	0·848
Abscess of ankle	Following a splint sore	Steward, 134, 1910	107	0·812
Mammary abscess	—	Rowlands, 193, 1910	108	0·819
Abscess of hand	Streptococcus longus	Steward, 80, 1911	98	0·747
Abscess of back	Abscess had already broken	Rowlands, 199, 1910	97	0·740
Pyoceles—				
Empyema	White, milky pus	Shaw, Ryell, 1911	97	0·740
Empyema	Pneumococcal septicæmia	Lane, Shaw, 1911	89	0·681
Empyema	Pneumococcal	Perry, 475, 1910	86	0·660
Suppurative arthritis of knee-joint	Micrococcus aureus and streptococcus	Turner, Redfern, 1911	86	0·660
Purulent cerebro-spinal fluid	Lateral sinus, thrombosis, and suppurative meningitis. Operation had been performed. Streptococcus longus in blood	Mollison, 40, 1910	94	0·719
Purulent cerebro-spinal fluid	From the same case a few days later. Patient died shortly afterwards	Mollison, 40, 1910	79	0·611
Non-suppurative inflammatory effusions—				
Pleuritic effusion	Aspirated	Pitt, Chason, 1911	88	0·674
Pleuritic effusion	Aspirated	Pitt, Bilcher, 1911	91	0·698

In the pyomas—that is, abscesses in connective tissue—there is some increased molecular concentration. Thus, the average concentration of the pyomas corresponds to ·836 per cent. NaCl, as against ·739 per cent. NaCl, the average of twelve non-inflammatory body fluids (Table B). This is in accord with what might be expected from experiments 1 to 10. It is in agreement with Ritter's cryoscopic results. But in the pyoceles, where suppuration takes place in some serous space, the tendency is all the other way, and the molecular concentration falls. Thus, the average concentration of six pyoceles corresponds to ·678 per cent. NaCl. The inflammatory serous collections which have not proceeded to suppuration show the same tendency to dilution.

The tension in pyomas, then, might be due to the hypertonicity of the pus, a difference of 0·1 per cent. being more than sufficient to produce all the pressure effects observed. But the tension in pyoceles must be due to a watery effusion into the pus from without. Perhaps this represents secretion, at any rate in the case of the cerebro-spinal fluid. Or it may mean increased permeability of the capillary walls, or else capillary leakage from increased intracapillary pressure as a result of vaso-dilatation. Probably more than one factor is concerned.

The action of the wall of the abscess remains to be considered.

It must act to some extent as a semipermeable membrane, otherwise differences of molecular concentration inside and outside could hardly be maintained. On the other hand, it does not partake of the nature of a *perfect* semipermeable membrane, for if so, toxæmia due to infusion of pus products would not take place. The abscess wall, then, usually acts as an imperfect semipermeable membrane.

Animal or vegetable parchments are imperfect semipermeable membranes, and to that extent may be taken to represent an abscess wall. In the following experiments the passage of sodium chloride through parchment under varying conditions of pressure

and concentration were studied. The results are only suggestive, they prove nothing, for the conditions only resemble those in the body to the extent that toxins are probably crystalloids (as is sodium chloride), and the abscess wall usually acts as an imperfect semipermeable membrane, as also does the parchment.

Experiment 11.—The bottom of a test-tube was replaced by parchment, which was hermetically sealed to the glass by means of paraffin wax. The test-tube was then suspended in a larger glass vessel. The concentration of the solutions inside and outside are expressed in terms of electrical conductivity (reciprocal megohms).

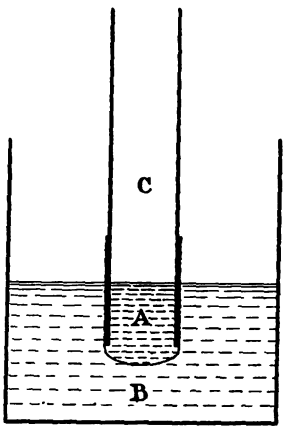

FIG. IV.

10 cc. of saline of a concentration of 31,333 units was placed in A.

150 cc. of slightly impure water of a concentration of 36 units was placed in B.

At the end of 12 hours the water in B had a concentration of 1,650 units. The level of A had risen slightly.

Experiment 12.—Experiment 11 was then repeated with exactly similar details, except that in C, above A, 5 inches of olive oil were placed, thus exposing the solution in A to a moderate

pressure. At the end of the 12 hours, the water in B had a concentration of 2,000 units. The level of oil had fallen slightly.

Experiment 13.—Experiment 11 again repeated with exactly similar details, except that a much more dilute solution was employed in A—one of 4,100 units. At the end of the 12 hours the water in B had a concentration of only 525 units. The level of A had risen very slightly.

From these experiments it seems clear that dilution of the solution in A (comparable to the pus in an abscess) means diminished leakage of the contained crystalloids, but that increased pressure means greatly accelerated leakage.

We wish to express our thanks to Mr. W. P. Digby and Dr. Boycott and Dr. Eyre for the use of their laboratories; to Dr. Wade and Dr. Hertz for advice; to Mr. E. G. Schlesinger for assistance with German papers; to Sister Theatres for help with sterilisation; and to the Resident Surgical Officer and many House Officers and others for their assistance. We are aware that some of our deductions rest on a very small bulk of evidence, and, with that reservation, submit the following—

SUMMARY.

(1) That acute suppuration is accompanied by local tension or pressure.

(2) That this pressure is evidenced by distension in loose tissues, or by compression in rigid compartments of the body.

(3) That this increased pressure is a factor in—

a. The local spread of suppuration.

b. The degree of toxic absorption.

c. The local pain and tenderness.

(4) That treatment aims at the relief of this tension.

(5) That all the processes in an abscess tend to increased molecular concentration and so tend to raise the osmotic pressure.

(6) That abscesses in connective tissue actually show some hypertonicity.

(7) That suppuration in serous spaces may, on the other hand, show hypotonicity.

(8) That the pressure of pus in pyomas may be due to raised osmotic pressure, but that in pyoceles it is probably due to an aqueous outpouring from the surrounding tissues.

(9) That an abscess wall usually acts as an imperfect semipermeable membrane; and, by analogy with another imperfect semipermeable membrane, probably allows increased leakage of contained solutes when either the concentration of the solution is increased or the pressure raised.

PONTINE HÆMORRHAGES.

By

H. L. ATTWATER, M.A., M.B., B.C.

As the basis of this paper on Pontine Hæmorrhages I have taken the clinical reports and pathological findings of the cases which have occurred at Guy's Hospital during the past 36 years —in all, 67 cases. I have divided the paper up into eight main sections, giving, first, a very brief sketch of the anatomy and physiology of the pons, so that the symptoms and signs which occur may be compared with those which might be expected to occur, according to experimental facts. The next section is devoted to a discussion of the diseases from which these patients have suffered, before they have shown any signs of a cerebral hæmorrhage, emphasising any factors which may cause a tendency to cerebral hæmorrhages in general. Next, a section of the paper is devoted to certain premonitory symptoms and signs which a few of these patients have shown for some considerable period before they have actually been struck down by the hæmorrhage into the pontine tissue. The next section attempts to show what have been the immediate causes of the hæmorrhages into the pons itself, in contradistinction to any other part of the brain. The next two sections are devoted to the clinical symptoms and signs of a case of hæmorrhage into the pons varolii, and the last two sections are devoted to the appearances that have been found in the post-mortem room.

The Anatomy and Physiology of the Pons Varolii.

The pons, being situated between the medulla oblongata and the mid-brain, must of necessity contain within its substance all those nervous tracts which are passing between the higher centres of the cerebrum and the lower parts of the nervous system. Furthermore, it contains several important nerve nuclei, which form intermediate cell stations in various tracts. All these nerve elements are exposed to injury or destruction from any disruptive lesion within the pontine substance, such as a hæmorrhage from a broken blood vessel. These nuclei and tracts will be discussed in order.

First, there are the nuclei of the third and fourth nerves. These are situated in the upper part of the pons, near its dorsal aspect, quite close to the aqueduct of Sylvius. Being situated here they do not seem so liable to injury as those nuclei which are situated lower down and nearer the middle of the pontine substance.

With regard to the fifth nerve nucleus, detailed description of this is not required, but, considering its ascending and descending roots, the motor and sensory portions, it occupies a position in practically every cross section of the pons, so that part of it is quite likely to suffer injury in a case of hæmorrhage, though it would have to be a very large hæmorrhage which would cause injury to the whole of the fifth nerve nucleus. A destructive lesion of the motor portion would cause paralysis and flaccidity of the muscles of the jaw, and a lesion destroying the sensory portion would cause anæsthesia of the same side of the scalp and face. Both of these symptoms will be noticed later.

The nucleus of the sixth nerve is sometimes injured, and should this occur there will be a paralysis of the external rectus muscle on the same side as the lesion.

In like manner the nucleus of the seventh or facial nerve, being situated quite close to the nucleus of the sixth nerve, is frequently subject to injury. If the facial nucleus be damaged, the ensuing paralysis affects the side of the face on the same side

as the lesion in the pons. If the nucleus of the eighth nerve be injured, then there will be signs of nerve deafness in the corresponding ear, and, owing to interference with the vestibular portion, there would be loss of power of maintaining equilibrium. Giddiness is a symptom which these patients complain of quite frequently, but it is rarely possible to inquire into such symptoms accurately, because these patients are usually rendered comatose and quite incapable of answering questions much too rapidly for an exhaustive research to be made into their subjective sensations. But the two components of the eighth nerve, namely, the cochlear and the vestibular divisions, are connected with nuclei which are in danger of injury in a case where the pons is widely lacerated with hæmorrhage. The cochlear division is apparently closely connected with the superior olive, a nucleus situated in the lower part of the pons; whilst the vestibular division is closely connected with Deiter's nucleus, which is also situated in the pons. Destruction of Deiter's nucleus would be liable to cause disturbance of equilibrium and also apparently some loss of tone in the muscles of the body. Another nucleus which is somewhat noticeable in cross sections of the pons is the nuclei pontis, situated anteriorly to the pyramidal tracts, amongst the transverse fibres of the trapezium. It is of quite unknown import, and is apparently an intermediate cell station in a collection of fibres passing from one cerebral hemisphere to the opposite side of the cerebellum. Another nucleus of importance, although it is not strictly pontine, is the so-called "red nucleus," situated in the region of the superior quadrageminal bodies, dorsal to the substantia nigra. Apparently it is a cell station in a large tract of fibres which pass from the cerebellum to the red nucleus by way of the superior peduncles, and thence down through the pons, medulla, and spinal cord as Monakow's bundle or the prepyramidal tract. The effect of section of Monakow's bundle seems to be a loss of tone of the muscles supplied by the corresponding pyramidal fibres. What is not at all clear is whether or not the red nucleus has within it the centre for the regulation of heat production or loss. Possibly the whole

question of temperature in these lesions is simply one of the state of activity of the body muscles. The discussion of this question will be left, however, until later.

Besides the nuclei in the pons, we have several important nerve tracts passing through its substance, connecting higher parts of the brain above with the spinal cord below, all of which are liable to irritation or destruction by a hæmorrhage occurring into this part of the brain.

The most important of these are the two pyramidal tracts, which, in this situation, are above their decussation, so that a lesion of the pons which is confined to one side and affects that pyramid only, will cause some form of paralysis on the opposite side of the body.

Another pair of equally important tracts are the fillets, which are responsible for the carrying of afferent impressions from the skin, etc., to the opposite cerebral cortex. A lesion which destroys the fillet on one side would cause anæsthesia on the opposite side of the body, though this symptom, again, is difficult to determine, because these patients are so often incapable of speech or deeply comatose.

The third nerve as it makes its exit through the substance of the mid-brain just above the pons is liable to injury. This sometimes occurs, causing paralysis of the corresponding eye muscles on the same side as that on which the nerve is injured.

The fourth nerve, as a rule, tends to escape injury, its course differing from that of the other nerves, so that it is out of the way of injury by any ordinary lesion in the pons.

There are also several other smaller tracts passing through this region. Of these, an important pair are the two posterior longitudinal bundles, which are situated close to the iter, and serve as commissural connections between the nuclei of the third, fourth and sixth cranial nerves, and also with the nerves of the spinal cord which are concerned in supplying the muscles which cause rotation of the head and neck. The posterior longitudinal bundle also has intimate connection with the eighth cranial nerve, and it is through this bundle that any loud noise stimula-

ting the eighth nerve causes conjugate deviation of the head and eyes to that side. If a pontine lesion causes destruction of the posterior longitudinal bundle, then there will be no conjugate deviation of the head and eyes, because the centres which are responsible for producing this complicated position are no longer connected up by the usual association of fibres.

The restiform bodies are simply the upward continuation of the direct cerebellar tract carrying afferent impulses from the lower parts of the spinal cord to the same side of the cerebellum by way of the inferior cerebellar peduncles. Their section causes symptoms of inco-ordination.

A great portion of the central part of the pons consists of a mass of transversely coursing fibres passing from one side across to the other, and dividing the pyramids up into bundles. They serve as connections between the two halves of the cerebellum, and their function is quite unknown. The fibres connected with the nuclei pontis also run amongst these transvers fibres, this nucleus being situated in their midst. Another portion of these transverse fibres has received a special name—the trapezium. Its fibres pass from the superior olive and trapezoid nuclei on one side of the pons across to the opposite side, and thence turn upwards to form connections with the nuclei in the region of the mid-brain. These nuclei and tracts are mainly concerned in conveying auditory impulses to the higher centres.

Of the two tracts conveying impulses from the spinal cord to the cerebellum, namely, the tract of Flechsig, or the direct cerebellar tract, and Gower's tract, or the indirect cerebellar tract, the former goes to the cerebellum by way of the inferior peduncles, whilst Gower's tract passes upwards through the pons to the cerebellum by way of the superior cerebellar peduncles, so that it is particularly liable to injury by a pontine hæmorrhage, the lesion giving rise to symptoms of inco-ordination.

As has been mentioned, the red nucleus, which is concerned in the maintenance of tone, is connected with the lower parts of the central nervous system by means of Monakow's bundle. These bundles are situated near the mid line in anterior sections

of the pons, but in more posterior sections they are situated laterally. They are therefore liable to injury, especially in the upper part of the pons, where they are situated in the middle of its substance. Should destruction occur, there would be loss of regulation of tone in the corresponding body muscles, and it has been found that lesions which advance high up into the pons are rather more prone to cause elevation of temperature than those occurring lower down, suggesting that when the tracts which regulate the condition of muscular tone are destroyed, then the temperature may rise owing to unregulated muscular activity.

In the upper part of the pons and mid-brain is a region called the tegmentum, which is merely the upward continuation of the formatio reticularis of the pons and medulla.

Age and Antecedent Illnesses in Relation to the Ætiology of Pontine Hæmorrhages.

Pontine hæmorrhage is a disease of middle and later life, its occurrence before thirty being exceedingly rare. It is also very rare after the age of sixty-five, the great majority of cases appearing between the ages of forty and fifty-five. The following is a table of the cases examined, showing the percentage of pontine hæmorrhages which have occurred in each decade of life between the ages of thirty and seventy:—

Age.	Percentage.
30—40	7·5
40—50	39
50—60	24
60—70	15

It is also much more common in the male sex than in the female; thus, of the cases recorded 78 per cent. have been found in males and the remaining 22 per cent. in females.

With regard to antecedent diseases in these patients, as a rule they have been fairly healthy individuals up to middle age, and have not exhibited any one disease in their early life which might be looked upon as being a marked factor in the causation of hæmorrhage into the pons Varolii. A few have

suffered from tuberculosis of one form or another, some having merely given a family history of phthisis, whilst others have shown signs of active tubercle in themselves; one case exhibited all the signs of Addison's disease, and at the post-mortem it was found that both suprarenal capsules were destroyed by masses of caseous material.

Syphilis also has occurred in about an equal number of cases. Epilepsy was present in a few cases. One of these appears to have had an epileptic seizure, and, having fallen from a considerable height, to have sustained a fracture of the base of his skull, as the result of which he got hæmorrhages into the pons. But apart from this sort of coincidence it does not appear that epilepsy is in any way a more predisposing factor in pontine hæmorrhages than either tubercle or syphilis.

A rather larger number of patients, about 7—8 per cent., gave a history of gout; two or three, also, had had attacks of lead poisoning. Both of these conditions may have been the primary cause of the chronic nephritis and arterial degeneration which had ultimately led to their having a cerebral hæmorrhage.

A much more potent factor in the antecedent history of these cases is alcohol. Thus, well over 20 per cent. gave either a history of having been excessive drinkers, or were found to be suffering from the effects of chronic alcoholism. Several had a marked degree of cirrhosis of the liver, which was either observed clinically or discovered at the autopsy. This shows that the individual who gets a pontine hæmorrhage does not differ in type to any great extent from one who is recognised as being prone to suffer from a cerebral hæmorrhage of any description; the patients are often big fat persons with short necks and heavy florrid features.

Recent worry was put down by one as the cause of his trouble. He was, however, suffering from a marked degree of arterio-sclerosis and granular kidney, and it is more than probable that his worry did no more than cause alterations of blood pressure, which, on one occasion, proved sufficient to cause a rupture of one of his pontine blood-vessels.

Antecedent Symptoms and Signs.

For a week or two before their hæmorrhage, a few cases have exhibited slight alterations in their mental character; a few of them complained of feeling very nervous and irritable; others appeared to suffer from considerable loss of judgment in business and in their ordinary occupations. Occasionally, for periods of varying duration before the hæmorrhages they have complained of a sensation of tingling or actual pain in the limbs, which were eventually paralysed by the hæmorrhage into the pons.

The majority of these patients appear to have suffered from the effects which are usually found with various degrees of arterio-sclerosis and granular kidney; a few are very anæmic, some are actually œdematous. Albumen has been found in the urine in well over 40 per cent. of all the cases investigated, being occasionally present in large quantities, but mostly in small amounts or as a slight trace. Various stages of albuminuric retinitis have been found, and one patient had been losing his sight from this cause for a week before his attack.

As in all cases of cerebral hæmorrhage following arterio-sclerosis and granular kidney, it is usually found that the tension of the pulse is considerably raised; furthermore, the arteries can be felt to be thickened, tortuous and unyielding, and in the post-mortem room it is almost a universal rule to find every degree of atheroma. This is especially well seen in the arteries situated at the base of the brain, because in this position the vessels are exposed to view in a thin sheet of pia mater.

The Immediate Causes of Pontine Hæmorrhages and the Positions of the latter in the Substance of the Pons.

Many of the cases of pontine hæmorrhage investigated have apparently occurred simultaneously with or, what is more probable, immediately following large cerebral hæmorrhages into the internal capsule. This seems especially liable to be the case where the hæmorrhage into the internal capsule has ruptured out of the cerebral substance into the lateral ventricles, both of which may be found to be full of blood clot. In these cases, the blood,

passing into the third ventricle and iter, may actually reach the fourth ventricle. Pontine hæmorrhages have also been observed apparently secondary to large meningeal hæmorrhages, which makes one suspect that the cause is the increase of intracranial tension caused by the rapid entry of a considerable quantity of blood into the closed cranial cavity.

The type of pontine hæmorrhage which occurs in these cases often differs somewhat from the ordinary primary type, which most often occurs as a definite hæmorrhage of considerable size into the substance of the pons, for it often happens that not one single hæmorrhage, but many small hæmorrhages are found, quite independent of each other. A single secondary pontine hæmorrhage is not unknown, and may itself burst its way out of the pontine substance either into the fourth ventricle, from which it may escape by bursting through the roof, and spreading over the base of the brain beneath the meninges; or it may force its way through the pontine substance into the subarachnoid space.

In some cases there was a recent history of injury to the head, usually the result of a fall. Some of the injuries were probably caused by the patient being rendered suddenly unconscious by the commencement of a cerebral hæmorrhage. What is interesting, however, is that two of these cases were known to be epileptics; one of them was seen to fall from a ladder, biting his tongue in the descent; the other also fell from a scaffold. On reaching the ground they both struck their heads. It was found at the post-mortem that both of them had fractured the base of the skull. One of them possessed only one kidney, which showed marked degrees of chronic nephritic change. In his case, therefore, his fall was probably the result of his hæmorrhage, especially as he also had a large hæmorrhage into one hemisphere, which may have been the primary lesion. The other, however, had absolutely healthy viscera, and he had always been a healthy man, except for the history of epileptic seizures, which had been occurring off and on for several years; his arteries were perfect, and there was absolutely no sign of any kidney change whatever. It seems fair, therefore, to conclude

that in the case of the latter, whilst he was on his ladder he had an epileptic fit, and falling, fractured the base of his skull. He fell, apparently, on to the back of his head, because there was a large occipital hæmatoma towards the left side. At the moment of impact there would be a sudden violent tendency for the brain and intracranial contents to move from the frontal region downwards and backwards towards the foramen magnum, because this direction is approximately opposite to the line of impact, and is in the direction along which the force of inertia would act; this would, of course, cause a considerable rise of pressure in the neighbourhood of the pons. If the shape of the brain be considered as a whole, it will be seen to be very roughly conical, and a force applied in the direction from base to apex, as described above, would be most felt in the region of the apex, where the pons is situated. The reason why the medulla does not suffer so much as the pons would seem to be its being situated nearer to the foramen magnum, so that it is afforded a means of escape from these sudden rises of intracranial tension.

There is apparently no doubt that a severe injury to the skull, if of sufficient violence, may cause a pontine hæmorrhage in an otherwise healthy individual. Thus, a young navvy working on the railway had his head smashed by the buffer of an engine, which killed him instantly. At the autopsy, the whole of the vault of the skull was found smashed into small pieces, and the brain beneath this was pulped and reduced to a structureless mass. The base of the skull, however, had escaped all injury, the pons and cerebellum, as far as external observation went, being apparently uninjured; but on making a section of the pons it was found to be full of punctiform hæmorrhages. In this case, at the moment of the impact between the buffer of the engine and the man's skull, the first event that would occur would be that the whole of the top of the skull would be forced inwards, compressing the intracranial contents. This would tend to force the brain violently out through the foramen magnum, and the pons being relatively more fixed than the neighbouring parts of the brain would be subjected to a sudden difference

of pressure and tension, which might very well be the cause of the laceration of the small vessels in its substance. Another example is that of a busman, whose horses were frightened by some event over which he had no control, and which caused them to bolt and throw him from his dicky to the ground, where he fractured the base of his skull. After death he was found to have several small hæmorrhages in the pons.

Pontine hæmorrhages, apparently caused by violence, tend to be multiple and to be distributed fairly uniformly throughout the pontine substance. This also suggests that the cause is in some way connected with changes of pressure, because when the intracranial tension is suddenly raised there is no reason why one part of the pons should suffer more than another.

With regard to the rapidity of onset of a case of pontine hæmorrhage, some cases advance with the utmost rapidity. The man has a hæmorrhage into his pons, falls down, and dies within half an hour, and at the post-mortem the pons is found to be totally disintegrated. It is obvious that a hæmorrhage into the pons, even though it is quite small, may yet contain within its limits many of the tracts which connect the higher centres in the brain to those lower down in the spinal cord. It will, therefore, cause much more severe, immediate, and profound disturbance than will the same sized lesion occurring in any other part of the brain except the medulla. The hæmorrhage may, however, be a very small one, and occur exceedingly slowly, probably in the first instance being an almost invisible speck. These cases may show symptoms of intracranial disturbance lasting over considerable periods; thus, they may first complain of headaches of greater or less severity, followed by the onset of giddiness and vomiting, which may go on for hours before the patient slowly drifts into unconsciousness, and finally dies. The relative proportion of cases which die rapidly in the course of minutes to those which last for hours or more is 1·32 to 1. Or, expressed in words, very rapid death is rather more frequent than partial recovery, or death after some hours or even days. It is from the less rapidly fatal cases that it is

possible to obtain information as to the patient's subjective symptoms. It sometimes occurs that after a patient has had a small hæmorrhage into the pons, with symptoms which have progressed to a greater or less extent, the hæmorrhage ceases to spread further, and the patient may recover with a partial paralysis or even without further symptoms, and continue to live for some considerable time longer. If an autopsy be made, the evidences of the old hæmorrhage will be found. These cases, however, are not very common, and the usual thing is that after a hæmorrhage into the pons the patient dies sooner or later in the first attack. Nevertheless, between 10 and 12 per cent. of the cases were found at the autopsy to exhibit signs of previous hæmorrhage into the pons. There may even be more than one of these old hæmorrhages in the pons, which have occurred either simultaneously or at different times. Occasionally where a history of illness was obtained from the patient or his friends, stating that he had been seized with an attack of coma and paresis some months or years previously, the pontine lesion which caused this attack was discovered at the post-mortem. In some of the acute cases the patients have been at their work, when they have fallen down quite unconscious and died within half an hour, almost before they could be taken to hospital.

The position of the hæmorrhage within the pons varies, no one spot appearing to be particularly susceptible, though mid-pontine hæmorrhages near the iter or fourth ventricle seem to be rather more common than hæmorrhages near the periphery.

Symptoms of the Attack.

This section is devoted to a discussion of the symptoms affecting the systems of the body, other than the nervous system, which occur in a patient actually suffering from a hæmorrhage into the pontine tissue. The hæmorrhage may be so severe as to be almost immediately fatal. The patient staggers, falls, rapidly becomes unconscious, and may be dead in the course of a few minutes. In these cases it is often very difficult to discover what has happened, as the patient may be universally paralysed

with widely-dilated pupils, and deep stertorous breathing, and practically nothing else can be made out about the case.

There are, however, many cases in which the hæmorrhage is initially small and advances slowly. In these cases it is possible to record symptoms, and even the subjective sensations of the patient, until he becomes unconscious. The progress of the hæmorrhage can be observed up till the time of death, when the clinical observations may be confirmed by a post-mortem examination.

Pain.—With regard to pain, it is seldom acute, but a few patients have complained of severe headaches for some hours before the appearance of further symptoms; and some, after the attack had commenced, complained of the very severe pain they felt in the head. In one or two cases severe lumbar or sub-costal pain was felt, but probably this was a mere coincidence; in one case, at least, the patient was found to be suffering from multiple aneurysms of the abdominal and thoracic aorta, and the pains did not coincide with any very definite nervous distribution.

Behaviour.—Another symptom which occasionally occurs is that the commencement of the attack is ushered in by a period of erratic behaviour. Thus, a carman, who was observed to be quietly driving his van, suddenly began to drive his horses wildly all over the place, and to sway from side to side in his dicky. Occasionally irritability of temper is a marked feature at the commencement of an attack, but, on the other hand, extreme drowsiness may be exhibited in the earlier stages of the malady, the patients rapidly becoming intensely lethargic, and eventually drifting into a condition of coma.

Coma.—Sometimes a patient will fall down unconscious, and a little later recover gradually, only to fall into coma once more after a period of longer or shorter duration. This is probably due to a small hæmorrhage, which immediately ceases to spread and causes momentary unconsciousness lasting for a short time, the patient then partially recovering, only to become comatose once more when the blood recommences to flow.

Falling down.—Sometimes whilst the patients are walking along the street they suddenly fall to the ground and are quite unable to get home or to a place of safety, though they remain quite conscious of all their surroundings.

Giddiness.—In others, again, the initial stage is still further prolonged. They complain of giddiness, and are obliged to cling to something for support, or they may even reach their homes, tell their friends that something is wrong and describe their sensations. Indeed, consciousness may persist for a period varying from a few minutes to hours or even, in a few cases, to days, during which the patients suffer from various more or less marked pareses, but are able to express their feelings and answer questions. More often they are only semi-conscious, and can only be roused by the strongest stimuli.

Convulsions.—When the attack begins with a general convulsion, the hæmorrhage is usually found at the post-mortem to be of great extent, and to be destroying a great part of the pons; or, what is just as common, is to find that the pontine hæmorrhage is secondary to a large hæmorrhage into the internal capsule. This type of case runs a rapidly fatal course. On examining these patients, it is often noticed that they belong to the "apoplectic" type, and have a suffused drunken appearance about the face.

Vomiting.—These patients often vomit a great deal during the course of the illness, and nausea and vomiting may be absolutely the first symptom of which they complain. Thus, one man vomited severely in the morning, but managed to do a day's work, at the conclusion of which he again began to vomit, and continued to do so for a considerable period after he had passed into a condition of coma. Vomiting occurs in about 15 to 20 per cent. of the cases, and is apparently due to irritation of the medulla. In a few cases, incontinence of fæces has been observed, but these patients are more often constipated.

Pallor and Coldness.—It may sometimes be noticed that these patients are exceedingly pale, and the surface of the body may feel cold; also, the patients themselves may complain of feeling

very cold, although the actual temperature is about normal. These vaso-motor disturbances, which are due to pressure on the vaso-motor centres, are of rare occurrence, and do not always affect the whole of the body. They may be unilateral or even confined to one limb, and differences of temperature can be recorded if the thermometer be applied to the surface of the skin in the several localities. If the centre for vaso-constriction be destroyed, then vaso-dilation, flushing, and a rise of the surface temperature will be noticed; whilst, on the other hand, if it is merely irritated vaso-constriction, pallor and a fall of the surface temperature will follow. Neither, however, are very common, but the irritative symptoms are perhaps the commonest.

Exophthalmos, proptosis.—In one case of severe pontine hæmorrhage there was the most marked double exophthalmos, and in another unilateral proptosis occurred. In the latter the pontine hæmorrhage had burst through the pontine substance, and passing forwards and upwards in the membranous space, had eventually pressed upon the cavernous sinus on the same side, causing congestion of the orbit and a pushing forward of the eye. In the former case the cause might either be congestion of the orbits owing to increased intracranial pressure, or it may have been a reflex nervous effect causing contraction of the muscle fibres in the capsule of Tenon.

The Pulse Rate.—Another interesting point is the rate of the pulse. Apparently, if the hæmorrhage be large and much pontine substance be destroyed, the pulse may be rapid, 120, 130, or more; occasionally it is most markedly irregular in rhythm, without any corresponding cardiac disease to account for the irregularity. Sometimes, on the other hand, the pulse rate is much diminished, and may fall as low as 36 beats in the minute; this is probably caused by direct stimulation of the vagal centres in the medulla, and will occur if there be much pressure from hæmorrhage in the neighbourhood. It is most frequently associated with those cases in which there is a large initial cerebral hæmorrhage into the internal capsule, and in which the intracranial tension is raised as a whole. In cases

in which the hæmorrhage into the pons is small and not much destruction has occurred, the pulse rate is not disturbed.

Respiration.—Stertorous breathing occurs in about 40 per cent. of the cases, and is due to the falling together of a paralysed tongue and soft palate, which causes the usual loud snoring noise with each respiration. It indicates that the hæmorrhage is causing paralysis as low as the twelfth cranial nerve. The rhythm of respiration varies a good deal in cases of this character; in some, instead of being noisy and stertorous it is feeble and shallow, and may be of a particularly irregular character. If there be much increase of the intracranial tension, so that the medulla is compressed, the respiration rate will often be much reduced (10—12 per minute). This is most common where the pontine hæmorrhage is of great size, or is secondary to a large capsular hæmorrhage. If there be much obstruction to respiration from paralysis of the tongue and palate, the patient may suffer from lack of efficient respiratory exchange, and will become cyanosed. When the respirations become feeble and shallow, and the pulse is beginning to fail, there is a tendency for the fluid secretions to accumulate in the lungs, giving rise to multiple moist sounds in the chest; and in a few cases this sodden lung has become infected with micro-organisms and pneumonia has supervened as a terminal event. Another respiratory phenomenon which occurs in a good many cases, and is often associated with increased intracranial tension and deficient aëration of the blood, is Cheyne-Stokes' breathing.

Incontinence of Urine.—Urinary symptoms are uncommon; about 12 per cent. of the cases had incontinence of urine, and a few of these both of urine and fæces. The cases in which these symptoms occur are, as a rule, of the rapidly fatal kind, and it may be regarded as an exceedingly grave symptom. Of this 12 per cent. of the cases, eight were associated with large cerebral hæmorrhages situated initially in one or other internal capsule.

Glycosuria.—Glycosuria occurred in two cases.

Sweating.—Sweating occurred in about 10 per cent. of the cases; sometimes of the whole body, and sometimes of the paralysed side. It is probably due to stimulation of the sweat centre in the medulla by the pressure of the adjacent hæmorrhage. General sweating is probably often due to the condition of profound shock into which these patients fall.

Pyrexia.—Pyrexia is a very interesting symptom of this disease, and has often been looked upon as one of the diagnostic features of the condition. So far from this being the case, it has only been observed to occur in some 20 per cent. of the cases recorded. Below are two tables, in one of which the high temperatures are recorded, and in the other the abnormally low temperatures. Against these are placed the nature of the pontine lesion, and the condition of the muscles found in each case, because it is thought by many that the whole phenomenon is to be explained by the supposition that the lesion in the pons injures or irritates certain fibres which control the amount of tone and activity of the muscles, and consequently the output of heat from this source.

Case.	T. (Fahrenheit).	Size and Position of Pontine Lesion.	Condition of Muscles.
1	102	Large upper mid-pontine, implicating pyramids	Not recorded.
2	103	Large mid-pontine	Not recorded.
3	103·8	Large mid-pontine	Spastic.
4	101·4	Large mid-pontine	Not recorded.
5	107	Large mid-pontine	Spastic.
6	108·2	Large pontine, destroying pyramids	Spastic.
7	107	Very large pontine	Increased tone.
8	103·6	Multiple	Slight universal movements
9	106·2	Large pontine	Spastic, constant movements.
10	107·8	Large pontine	Convulsions.
11	108	Mid-pontine	Spastic.

From this it would appear that if there is a large mid-pontine hæmorrhage which irritates the pyramids, and at the same time the fibres which regulate the degree of tone of the muscles, probably those of Monakow's bundle, then the temperature of the patient will rise.

Case.	T. (Fahrenheit).	Size and Position of Pontine Lesion.	Condition of Muscles.
1	97	Large double pontine causing total destruction of substance	Fibrillary contractions of all muscles.
2	96·2	Small upper pontine passing into crusta	Flaccidity.
3	95·6	Large upper pontine; right greater than left	Clonic convulsions at commencement. Loss of tone left side.
4	Below 95	Small right pontine	Spasticity left side.
5	95·4	Two small pontine situated on one side	Slight spasticity opposite side.
6	97	Lower dorsal right pontine ...	Fit.

From this table we see that the opposite effect is by no means as certain; apparently, if there be absolute total destruction of the pontine contents, then the temperature will fall, though in the first case it was maintained at a little below normal by the fibrillary contractions of the muscles. From an examination of the rest of the table it will be noticed that all the hæmorrhages in this table, except the first, which has been discussed, are unilateral, leaving one side of the pons to convey controlling impulses by way of Monakow's bundle and the pyramids, which will prevent any undue rise of temperature from the increased tone of the muscles on the paralysed side. There is also reason to believe that not only may this actually prevent any rise of temperature, but that by throwing the non-paralysed limbs into a condition of flaccidity there may be an actual over correction, and the temperature may fall below normal. If the shock be severe, then there is, as in all cases of shock from whatever cause, a marked tendency for the temperature to become subnormal.

Symptoms Presented by the Nervous System.

The next section of the paper is devoted to a continued description of the symptoms of a case of pontine hæmorrhage, and deals in particular with those which are found on examining the central nervous system.

Vertigo.—These patients frequently complain of feeling exceedingly giddy, a feeling which may last for some time before unconsciousness supervenes. That this might be expected to

occur is at once obvious, if it be remembered that the vestibular nerve and its controlling nuclei are often injured in cases of hæmorrhage into the pons, Deiter's nucleus being especially concerned in these cases.

Deafness.—Sometimes the patients are quite deaf in the ear which corresponds to the lesion due to injury of the corresponding cochlear division of the eighth nerve.

Dysarthria.—Aphasia in a pure case of pontine hæmorrhage does not exist; if it occurred, then a left-sided cerebral lesion was present on every occasion. But what happens very often is that the patient seems to understand what is said to him, though he is quite unable to make himself intelligible, because of the paralysis of the lips, tongue and palate.

Coma.—Unconsciousness occurs in practically every case. It supervenes at an earlier or later period according to the degree of severity of the hæmorrhage into the pontine substance. One case alone of those investigated apparently remained conscious right up till the moment of death. The condition is, of course, due to the enormous disturbance caused by even a small hæmorrhage into a region which contains practically all the important communications between the higher centres and the rest of the nervous system.

Cranial Nerve Paralysis.—A pontine hæmorrhage is apt to affect certain of the cranial nerves, and the first of these to be considered is the third or motor-ocular nerve. An important feature in these cases is the size of the pupils, which are usually constricted and practically pin-point in size. This is due to stimulation of the constrictor fibres of the iris. These are innervated from the third nerve, which is more often irritated than destroyed. Quite a small hæmorrhage into the pons is sufficient to cause the pupils to become pin-point, although it may be situated quite close to one side of the mid-line, and may only cause actual stimulation of one centre; nevertheless, owing to the two oculo-motor centres being connected so closely by association fibres, both pupils usually respond to a stimulus of either. Of course, it often happens that the hæmorrhage into the pons is not uni-

lateral, but spreads across to the opposite side, or is situated in the mid-line, with the result that the centres of both third nerves are stimulated, causing both pupils to be constricted. In some cases the pupil on the side of the lesion was constricted as above, but the opposite pupil was of medium size, and behaved normally. This may have been because the hæmorrhage had injured the connection between the two centres situated on opposite sides of the mid-line.

If one side of the pons be absolutely reduced to pulp and destroyed, and the other side injured, but not exterminated, then there will be a large dilated pupil on the side on which the lesion has destroyed the nucleus of the third nerve, whilst on the opposite side there will be a pin-point pupil from irritation of its nucleus.

If there be a large hæmorrhage into the internal capsule, then, as a rule, the pupil is found to be dilated on the side of the hæmorrhage without there being necessarily much destruction of the pons. Suppose that there is a small progressive hæmorrhage in the left side of the pons, the first thing that will be noticed about the eyes is that the left pupil has become pin-point, a little later the right pupil also contracts; as the hæmorrhage progresses and advances towards the right side, the next thing that happens is that the left pupil dilates as soon as the pons on the left side is destroyed, and if the right side of the pons be destroyed, then the right pupil will dilate also.

Sometimes when the hæmorrhage is very violent, and usually just before death, both pupils are equal in size, widely dilated, and fixed. If this occurs, there is, as a rule, much destruction on both sides of the pons, and the patient is almost certain not to recover consciousness.

Ptosis occurred in three cases, in which the hæmorrhage filled very nearly the whole of the pons; in one of these the ptosis was on the opposite side to the hæmorrhage. This may occur either in cases of paralysis of the third nerve, or as the result of paralysis of the muscle fibres in Tenon's capsule and the upper eyelid, which are supplied by the sympathetic, in the same

manner as stimulation of these fibres may cause exophthalmos. It is a rare symptom, and was only noticed in about 4 per cent. of the cases.

Any of the ocular muscles may be thrown out of action by damage to the nerves supplying them, causing squints. The third and sixth nerves are the two most frequently involved; these paralyses are, however, uncommon.

Another ocular symptom which sometimes occurs is nystagmus, either in the vertical or horizontal plane. This, again, is a very rare symptom, and it is not always easy to be sure of its presence. Occasionally conjugate deviation of the head and eyes to one side or the other is noticed, and very often at the autopsy these cases are found to be associated with a primary capsular hæmorrhage. The symptom does occur, however, in pure cases of hæmorrhage into the pons, but in these cases the deviations are in the opposite direction to those which occur with a hæmorrhage into the internal capsule.

Thus, with a left capsular hæmorrhage causing right hemiplegia, the deviation will be to the left in paralysis, but to the right during spasm, whilst in the case of a left pontine hæmorrhage causing a right hemiplegia, the deviation will be to the right during paralysis and to the left during spasm. The reason why the head and neck and both eyes all share in these movements is that the nucleus of the nerve supplying the external rectus muscle of the eye on one side, and the nucleus supplying the internal rectus muscle of the opposite eye and the centres for rotation of the head, are all closely connected by association fibres, and the deviations in a case of pontine hæmorrhage are opposite to those which occur in a case of capsular hæmorrhage, because the sixth nerve in the pons is below its decussation, so that injury causes paralysis on the same side as the lesion.

In a few cases the fifth or trigeminal nerve has been found torn and destroyed by the hæmorrhage, which has ploughed up the pons. The effect of this is to produce anæsthesia on the same side of the face, but as the hæmorrhages which produce these lesions are necessarily severe, the patients are usually

unconscious, and anæsthesia is not apparent. The paralysis of the fifth nerve attracts notice sometimes from the fact that the corresponding cornea becomes insensitive, cloudy, and œdematous, whilst there is a loss of corneal reflex on this side. Also, if the motor portion be involved, the masseter and pterygoid muscles will become paralysed and the jaw will fall.

The facial nerve is almost always involved in cases of pontine hæmorrhage, and the ensuing paralysis of the face, being due to an infranuclear lesion, occurs on the same side as the lesion in the pons, and on the opposite side to the paralysis of the body, a condition usually spoken of as "crossed paralysis." A definite crossed paralysis at once places the lesion in the pons, with a few exceptions which will be indicated later. As an example, suppose there is a left flaccid paralysis of the trunk with a right facial paralysis, whilst at the same time the right side of the body shows irritative symptoms, then there will be a right pontine hæmorrhage, destroying that side of the pons and spreading towards the left, causing irritative symptoms on the right side of the body. An interesting case is described in the *Revue Neurologique* by Delini, in which the fibres of the facial nerve which supplied the lower half of the face alone were destroyed, whereas usually the whole face is affected. Possibly in this patient the facial fibres which supplied the upper part of the face followed an abnormal course.

If the hæmorrhage is in the superior part of the pons or crura, it may give rise to a supranuclear lesion of the facial nerves before the fibres have decussated. In this case the facial paralysis and the paralysis of the trunk will be on the same side, opposite to the lesion in the pons. Irritation of the facial nerve manifests itself by twitchings of the lips, cheek or eyelids.

The twelfth nerve, though situated in the medulla rather below the pons, is often paralysed through involvement of its supranuclear fibres. In these cases the paralysis is, as a rule, on the same side as the lesion in the pons, which would seem to indicate that the pons is below the decussation of the twelfth nerve fibres.

With regard to the ordinary superficial reflexes, it is found that almost as soon as the patient loses consciousness these are in abeyance; thus the conjunctival, abdominal and cremasteric reflexes disappear, and if the soles of the feet be stimulated, as a rule there is no response.

If the hæmorrhage be of any size, the pyramidal tracts are usually involved at once, either on one or both sides, sometimes suffering total destruction; though, apparently, the blood tends to make its way in between the individual fibres without actually breaking them, causing signs of irritation. Again, one side of the body may be spastic, whilst the other side is flaccid without any corresponding lesion to account for the flaccidity. This is probably due either to the loss of tone which occurs in all unconscious persons, or to the influence of Monakow's bundle. Again, if the hæmorrhage causing the spasticity progresses to complete pyramidal tract destruction, the muscles will lose their tone and become flaccid. Thus spasticity may be followed by flaccidity, and the opposite side may, in its turn, become first spastic and then flaccid, until both sides of the face and trunk become atonic and paralysed, owing to the complete destruction of both sides of the pons.

The muscles of the trunk, such as the abdominal muscles, may become rigid during the irritative stage, and the abdomen may, in a few cases, become retracted and assume the scaphoid form as in the cases of meningitis.

It is occasionally quite difficult to account for the hemiplegia, the pontine hæmorrhages being so small and not being situated near the pyramids. Death may even occur where the lesions are so small as only to give rise to slight irritative symptoms. As a rule, however, in cases of pontine hæmorrhage it is not difficult to account for the cause of death. Irritative symptoms, such as spasticity and twitchings alternating with periods of quiet and flaccidity, were marked in about 20 per cent. of the cases, frequently lasting till within a few minutes of death, and occasionally so exaggerated as to appear as actual convulsions.

Anæsthesia of the paralysed side is noticed occasionally, but a lesion in the pons which destroys the fillet is generally a large one, so that, as a rule, these patients are unconscious, making it impossible to demonstrate the anæsthesia. The knee jerks may be present and equal on both sides; in these cases the lesion in the pons is small and not situated near the pyramidal tracts. With a unilateral hæmorrhage only, the jerk on the opposite side to the lesion may be exaggerated, but if both pyramids be irritated, both jerks will be exaggerated. If, however, one pyramid be absolutely destroyed, then the opposite knee jerk will be absent, and occasionally in severe cases this condition is bilateral. Where the destruction of the pyramids is not complete, the plantar reflex is usually extensor, either unilaterally or bilaterally according to the size and position of the hæmorrhage in the pons.

In company with increased jerks and Babinski's sign it may be possible to elicit ankle-clonus, though this is rare. If it occurs there is, as a rule, a primary hæmorrhage in the internal capsule with a secondary pontine hæmorrhage. In the severer forms the irritative symptoms due to pressure on the pyramidal tracts manifest themselves either in fibrillary contractions, usually associated with complete ploughing up of the pontine substance, or as twitchings of individual muscles, or as convulsions either of a single limb or even of the whole body.

Pathological Appearances apart from the Intracranial Lesions.

The pathological conditions which are found in connection with the circulatory system will now be considered. Almost without exception in those cases which occurred as the result of the bursting of an atheromatous artery the heart was much hypertrophied, especially as to the left ventricle. In 12 per cent. of the cases there was marked atheroma of the mitral valves and in a few actual stenosis. Most of these cases of mitral stenosis were associated with a granular condition of the kidney. In a few cases the coronary arteries were markedly athero-

matous; a part of the general systemic arterial degeneration, which was found to be present in over 60 per cent. of the cases, was often most apparent in the small vessels at the base of the brain. Occasionally aneurysms have been found. One case had both a thoracic and an abdominal aneurysm, and his pontine hæmorrhage was possibly the result of a burst cerebral aneurysm. In this particular case there was a history of syphilis about 14 years before. Two of the cases were found to have widely adherent pericardia, and in one the heart was discovered to be markedly fatty.

Sometimes where the hæmorrhages in the pons were multiple, this condition was merely a part of a general tendency to minute extravasations of blood; thus, one of these was a case of fatal septicæmia in a child of 14 years who had acute nephritis with sloughing and ulceration of the tonsils. She had had chronic nephritis for over a year, and was the only case investigated which was under the age of 20.

With regard to the pathological conditions which were noted in the respiratory system, 6 per cent. of the cases were found to possess signs of old or recent tuberculous disease, either in the lungs or elsewhere; in one case, as mentioned above, the suprarenal capsules were caseous and practically destroyed, as the result of which the patient was suffering from a marked degree of Addison's disease. Some of these cases had been the subject of chronic bronchitis for many years, and were found to be markedly emphysematous, and in a few the signs of antecedent pleurisy were discovered; but, bearing in mind that the majority of these patients are well on in middle life, they do not seem to be particularly prone to illness, and most of the viscera were, as a general rule, remarkably healthy, apart from the arterio-sclerosis and renal conditions. One case, which remained alive for a week after the onset of his hæmorrhage, was found post-mortem to have considerable areas of broncho-pneumonia in the lungs. This was probably a terminal infection of the lungs, which were becoming waterlogged from a tendency to respiratory failure. In one case primary sarcoma of the bronchial glands was discovered.

Well over 60 per cent. of the cases exhibited various degrees of granular kidney, and this appears on every hand to be the most potent antecedent condition in these cases; a few of these kidneys also showed cystic changes of a more or less advanced type. There were two cases in which the kidneys were almost destroyed by growth or aneurysm. The generative organs were healthy, as a rule, only one case of ovarian cyst being recorded.

Intracranial Pathological Conditions.

A few cases showed cerebral softening of a date considerably prior to the occurrence of the pontine hæmorrhage; probably, therefore, these lesions took no part in the production of the lesion in the pons. One case showed considerable thickening and fibrosis of the meninges over the motor area, possibly due to the marked degree of arterio-sclerosis which was present, because he had shown no untoward symptoms, except a transient attack of unconsciousness two years previously, apparently due to a small hæmorrhage into his internal capsule, of which traces were found at the post-mortem. It happens frequently that in addition to the recent pontine hæmorrhage, traces of several previous hæmorrhages are found situated in various parts of the brain, the most common places being the internal capsules and basal ganglia.

In about 30 per cent. of the cases there was a small secondary pontine hæmorrhage with a large primary hæmorrhage into the internal capsule, which had caused considerable local destruction, and then, bursting into the lateral ventricle, had flooded the whole of the ventricular system. In some of these cases the hæmorrhage was not quite so extensive, but was confined to the lateral ventricles. These primary capsular hæmorrhages had occurred with almost equal frequency on the two sides, so that there did not seem to be any greater tendency for a hæmorrhage on one side more than the other to produce a secondary pontine lesion. In fact, a pontine hæmorrhage may apparently be secondary to any large hæmorrhage occurring anywhere within the cranium; thus, it was found with a large hæmorrhage in the

frontal lobe, or in the sphenoidal lobe, or even occasionally with a large meningeal hæmorrhage which, in one case, was responsible for considerable destruction of one optic nerve.

Occasionally the pontine hæmorrhage is but an instance of many hæmorrhages occurring simultaneously throughout the brain. One interesting case was that of a patient who had perforated his orbit with the spoke of an umbrella, and had lacerated his ethmoid sinus, causing a large hæmorrhage into the anterior and middle fossa, with a secondary hæmorrhage into the pons. The converse phenomenon of a small cerebral hæmorrhage in the internal capsule occurring secondarily to a large pontine hæmorrhage was found in only one case. In one case, also, where there was a very large pontine hæmorrhage there were two small secondary hæmorrhages situated one in either crus, possibly caused by the tension set up by the big hæmorrhage close by.

Twelve per cent. of the cases of pontine hæmorrhage appeared to be the direct result of severe injuries to the skull, causing in most of them fracture of the base. Of these, four apparently occurred as the result of falls caused by the patient being rendered unconscious by a big hæmorrhage into his internal capsule. In the remaining eight cases, however, the injury to the base of the skull appears to have been the initial lesion, the patient having been injured through no fault of his own, and there being no reason found which might be supposed to predispose him to hæmorrhage. The injuries causing these hæmorrhages were not necessarily confined to the base of the skull; thus, a pontine hæmorrhage was discovered in a case where the vault of the skull had been badly smashed.

With regard to the pontine hæmorrhages themselves, they often begin on one side, and then, spreading slowly, destroy more and more of the pontine substance, first on one side and then on the other, until ultimately the whole pons is disintegrated. Sometimes the blood had spread back into the medulla, but did not seem to have destroyed the vital centres, as their function was carried on till the last; many cases, however, died of failure of respiration.

Frequently the hæmorrhage was not confined to the pons, but, having burst its way into the fourth ventricle, filled it, and having burst through the roof, had become a submeningeal hæmorrhage, spreading over the cerebellum and base of the brain; it may also pass up the aqueduct of Sylvius to the third ventricle. At other times it passed straight into the subarachnoid space by bursting out laterally through the pontine substance. The fourth ventricle may contain blood from two sources: first, it may have descended from the lateral ventricles, flooded by a large hæmorrhage into the internal capsule which has burst into them; or secondly, it may be filled by blood which has burst straight into it from the pons. Sometimes a pontine hæmorrhage ruptures straight into the aqueduct of Sylvius, and then spreads upwards and downwards into the third and fourth ventricles respectively. These ventricular hæmorrhages may be of any extent, from a complete flooding of all the cavities to a small hæmorrhage confined to the fourth ventricle. As a rule, it is rare for much blood to reach the lateral ventricles from the hæmorrhage into the pons, which usually bursts, and escaping beneath the membranes, ceases to pass upwards into the ventricular system. It is clear, therefore, that the cases of hæmorrhage into the internal capsule, which seem most likely to cause a secondary pontine lesion, are those which first destroy the internal capsule and then burst into and flood the ventricular system.

In some cases, where the hæmorrhage into the pons or internal capsule was extensive, but had failed to burst into the ventricular system, nevertheless, the ventricles have been found to be filled with an excess of blood-stained fluid; the cause of this is undetermined, but may be due to congestion of some of the vessels near the ventricles by the pressure of the hæmorrhage upon them.

Sometimes two hæmorrhages, one on each side of the pons, or two in one half, or even many at the same time, apparently commence quite independently of each other. When the hæmorrhages in the pons are multiple, they vary in size from mere

ecchymoses of any number to perhaps two or three relatively large hæmorrhages. They often occur as a group of small hæmorrhages situated in the middle of the pons near the iter. Where the cause of the hæmorrhage into the pons has been a cranial injury, then the pontine hæmorrhages are rarely single, but tend to be multiple, punctiform in size, and to be distributed equally throughout the pontine substance. The condition of multiple punctiform pontine hæmorrhage is determined apparently by a very sudden change of pressure within the cranium. One case reported in France in the *Revue Neurologique* is that of a young man who fell off a scaffold, and did no actual bony injury to the skull, but was found to have punctiform hæmorrhages throughout his pons. As has been mentioned, multiple hæmorrhages in the pons may be but a part of a general tendency to hæmorrhage, as in an acute case of septicæmia or nephritis. The diagnosis of multiple pontine hæmorrhages is almost impossible, as there will be no definite localising symptoms.

Summary.

It remains to recapitulate the main points which have been mentioned above. It has been shown from anatomical and physiological considerations that hæmorrhages into the pons might be expected to cause paralysis of certain cranial nerves, and also if the hæmorrhage be unilateral it will cause a paralysis of the same side of the face as that on which the lesion occurs, and of the opposite side of the body. It is also clear that, owing to the small size of the pons and the great number of important structures within it, the disturbance produced by even a small hæmorrhage will be exceedingly profound, causing with great rapidity wide-spread paralyses and a condition of the deepest coma. The great majority of cases of pontine hæmorrhages die in the first attack after a longer or shorter interval, but evidence of old antecedent pontine hæmorrhage has been found in a few cases. Again, owing to the involvement of Monakow's

bundle, there is often considerable disturbance of muscular tone, and should Monakow's bundles be destroyed and the pyramidal tracts stimulated, then the corresponding muscles will become markedly spastic and even convulsed if the irritation be sufficiently severe. This will give rise to a considerable increase in the muscular heat, and consequently the temperature of the patient will rise. But if one side of the pons be intact, then the opposite side of the body will become markedly hypotonic, causing a diminution of muscular heat on that side, and correcting the increased output of the spastic side of the body. Further, if the whole pons be destroyed, then, owing to total loss of muscular tone there will be a fall of the patient's temperature. It has been noticed that in those cases in which the temperature has risen, the lesion often injures the anterior part of the pons, where Monakow's bundles are most exposed to injury, and that signs of irritation of the pyramidal tracts, such as spasticity and tremors, are present.

The only antecedent conditions which predispose a patient to an attack of pontine hæmorrhage are those which might cause any kind of cerebral hæmorrhage, namely, alcoholism, arteriosclerosis and granular kidney. Other diseases also occur, but are too infrequent to be important.

There appear to be two other main causes of hæmorrhage into the pons itself. First, any large intracranial hæmorrhage —most often one which, situated in the internal capsule, has burst into the ventricular system—may cause a rise of intracranial tension and a secondary pontine lesion. In these cases there are two factors, the increase of intracranial pressure and the degenerate condition of the arteries in the pons. Secondly, a severe blow on the head, which is usually sufficiently violent to fracture the base of the skull, may cause a pontine hæmorrhage in an otherwise healthy individual owing to the sudden changes of tension set up in the neighbourhood of the pons.

Pontine hæmorrhage is a disease of middle life, affecting more men than women, and, as a rule, the patients are remarkably healthy right up to the time of the hæmorrhage.

With regard to symptoms, perhaps the most common clinical picture is as follows: The patient suddenly has an attack of giddiness and vomiting, followed by unconsciousness; on examination, paralysis of one side of the face and of the opposite side of the trunk may be discovered, or even a total flaccid paralysis of the whole body; the superficial reflexes will have disappeared, and one or both pupils will have become pin-point in size. The pulse rate varies a great deal, but the arterial tension is usually high, the respirations are deep and stertorous, and evidence of chronic nephritis may be obtained from the discovery of albumen in the urine. Further, as explained above, the temperature of a few of these patients is raised. Finally, the patient frequently dies as a direct result of failure of respiration.

No particular portion of the pons appears to be especially susceptible to hæmorrhage, but perhaps rather more hæmorrhages occur in the centre of the pons near the iter than towards its periphery. The hæmorrhage often ruptures into the fourth ventricle or into the submembranous space. In the former case it may also reach this space by bursting through the roof of the fourth ventricle, or may pass upwards through the iter into the ventricular system.

The most important pathological conditions found in the rest of the body are those which are due to the granular condition of the kidneys and the arterial degeneration. By far the most important of these is the hypertrophy of the left ventricle of the heart.

SUMMARY OF NOTES OF THE 67 CASES.

Case 1. Male, aged 35, under Dr. Hilton Fagge, admitted September 13th, 1882 (Ref. No. 94).—He gave a doubtful history of syphilis and rheumatism, and was much addicted to alcohol. He had had two previous fits, after the second of which he had been unable to work for two years, having a slight right hemiplegia. He had suffered from pain in head for 3—4 years. After a feeling of slight nausea he had a severe fit, and became rapidly unconscious, with laboured, puffing respiration. He lay motionless, but his reflexes were present, and the arms were

somewhat rigid. Sugar was found in the urine. The day after admission the temperature rose to 102·2° F., and pulse was 130 and respiration 45. He died on the second day after admission.

Post-mortem.—Adherent pericardium. Two old pontine hæmorrhages. A large recent hæmorrhage into the mid-upper pontine region bursting into the fourth ventricle and thence through the iter to the third and lateral ventricles. The blood had also escaped beneath the membranes into the interpeduncular space.

Case 2. Male, aged 40, admitted into Clinical, November 11th, 1883 (Ref. No. 106).—Gave a history of alcohol. He had fallen on to his head a few days before admission. The day before admission he was sick, but drove his van eighteen miles out and then back. He then began to feel very ill, and was thought to be drunk at 5.30 p.m. Next day, on admission, he was partially conscious, and moving the right arm and leg. The eyes were closed, and there was slight nystagmus of the left eye (the right eye squinted downwards and inwards), the right pupil was dilated and the left constricted. There was a right facial paralysis. He was constipated, and his temperature was 101·2°, his pulse 72, and respiration 28. He had convulsive twitches of the right side. On November 12th his temperature was 103·4°, and he died 3 days after admission. His right cornea became clouded before death.

Post-mortem.—Vessels degenerate and kidneys granular. There was blood clot in right side of pons and also in left. The blood had escaped out of the pons on the right side into the submembranous space, and had damaged the 3rd, 4th, 5th, 6th, and 7th cranial nerves.

Case 3. Male, aged 84, admitted January 23rd, 1884, into Clinical (Ref. No. 119).—He was a cashier and became unconscious whilst at work. On admission he was comatose, his pupils were constricted and his breathing stertorous and jerky. He died shortly after admission.

Post-mortem.—Liver cirrhotic, and heart was hypertrophied and vessels were bad. The pons was filled with clot which extended into the medulla, and the ventricles of the brain were filled with blood-stained fluid.

Case 4. Male, aged 50, admitted on January 2nd, 1884, into Clinical (Ref. No. 120).—Gave a history of alcohol. Two hours before admission he began to lose his speech and could not protrude his tongue. On admission he was semiconscious, and was paralysed on the right side of the face and trunk, his pupils were pinpoint, and the head and eyes were turned to the left. He was vomiting, and his breathing was stertorous, and he had incontinence of urine. Four hours after admission his left leg and arm became rigid, and he became deeply comatose and died of respiratory failure.

Post-mortem.—Degenerate arteries. A large hæmorrhage into the left corpus striatum, which had burst into the ventricular system. The pons was full of multiple hæmorrhages of sizes varying from mere ecchymoses to the size of a small pea.

CASE 5. Male, aged 50, admitted December 23rd, 1885, under Dr. Taylor (Ref. No. 102).—He fell down and vomited. On admission he was comatose, his head was turned to the left, and the pupils were somewhat contracted. There was a right hemiplegia, and tremors of the right sterno-mastoid, the right arm and both legs were observed; these lasted for from one to two minutes and occurred frequently. His left knee-jerk was brisk, and the superficial reflexes had disappeared; his abdomen was retracted, and he had incontinence of urine. He vomited continually, and gradually the right side of his body became flaccid. Death occurred in a few hours from respiratory failure. Just before death the left pupil first constricted and then dilated.

Post-mortem.—Bad vessels; albuminuria; and hypertrophied heart. Hæmorrhage into the left corpus striatum and lateral ventricles, and blood-clot in the fourth ventricle. There was a small hæmorrhage near the posterior cornu of the right lateral ventricle and in the motor part of the pons. There were signs of old hæmorrhages in the right optic thalamus.

CASE 6. Male, aged 55, admitted November 20th, 1885, under Dr. Taylor (Ref. No. 104).—Gave a moderate alcoholic history. He had had tingling for three weeks in his right leg, which had become weak two days before admission. On the day of his admission he fell down and became drowsy, vomited and complained of pain all over the head and back of neck. On admission he had a right hemiplegia and pinpoint pupils; his pulse was slow (48), and he was sweating. At first he improved, but later got worse, his breathing being stertorous, and finally he became deeply comatose and died a week after admission.

Post-mortem.—Growth of left kidney; aneurysm of septum interventriculorum of heart. There was a left meningeal hæmorrhage which was passing along the sheaths of the optic nerve. There was a cavity filled with blood-clot under the left orbital lobe. There was a recent small pontine hæmorrhage.

CASE 7. Male, aged 44, admitted November 5th, 1885, into Clinical (Ref. No. 83).—Gave an alcoholic history, and had had a left hemiplegia eighteen months before admission. He was a big man, and on the day of admission he had a convulsion, became comatose, and passed both his urine and fæces unconsciously. On admission he was stertorous, his head and eyes were turned to the left, his pupils were pinpoint; later on an external strabismus of the left eye was noticed. There were convulsive movements of the flexors of the right fore-arm; the right knee-jerk was absent; there was a complete right-sided paralysis of the face and trunk; and albumen was found in the urine. Temperature, 97·6°; pulse, 56; respiration, 32.

Post-mortem.—Multiple hæmorrhages in the lungs, a hypertrophied heart, and cystic kidneys. There was an extensive hæmorrhage into the left internal capsule, which had ruptured into the ventricular system. There were two small recent pontine hæmorrhages situated in the mid-line about the size of a big pin's head, and traces of an old hæmorrhage of about the same size which had probably caused his hemiplegia eighteen months before. Weights: brain, 55 oz.; heart, 26½ oz.

CASE 8. Female, aged 44, admitted February 15th, 1886, under Dr. Pitt (Ref. No. 74).—The day before admission she felt faint, and had pain and twitching of the left eye. On admission the right arm was weak, and speech was difficult. She was drowsy, and the right side of tongue and face were paralysed; there was also some weakness of the right leg. The right pupil was dilated, and there was vertical nystagmus. Anæsthesia of the right side was present; she got steadily worse, and died after seven days.

Post-mortem.—Bad vessels; mitral stenosis; pneumonia; and granular kidneys. There were old hæmorrhages: (1) the size of a pea in the left centrum ovale, passing upwards and forwards into the corpus striatum; (2) a cyst in left lenticular nucleus; (3) two cysts in the right pyriform nucleus. There was a recent hæmorrhage which was pulping most of the pontine substance, rather more so on the right side than the left, and passing up into the right crus for a quarter of an inch and backwards into the whole half of the mid-cerebellar region. This hæmorrhage seemed to arise from a small old hæmorrhage in the lower posterior part of the pons.

CASE 9. Male, aged 51, admitted October 9th, 1887, into Clinical (Ref. No. 111).—Gave a history of alcohol. He had suffered from a right hemiplegia for eighteen months before admission, and during this period he had had two attacks of unconsciousness. He had also been troubled with headaches, misty vision, and loss of judgment. The day before admission he had a convulsion and became comatose, and his right side was seen to twitch; he was admitted, and died in the course of an hour or so.

Post-mortem.—Bad vessels. A large hæmorrhage in left frontal lobe and a small one of antecedent date on the right side. There was a single secondary pontine hæmorrhage.

CASE 10. Female, aged 44, admitted July 13th, 1887, under Dr. Pye-Smith (Ref. No. 79).—She had lumbar pain and phthisis for some time. She suddenly became unconscious, preceded by ptosis of the left eye. On admission she was comatose and breathing stertorously; her temperature was 103·8°, and her left side was spastic. Three hours after admission the conjunctivæ were insensitive, but an hour later became sensitive.

Three hours later, again, she became deeply comatose, and had incontinence of both urine and fæces, and died.

Post-mortem.—Tubercular disease of the lung was discovered, and a large pontine hæmorrhage.

CASE 11. Female, 52, admitted July 24th, 1891, under Dr. Goodhart (Ref. No. 79).—She had had a great deal of recent worry, and had been paralysed for a few days before admission, and had also been aphasic. On admission she was drowsy; and the head and eyes were turned to the left. There were occasional movements of the left leg. The right side of the body was paralysed, and seemed to be anæsthetic. She had incontinence of both urine and fæces. She rapidly got worse, with stertorous breathing and deep coma, and finally died. Albumen was found in the urine.

Post-mortem.—Bad vessels, and a large pontine hæmorrhage.

CASE 12. Female, aged 40, admitted July 14th, 1893, into Clinical (Ref. No. 81).—She suddenly became deeply comatose. On admission she showed various signs of syphilis; she was vomiting and stertorous; and her arms were flaccid. The left leg was spastic, and the pupils were constricted. She rapidly died of cardiac failure.

Post-mortem.—Showed an hypertrophied heart, and very advanced granular kidneys. The vessels were very bad. There was a very large hæmorrhage in the midst of the pons, reaching up into both crura, and nearly down as far as the medulla. There was a small secondary hæmorrhage in one lenticular nucleus.

CASE 13. Male, aged 40, admitted November 28th, 1894, under Dr. Taylor (Ref. No. 352).—Gave a history of epilepsy. Became suddenly unconscious. On admission, was pale, with stertorous breathing, 12 per minute. The knee-jerks were much exaggerated, but the limbs were flaccid. Both pupils were dilated and fixed. He rapidly died of respiratory failure.

Post-mortem.—The heart was hypertrophied, and both lungs were engorged. The left kidney was absent and the right was granular. There was a large hæmorrhage in the left hemisphere coming from the anterior part of the external capsule, and passing into the lateral ventricles through a small hole above the caudate nucleus. The lateral and fourth ventricles contained a small amount of blood-clot and blood-stained fluid. There was a large hæmorrhage in the anterior part of the pons bursting its way into the iter.

CASE 14. Male, aged 45, admitted March 23rd, 1896, under Dr. Washbourn (Ref. No. 124).—Patient had been nervous lately. On the day of admission he was suddenly seized with vomiting, and became comatose.

On examination, the right pupil was constricted and the left was dilated: his respirations were stertorous, and he had bitten his tongue; his pulse was 70. Both knee-jerks were much exaggerated, and albumen was present in the urine.

Post-mortem.—His vessels were bad, and a large pontine hæmorrhage was found.

CASE 15. Male, aged 60, admitted February 15th, 1896, into Clinical (Ref. No. 108).—Patient thought he was going to have a fit, and became unconscious on his way up to the hospital. On admission his respirations were stertorous and 15 per minute. The limbs had occasional attacks of spasticity, and both knee-jerks were rather brisk. He was somewhat cyanosed. His pupils were fixed, and the left was constricted; the right was medium in size, and oval in shape. He had a convergent strabismus, and his conjunctival reflex was absent. He died twenty minutes after admission.

Post-mortem.—Bad vessels. Submucous hæmorrhage at the lower end of ileum. Several superficial extravasations in the brain, and a large hæmorrhage in the pons, more extensive on the right side than on the left.

CASE 16. Male, aged 43, admitted April 27th, 1896, into Clinical (Ref. No. 213).—At 9 a.m. patient fell and became unconscious. At 1 p.m., after admission, he was in a comatose condition, with no superficial reflexes; his pupils were constricted, and his temperature was 100°F. His respirations were stertorous and jerky; his pulse was 80 per minute. Albuminuria was found. He died at 6 p.m., with a temperature of 101·4° F.

Post-mortem.—General arterial degeneration, and a large pontine hæmorrhage passing into the fourth ventricle.

CASE 17. Male, aged 44, admitted May 31st, 1899, under Dr. Pye-Smith (Ref. No. 175).—He gave a history of gout, gonorrhœa, and of a "liver" attack. He was also addicted to alcohol, and had been suffering for some time from loss of strength and from œdema of the legs. He was admitted for plumbism and chronic interstitial nephritis. For five weeks he had felt very weak and had been short of breath, suffering from a bad cough. His sight had been failing for eight days. On admission he was very anæmic, a blue line was seen on the gums, and his liver was enlarged. His vessels were thickened and tortuous, and his pulse tension was raised; his heart was hypertrophied, and his legs were œdematous. Albumen was found in the urine. A fortnight after admission he suddenly vomited, and had a left-sided convulsion, followed by a left-sided paralysis. His right pupil was larger than the left. In the course of the next few hours he had two more of these seizures and became comatose. His pupils were equal and fixed, and the conjunctivæ became insensitive, and he finally died.

Post-mortem.—Bad vessels. An old hæmorrhage into the right internal capsule and a more recent one into the left internal capsule. A large pontine hæmorrhage, the right side being more extensively damaged than the left.

CASE 18. Male, aged 63, admitted August 6th, 1901, under Dr. Hale White (Ref. No. 266).—He was found unconscious in the street. His respirations were stertorous and of the Cheyne-Stokes' variety. His pulse was irregular, and his pupils were constricted.

Post-mortem.—A pontine hæmorrhage was found.

CASE 19. Female, aged 39, admitted July 27th, 1901, into Clinical (Ref. No. 424).—She suddenly had a fit, and rolled her eyes and threw herself about. On admission she was comatose and had double exophthalmos; her right hand was twitching and being occasionally moved up to the head. Her face, arms, hands, nipples and thighs were pigmented. Her pulse was 150 per minute and irregular, and she was cyanosed; her respirations were stertorous. Her pupils were constricted, and the conjunctival and superficial reflexes were absent. She was spastic all down the right side, and the head was turned to the right side. She died quite suddenly.

Post-mortem.—Aortic atheroma and dilated heart. The suprarenal bodies were caseous and calcareous. The pons was occupied by a large clot which had completely destroyed it.

CASE 20. Male, aged 43, admitted October 10th, 1901, into Clinical (Ref. No. 580).—His father died of fits. He himself was alcoholic, and had lived very badly, and was greatly troubled with asthma. He suddenly became unconscious and was admitted. He was lying on his left side, which was motionless except the wrist. The right side showed marked fibrillary contractions of the muscles. His breathing was stertorous and of the Cheyne-Stokes' variety, and there were many moist sounds in the chest. The pupils were small, the left being somewhat larger than the right, and both reacted to light. His corneal reflexes were present, and the left knee-jerk was brisker than the right. He died in a few hours.

Post-mortem.—The pons was found practically destroyed by a double pontine hæmorrhage.

CASE 21. Male, aged 56, admitted May 9th, 1902, under Dr. Hale White (Ref. No. 177).—Patient had had anthrax twelve years before. Two years before his attack he had a transitory left hemiplegia, which completely cleared up in the course of a short interval. He swayed and fell down, and felt very cold. On admission he was conscious, and his eyes were open and his head was turned to the right. His articulation was imperfect, but he could answer questions. The skin of the right

arm was flushed and sweating, and the abdomen was very rigid. His pupils were much constricted, and the muscles of the jaw were paralysed, allowing the jaw to fall. The right side of the tongue was paralysed; the right side of the body was quite flaccid and the left somewhat weak. Babinski's sign was present on the right side, and the right knee-jerk was somewhat increased. Albumen was present in the urine; temperature, 99·2°; respiration, 24; pulse, 84. He died after a few hours.

Post-mortem.—Vessels bad. Thickened pleura at both apices, and atheroma of the mitral valve of the heart. The kidneys were granular. There was considerable thickening of the meninges over both motor areas, and traces of two old hæmorrhages, one in each lenticular region. There was a recent hæmorrhage in the lower left pontine region, and also one in the tegmentum. The fourth ventricle contained blood.

Case 22. Male, aged 57, admitted September 20th, 1902, under Dr. Hale White (Ref. No. 323).—There was a family history of phthisis. The patient complained of pain in the right side, and had incontinence of urine. On admission he was unconscious; temperature, 96·2°; pulse, 60; respiration, 24. He was flaccid, especially on the left side. His breathing was stertorous and of the Cheyne-Stokes' variety. The pupils were fixed, the right being dilated and the left contracted. His plantar reflex was extensor on both sides, and his knee-jerks were absent. His vessels were hard and tortuous. Two or three hours later he was sweating and his face was flushed. Retinal hæmorrhages were seen. He rapidly sank and died.

Post-mortem.—The thoracic viscera were markedly jaundiced, and the liver was cirrhotic. He had a large meningeal hæmorrhage, chiefly confined to the base of the brain over the pons and both dorsal and ventral aspects of the cerebellum. There was a pea-like hæmorrhage in the crusta, spreading back into the pons. The lateral ventricles were full of sanguineous fluid, and there was blood in the third ventricle and iter.

Case 23. Male, aged 70, admitted May 2nd, 1904, into Clinical (Ref. No. 299).—Patient stated that several members of his family had died from thoracic diseases. He himself was gouty, and had led a very rough life, having passed through four wrecks and a fire at sea. On March 1st, 1902, he was drinking, when he had sudden pains in the forehead. and he felt his muscles twitch; he became very giddy and fell. He became unconscious, and was paralysed down the left side. He was admitted under Sir Cooper Perry (Ref. No. 94), and slowly recovered. He was aphasic, the left side of the face was twitching whilst the right side was paralysed. His tongue was tremulous. The abdomen felt hotter on the left side than on the right. He had incontinence of urine. He almost completely recovered in three weeks, and went out with a slight facial paralysis on the right side. On the day of his re-admission he was walking along when he staggered and became unconscious. On admission

he was vomiting, and his respirations were stertorous and of the Cheyne-Stokes' variety. His limbs were somewhat rigid. At first his pupils were fixed, the right being greater than the left; later on both were dilated. His temperature was 99° F. He rapidly died.

Post-mortem.—Bad vessels. Cardiac vessels atheromatous; kidneys granular. There was some external hæmorrhage on the ventral aspect of the right side of the pons, extending to the crusta and optic chiasma. This came from a pontine hæmorrhage which had ruptured straight through the pontine substance. There was an old hæmorrhagic cyst in the posterior part of the right lenticular region.

CASE 24. Male, aged 45, admitted October 16th, 1903, into Clinical (Ref. No. 677).—Was a very heavy beer drinker. He had been drinking until 12.30 a.m., when he went to bed. Next morning he went to work, and at 11 a.m. suddenly became unconscious. On admission, his pupils were pinpoint, and his reflexes were absent. His respirations were slow and shallow, and much albumen was found in a catheter specimen of urine. He lived for a few hours, during which time he had five attacks of tremor in the legs.

Post-mortem.—Bad vessels; granular kidneys; cirrhosis of liver. A pontine hæmorrhage greater on the right side than the left, and a subarachnoid hæmorrhage over the cerebellum and under the pons; the blood had escaped from the fourth ventricle, which in turn had been filled from the pontine hæmorrhage. His heart was hypertrophied, and there were signs of old phthisis in the lungs.

CASE 25. Female, aged 48, admitted November 13th, 1903, into Clinical (Ref. No. 744).—Had always suffered from headaches, which were very severe the day before admission. She suddenly became giddy and unconscious, and was first of all paralysed down the right side; later on both sides became paralysed. There was ptosis of the right eye, and the pupils were pinpoint and fixed. Her knee-jerks were brisk, the right more so than the left, and ankle clonus and extensor plantar reflexes were found on both sides. She was breathing stertorously, and lived for a few hours, during which interval her temperature rose to 107° F.

Post-mortem.—The cardiac vessels were atheromatous, and the heart was fatty. The kidneys were granular. The pons was largely destroyed by a hæmorrhage more on the left side than the right. The blood was oozing from the pons on the left side, and had burst into the aqueduct of Sylvius and thence into the fourth ventricle.

CASE 26. Male, aged 46, admitted March 21st, 1906, into Clinical (Ref. No. 176).—This patient was driving a van when he suddenly fell, but was caught before he reached the ground. On admission he was comatose, and exhibited occasional clonic convulsions of the right arm and hand. He was very cold, and his breathing was stertorous; he was markedly

cyanosed, and had incontinence of urine. He had a left hemiplegia and right facial paralysis, and his left knee-jerk was absent. The right corneal reflex was absent, and the pupils were unequal and constricted, the right being greater than the left. He died shortly after admission.

Post-mortem.—Bad vessels; hypertrophied left ventricle of the heart; granular kidneys. There was a hæmorrhage into the upper right pontine region spreading over towards the left side.

Case 27. Male, aged 59, admitted November 30th, 1907, under Dr. Hale White (Ref. No. 527).—He became faint at work, and rapidly became unconscious. On admission, temperature, below 95°; pulse, 52; respiration, 24. His abdomen was rigid, and his breathing was difficult and of the Cheyne-Stokes' variety. All his limbs were spastic, and Babinski's sign was present on both sides. The pupils were fixed, the left being constricted and the right dilated.

Post-mortem.—There was blood which had escaped from the fourth ventricle on the under surface of the brain and between the frontal lobes. There was considerable softening of the cerebral substance near the clot. The ventricles were all occupied with blood-clot, and the right caudate nucleus was destroyed by hæmorrhage. There was a small hæmorrhage into the right pontine region. The vessels were bad, and the heart was hypertrophied; and there were signs of old phthisis in the lungs. Both kidneys were granular. Weights: brain, 1,931 gms.: heart, 384 gms.; liver, 1,329 gms.; spleen, 107 gms.; kidneys, 206 gms.

Case 28. Male, aged 65, admitted November 4th, 1908, under Dr. Pitt (Ref. No. 417).—He became unconscious at 5.30 p.m. He had marked scoliosis. On admission, the right side was spastic and the left flaccid. The right side of his face was paralysed. His pupils were both pinpoint. Temperature, 97·4°; pulse, 72; respiration, 24. At 8.15 p.m., temperature, 102·4°. Venesection was performed, causing movements of both legs on incision. At 9 a.m., temperature, 108·2°, and he died.

Post-mortem.—Bad vessels and hypertrophied heart. Kidneys granular. There was a hæmorrhage into the left side of the pons just anterior to the fourth ventricle. Weights: heart, 478 gms.; kidneys, 234 gms.

In the following cases the particulars were obtained from the post-mortem reports :—

Case 29. Male, aged 40, admitted December 21st, 1875; died December 22nd (P.-m. 506).—He had had a rheumatic attack three years before, and had been suffering from Bright's disease for three months. He became suddenly unconscious, and was muttering to himself, and could with great difficulty be got to answer questions. On admission, there was ptosis of the left eye and external strabismus, and both pupils were constricted. The next day he was conscious in the morning, but in the evening he gradually drifted into coma and died.

Post-mortem.—The vessels were bad. The lungs were emphysematous. The heart was hypertrophied, and the mitral valve was calcareous. The kidneys were granular. There was a small superficial blood cyst on the left side of the floor of the fourth ventricle. There was a pontine hæmorrhage on the right side and rather posterior. The third nerves were apparently uninjured. Weights: brain, 53 oz.; heart, 14½ oz.; liver, 53 oz.; kidneys, 9 oz.

CASE 30. Female, aged 60, admitted January 22nd, 1879; died January 22nd, 1879 (P.-m. 27).—At 2 p.m. she stopped work, and became paralysed down the right side. At 3 p.m. she was spastic on the right side, semi-conscious, and aphasic. At 9 p.m. she was comatose and breathing stertorously. The left pupil was larger than the right. There was no facial paralysis, and the arm was no longer spastic. Her pulse was 44 per minute. She died at 11.20 p.m.

Post-mortem.—Granular kidneys, and left ovarian cyst. The brain was flattened, and the left hemisphere was full of blood-clot. The right lateral ventricle was full of blood-clot, but the left one was empty. There were two small hæmorrhages in the upper part of the pons. Weights: heart, 15 oz.; kidneys, 7 oz.

CASE 31. Male, admitted March 10th, 1879 (P.-m. 92).—He had a fit at 2.45 p.m., but remained conscious; he was quite unable to walk. On admission he was collapsed, but could answer questions. He was sweating, and had cold extremities, and he was vomiting. There was a left facial paralysis and there was a left-sided paralysis, which was most marked in the legs. The left pupil was constricted and the right dilated. He died suddenly, apparently without becoming unconscious first.

Post-mortem.—Granular kidneys. There was a large hæmorrhage into the right corpus striatum, and the ventricles were full of blood-stained fluid. There was also a hæmorrhage into the middle of the pons. Weights: heart, 13 oz.; kidneys, 7 oz.

CASE 32. Female, aged 63, admitted November 11th, 1879 (P.-m. 423).—She walked into the hospital and first of all refused to stay, but did so eventually.

Post-mortem.—The kidneys were granular, and the vessels were bad. Sugar was present in the urine. There was a fracture of the base of the skull running from before backwards and passing through the foramen ovale. There was a left-sided meningeal hæmorrhage and bruising of the brain above the fissure of Sylvius. There was a large pontine hæmorrhage.

CASE 33. Female, aged 49, admitted August 22nd, 1880 (P.-m. 304).—She had had chronic nephritis for two years. Her articulation became imperfect on August 17th, and she had a fit on August 22nd. She was

sweating, and the left arm was first of all flaccid, but afterwards it became spastic. She became comatose, and remained so for a day and then died.

Post-mortem.—Vessels bad and kidneys granular. The left lateral ventricle was dilated, and the right corpus striatum was softened. There was a hæmorrhage in the right mid-pontine region which apparently did not injure the pyramidal tracts. Weights: heart, 12 oz.; liver, 39 oz.; spleen, 3 oz.; kidneys, 6 oz.

Case 34. Male, aged 56, admitted June 8th, 1882 (P.-m. 159).—Patient gave a history of gout. On the day of admission he had a fit, but there were no definite pareses. On admission, the pulse was slow and strong; the respirations were laboured; and the temperature was 97° F. Albumen was present in the urine, and he died in the course of half an hour.

Post-mortem.—Vessels were bad, and the kidneys were granular. There was a hæmorrhage in the right lower dorsal pontine region passing upwards into the crus and downwards into the cerebellum, where there was a large cavity. It had also ruptured into the fourth ventricle, and the lateral ventricles were full of sanguineous fluid. Weights: brain, 60 oz.; heart, 19 oz.; liver, 85 oz.; spleen, 9 oz.; kidneys, 9 oz.

Case 35. Male, aged 46, admitted June 12th, 1882; died October 16th, 1882 (P.-m. 305).—Patient contracted syphilis 14 years before admission. He was admitted for lumbar pain, and was found to be suffering from an abdominal aortic aneurysm. Albumen was found in the urine. He remained alive for four months, and then suddenly died. Retinal hæmorrhages were seen.

Post-mortem.—The heart was hypertrophied, and there was an abdominal aneurysm excavating the twelfth dorsal and first lumbar vertebræ. There was also an aneurysm of the innominate artery, and the subclavian and carotid arteries were full of hard blood-clot. The abdominal aneurysm had almost destroyed the left kidney. There was a large pontine hæmorrhage which was infiltrating between the fibres, and damaging both pyramidal tracts. It was situated just above the medulla, and was bulging into the fourth ventricle. Weights: brain, 46 oz.; heart, 16 oz.; liver, 59 oz.; kidneys, 10 oz.

Case 36. Male, aged 62, admitted August 9th, 1883; died October 3rd, 1883 (P.-m. 343).—This patient had had ascites for three years, and had been a pronounced alcoholic. Albuminuria was present. On August 17th he was troubled by severe diarrhœa, which, however, got better. On August 21st a systolic apical bruit made its appearance. On September 4th his liver was found to be one and a half inches below the costal margin, and on the 21st, blood, in addition to albumen, was found in the urine. On October 1st he fell downstairs and injured the right side of his head; after this he slowly became comatose, and died on October 3rd.

Post-mortem.—Heart valves were thickened, the vessels were degenerated. and the kidneys were granular. There were small recent meningeal hæmorrhages over the right frontal region, over right temporo-sphenoidal lobes, and over the occipital cortex. There were signs of old hæmorrhage in the posterior part of the tail of the lenticular nucleus, and two small old hæmorrhages in the pons. Weights: heart, 13½oz.; kidneys, 9½ oz.

CASE 37. Male, aged 42, admitted November 27th, 1883; died February 28th, 1884 (P.-m. 77).—He was admitted for ascites and anasarca, from which he had suffered for two years. He gave a history of old urethral stricture, and of gout and alcohol. Albumen was found in the urine. He progressed more or less well until February 28th, when he awoke in the morning and felt stiff, and immediately became comatose, with a constricted pupil on the right side. He died in the course of an hour or so.

Post-mortem.—Degenerated vessels; hypertrophied left ventricle of the heart. The capsule of the liver was thickened, and the kidneys were granular, and had had recent acute inflammation. There was a hæmorrhage into the left crus which had made its way back into both sides of the pons, and had also ruptured out of the pons into the fourth ventricle. Weights: brain, 45 oz.; heart, 14½ oz.; liver, 67 oz.; spleen, 6 oz.; kidneys, 8½ oz.

CASE 38. Male, aged 53, admitted August 5th, 1884; died August 8th, 1884 (P.-m. 254).—He had been a painter for 5 years, and had had two attacks of lead colic. Two years before admission he had a convulsion with slight paresis. For sixteen days before admission he had been suffering from headache and vomiting, and on August 2nd he was found lying unconscious on the ground. On admission, on August 5th, temperature, 100°; pulse, 106; respiration, 28. He was hemiplegic down the right side, and had a left facial paralysis. His pupils were minutely contracted, the right being slightly larger than the left. His superficial reflexes were absent, and his breathing was stertorous. On August 6th he developed a paralysis of the right side of his tongue, and had to be fed with nasal tubes. On August 8th, temperature, 105·2°; pulse, 145; respiration, 42. Albumen was present in small quantities in the urine, and the pupils were most minutely contracted. His respiration was of the Cheyne-Stokes' variety. The temperature rose to 107° F. at the point of death.

Post-mortem.—Kidneys granular and cystic. There was a hæmorrhage into the left side of the pons extending right forward into the crus. Weights: brain, 51 oz.; heart, 16½ oz.; kidneys, 8 oz.

CASE 39. Male, aged 61, admitted March 10th, 1886; died March 10th (P.-m. 90).—He had a similar attack three months ago, but recovered. At 8.45 p.m. he staggered and fell. At 9 p.m. he was pale, and

breathing stertorously. Mucous was dribbling from his mouth, and there was slight œdema of his legs. He moved all his limbs spontaneously and reflexly, but facial paralysis was observed. His pupils were minutely constricted. At 9.5 p.m. the right pupil had dilated, and at 9.20 p.m. both pupils were dilated; further, the left side became spastic, and little later the right. At 9.30 p.m. he was quite flaccid, and at 9.35 p.m., after an interval of some respiratory irregularity, he died of respiratory failure.

Post-mortem.—Bad vessels; hypertrophied left ventricle of the heart; and granular kidneys, with a deposit of urates. There was about two ounces of recent blood in a cavity in the right centrum ovale outside the basal ganglia. Also there were three or four small recent clots in the right corpus striatum. There was also a fair-sized hæmorrhage in the upper half of the pons which had burst its way into the fourth ventricle. There were traces of old hæmorrhage in the left optic thalamus. Weights: brain, 55 oz.; heart, 20½ oz.; spleen, 9 oz.; kidneys, 12 oz.

Case 40. Male, aged 44, admitted April 1st, 1886; died April 1st, 1886 (P.-m. 119).—He fell down twenty steps, and was found lying unconscious at the bottom. His pupils were dilated, and he was bleeding from the nose and left ear. There were moist sounds all over the chest.

Post-mortem.—Atheroma of the mitral valves. The base of the skull was fractured on the left side, involving the middle ear. The brain was much bruised and covered with subarachnoid clot. There was a small pea-like hæmorrhage in the mid-pontine region. Weights: brain, 51 oz.; heart, 14 oz.; liver, 62 oz.; spleen, 2 oz.; kidneys, 11 oz.

Case 41. Male, aged 50, admitted and died April 15th, 1886 (P.-m. 131).—He had a severe fall, and became comatose, stertorous, and died.

Post-mortem.—The kidneys were not granular, but there was some atheroma of the coronary arteries. The base of the skull was fractured, one fissure running from the left side of the internal occipital protuberance to the foramen magnum, and another from the right jugular foramen towards the foramen magnum, which it partially encircled. There was blood-clot over both frontal lobes, and several small hæmorrhages into the pons and both crura. Weights: heart, 14½ oz.; liver, 62 oz.; kidneys, 15 oz.

Case 42. Male, aged 36, admitted and died May 25th, 1886 (P.-m. 177).—He had perforated the inner angle of the left eye with an umbrella spoke, opening up the ethmoidal sinuses and causing a meningeal hæmorrhage. He was found to have a small pontine hæmorrhage. The rest of the viscera were absolutely healthy.

Case 43. Male, aged 76, admitted July 19th, 1886; died July 21st (P.-m. 243).—He was admitted comatose, with contracted pupils and

slight paralysis of the right cheek. There were movements of the left side of the body. Temperature, 97·8°; pulse, 74; respiration, 28. He steadily sank and died.

Post-mortem.—Vessels bad. Signs of old pleurisy and emphysema. The pericardium was adherent, and the left ventricle of the heart was hypertrophied; the kidneys were granular. There was a large pontine hæmorrhage rather more on the left than the right, extending into the crus in front and almost back to the medulla. Weights: brain, 49 oz.; heart, 14 oz.; liver, 39 oz.; spleen, 2 oz.; kidneys, 9 oz.

CASE 44. Female, aged 50, admitted and died May 26th, 1887 (P.-m. 141).—No report on clinical condition or antecedent history.

Post-mortem.—The kidneys were granular. There was a hæmorrhage into the internal capsule on the right side, and also one into the right side of the pons near the iter. There were signs of an old hæmorrhage into the right side of the pons.

CASE 45. Male, aged 40, admitted and died June 20th, 1887 (P.-m. 172).—Unconscious. No history or clinical record.

Post-mortem.—The kidneys were granular. There was a hæmorrhage into the left internal capsule, and also a small hæmorrhage into the pons. Weights: brain, 57 oz.; heart, 14 oz.; liver, 51 oz.; spleen, 3 oz.; kidneys, 8½ oz.

CASE 46. Male, aged 54, admitted and died July 28th, 1887 (P.-m. 231).—He was unconscious and breathing stertorously; his pulse was 70 and the temperature 103·6° F., and there were slight movements of all the limbs. The left pupil was dilated and the right contracted.

Post-mortem. — Bad vessels. Hypertrophied heart, especially left ventricle. Granular kidneys. A hæmorrhage into the left internal capsule, and several small mid-pontine hæmorrhages, especially on the left side. Weights: brain, 53 oz.; heart, 23 oz.; liver, 62 oz.; spleen. 6 oz.; kidneys, 9 oz.

CASE 47. Male, aged 70, admitted and died February 1st, 1888 (P.-m. 30).—He had fallen out of a cart. His pupils were contracted; and ankle clonus was present on both sides. His pulse was 60 per minute, and his respirations of the Cheyne-Stokes' type. The left pupil dilated before death.

Post-mortem.—Bad vessels and old mitral regurgitation. Primary sarcoma of the bronchial glands. There was a fracture of the base of the skull on the left side and a hæmorrhage into the left internal capsule. The pons was filled with ecchymoses. Weights: brain, 51 oz.; heart, 14½ oz.; liver, 58 oz.; spleen, 3½ oz.; kidneys, 11 oz.

CASE 48. Male, aged 40, admitted and died February 22nd, 1888 (P.-m. 60).—There was a long history of fits. He fell 22 feet on to his head, and was picked up bleeding from the mouth, having bitten his tongue. There was a large hæmatoma in the left occipital region.

Post-mortem.—There was a fracture of the left occipital region causing rupture of the middle meningeal artery. There were several small hæmorrhages in the floor of the fourth ventricle affecting the nuclei of the sixth and seventh nerves on the right side. Also there were hæmorrhages in the mid-pontine and tegmental regions. The rest of the viscera were absolutely healthy.

CASE 49. Male, aged 40, admitted and died April 19th, 1889 (P.-m. 155). —He felt giddy, but walked some way before he fell down and vomited. He became unconscious with a right hemiplegia, and had incontinence of urine. His pupils were contracted; he died shortly after admission from respiratory failure.

Post-mortem.—Vessels bad; hypertrophied heart; granular kidneys. A large hæmorrhage into left internal capsule, which had burst into the lateral ventricle and had flooded the whole ventricular system. In addition there were several small mid-pontine hæmorrhages. Weights: brain, 53½ oz.; heart, 20½ oz.; liver, 71 oz.; spleen, 5 oz.; kidneys, 9½ oz.

CASE 50. Male, admitted and died May 7th, 1889 (P.-m. 174).—He was knocked down by a van and wounded in the occipital region. On admission he was comatose, with a pulse of 40 per minute, and spasticity on the left side. The left pupil was contracted and the right dilated.

Post-mortem.—Cirrhosis of liver. Old mitral valve disease. Several ribs were fractured, and the pleuræ were covered with ecchymoses. The base of the skull was fractured, tearing the dura and causing considerable hæmorrhage which had torn the pons. In addition there were several small hæmorrhages in the pontine substance possibly caused by splinters of bone. Weights: heart, 11 oz.; liver, 59 oz.; kidneys, 10 oz.

CASE 51. Male, aged 54, admitted and died May 18th, 1889 (P.-m. 188).—He suddenly staggered, fell, and became unconscious. On his admission he was generally flaccid, and his pupils were equally constricted. A short while afterwards he became generally rigid; both pupils dilated; and he died.

Post-mortem.—Bad vessels; hypertrophied left ventricle of heart; and granular kidneys. There was a very large hæmorrhage into the left internal capsule which had burst into and flooded the whole ventricular system. There was a small hæmorrhage into the left side of the pons. Weights: brain, 51 oz.; heart, 11½ oz.; liver, 57 oz.; spleen, 3 oz.; kidneys, 8 oz.

CASE 52. Male, aged 27, brought to hospital dead October 1st, 1890 (P.-m. 368).—He was a navvy, and was working on the line when the buffer of an engine struck his skull, and killed him instantly.

Post-mortem.—All viscera were healthy except the head. The whole of the vault of the skull was smashed to small pieces, and the brain beneath it was pulped and disintegrated. The base of the skull had, however, escaped injury, and the pons and cerebellum appeared uninjured. The pons, however, was full of many punctiform hæmorrhages. Weights: heart, 9 oz.; liver, 52 oz.; spleen, 4 oz.; kidneys, 11½ oz.

CASE 53. Male, aged 74, admitted and died December 13th, 1890 (P.-m. 476).—He was thrown off his bus whilst driving, and fell on his head. He remained partially conscious, but was very irritable. He had a large hæmatoma on the left side of his scalp, and some hæmorrhage from the left ear. He rapidly became unconscious, and vomited a considerable quantity of blood, and died.

Post-mortem.—The base of the skull was fractured, and the brain was ploughed up with hæmorrhage. There were four small independent hæmorrhages in the posterior part of the pons. Weights: heart 10 oz.; liver, 41 oz.; spleen, 3 oz.; kidneys, 9 oz.

CASE 54. Male, aged 34, admitted and died July 19th, 1892 (P.-m. 253).—He was alcoholic, and his legs were œdematous, and blood and albumen were present in the urine. He had become suddenly unconscious. He rapidly died.

Post-mortem.—Bad vessels; hypertrophied heart; and granular kidneys. There was a hæmorrhage into the right internal capsule, filling both lateral ventricles. There were several small hæmorrhages in the pons. Weights: brain, 49 oz.; heart, 18 oz.; liver, 47 oz.; spleen, 22 oz.; kidneys, 23 oz.

CASE 55. Female, aged 42, admitted September 1st, 1892; died September 6th, 1892 (P.-m. 306).—She was found clinging to some railings. Her face was flushed; the right hand was colder than the left, and the left leg was colder than the right. She was almost completely conscious. The right pupil was dilated, and the tongue was paralysed on the left side. There was loss of movement of the left arm and hand, and the left leg was rigid; the right arm and leg were being constantly moved. There was no anæsthesia; the knee-jerks were increased, more so on the left than on the right. Some albumen was found in the urine. September 3rd: The lungs were full of moist sounds. September 4th: She became comatose, breathing stertorously, and had complete paralysis of the right arm. September 6th: The temperature rose to 106·2° F., and the patient died.

Post-mortem.—The kidneys were granular; the vessels were bad; and those of the heart were atheromatous. There was a hæmorrhage into the

right internal capsule, extending downwards into the basal ganglia, and backwards into the crus and pons. There was also a separate pontine hæmorrhage more on the right than on the left. The ventricles of the brain were full of blood-stained fluid. Weights: brain, 41 oz.; heart, 12 oz.; liver, 41 oz.; spleen, 3 oz.; kidneys, 7 oz.

CASE 56. Male, aged 42, admitted January 18th; died January 23rd, 1893 (P.-m. 36).—He had been in the hospital in the previous October for aortic incompetence and a left hemiplegia of embolic origin. He improved and went out. He was re-admitted on January 18th, and died in a few days.

Post-mortem.—There was an embolism of the right cerebral artery, which was calcareous. The brain was softened in its distribution. There were two minute mid-pontine hæmorrhages, and there was a small amount of blood in the fourth ventricle, the source of which was not found.

CASE 57. Male, aged 75, admitted June 10th, 1893; died June 11th (P.-m. 213).—He fell down three steps, but sustained no injury, and walked home. He then felt giddy and told his friends about his accident. He then became unconscious. He breathed stertorously, and his pupils were constricted. He was rigid on both sides, and a small amount of albumen was found in the urine.

Post-mortem.—The viscera were healthy, except for some slight atheroma at the base of the brain. The right lateral ventricle was full of blood which had ruptured into the third ventricle and across into the left cerebral hemisphere. The blood had reached down as far as the fourth ventricle. There were two distinct fair-sized pontine hæmorrhages, one on each side of the middle line. Weights: heart, 10½ oz.; liver, 63 oz.; kidneys, 10 oz.

CASE 58. Female, aged 14, admitted September 25th, 1894; died September 29th, 1894 (P.-m. 383).—A year before admission she had acute nephritis, and for a fortnight before admission she was suffering from epistaxis. She had a systolic murmur at the apex of the heart. September 26th: She had a clonic convulsion with occasional general rigidity, and she ground her teeth. There was some hæmorrhage from the mouth. September 28th: She was breathing stertorously, and was quite comatose. September 29th: The extremities became cold, and she died.

Post-mortem.—The tonsils were enlarged, and the right one was ulcerated. The kidneys were granular. There were some petechiæ under the pleuræ. There were some pia-arachnoid hæmorrhages and innumerable punctiform hæmorrhages in the brain, especially in the pons and internal capsules. There was a small patch of softening in the left optic thalamus, and some inflammation of the optic nerve. Weights: brain, 53, oz.; heart, 10 oz.; liver, 48 oz.; spleen, 1½ oz.; kidneys, 4 oz.

CASE 59. Female, aged 40, admitted and died December 28th, 1894 (P.-m. 491).—She was alcoholic, and had swelling of abdomen and legs. Half an hour after her admission she suddenly became unconscious; she was breathing stertorously, and exhibited Cheyne-Stokes' phenomenon. Her pupils were widely dilated. She was totally flaccid, but there were occasional twitches of the left arm. Her knee-jerks were exaggerated. She rapidly died.

Post-mortem.—Bad vessels; the heart was hypertrophied, and the kidneys were granular. The pericardium was adherent. There was a hæmorrhage into the left internal capsule, which had filled the lateral ventricles and most of the frontal and parietal lobes. Weights: heart. 19½ oz.; liver, 54 oz.; spleen, 5 oz.; kidneys, 5 oz.

CASE 60. Female, aged 59, admitted and died January 24th, 1895 (P.-m. 25).—On admission she was unconscious, breathing stertorously, and paralysed down the right side. The pupils were contracted. She rapidly died.

Post-mortem.—Bad vessels; hypertrophied heart; and granular kidneys. There was blood-clot in the subarachnoid space, and a large hæmorrhage into the left internal capsule which had flooded the ventricular system. There were many small hæmorrhages in the pons. Weights: heart, 12 oz.; liver, 52 oz.; spleen, 4 oz.; kidneys, 11 oz.

CASE 61. Male, aged 50, admitted and died August 25th, 1897 (P.-m. 331).—For several months he had had swelling of the legs, and palpitations of the heart. Suddenly he lost the power of the right arm, and gradually became unconscious. He breathed stertorously, and respirations were of the Cheyne-Stokes' variety; his face was paralysed; his pulse was rapid and of high tension; his pupils were pinpoint; and he was generally paralysed, especially in the right arm. Whilst he was under observation he had a fit which commenced in the right arm. After this his temperature rose to 107·8° F., and he died.

Post-mortem.—Bad vessels; hypertrophied heart; and apparently normal kidneys. There was a large hæmorrhage into the pons more on the left side than on the right, tailing off both anteriorly and posteriorly. Weights: heart, 16 oz.; liver, 51 oz.

CASE 62. Male, aged 70, admitted and died March 18th, 1901 (P.-m. 90).—He was quite well in the morning, a little later he noticed that his legs felt weak. He very rapidly lost all power in his limbs. In the Surgery he was just conscious, but could not speak, and died on his way into the ward.

Post-mortem.—There were signs of old pleurisy. The aorta was atheromatous. The heart was hypertrophied, and the mitral valve was thickened. The kidneys were normal. The right side of the brain was larger than

the left, and the lateral ventricles were full of blood. There was a pontine hæmorrhage in the neighbourhood of the fourth ventricle, and also a hæmorrhage into the right side of the cerebellum, which had ruptured externally. Weights: brain, 1,328 gms.; heart, 450 gms.; liver, 1,422 gms.; spleen, 83 gms.; kidneys, 380 gms.

CASE 63. Male, aged 61, admitted and died November 3rd, 1902 (P.-m. 495).—Was admitted unconscious; his pulse was high tension; there was a corneal reflex on the left side; he had a right hemiplegia and a left facial paralysis.

Post-mortem.—Bad vessels; atheroma of the coronary arteries. The heart was hypertrophied; and the kidneys were granular. There was a large hæmorrhage into the left internal capsule bursting into the ventricles. There was a pea-like hæmorrhage in the upper left dorsal pontine region, and several mid-pontine hæmorrhages. Weights: brain, 1,286 gms.; heart, 710 gms.; liver, 1,879 gms.

CASE 64. Male, aged 38, admitted November 21st, 1902; died November 25th (P.-m. 525).—He had a somewhat similar attack four months before his admission, but recovered in the course of two months. He was seen to suddenly commence to drive his van wildly about, and on getting hold of him he was vomiting and complaining of severe pain in the back. In hospital he was quite unconscious; his head was turned towards the right; and most of his limbs were paralysed. His pupils reacted to light. His breathing was of the Cheyne-Stokes' variety, and stertorous; his knee-jerks were much exaggerated. Albumen was present in the urine, and he had incontinence. His temperature rose to between 107° and 108° F. before he died.

Post-mortem.—The lungs were emphysematous; the kidneys were granular; the blood vessels were bad; and the heart was hypertrophied. There were numerous petechiæ all over the brain. There were both a recent and an old hæmorrhage of small size into one internal capsule, and two small recent mid-pontine hæmorrhages, one anterior and the other posterior. Weights: brain, 1,320 gms.; heart, 636 gms.; liver, 2,161 gms.; spleen, 251 gms.; kidneys, 248 gms.

CASE 65. Male, aged 53, admitted and died February 13th, 1905 (P.-m. 80).—He was stated to be of temperate habits. Fifteen years before admission he had an attack of kidney trouble, but recovered, and seven years before admission he had several attacks of transient unconsciousness occurring three to five times every day. After a time, however, this ceased, and he remained well until a year before his death, when he was found to be suffering from Bright's disease. He was found collapsed and complaining of pain in his head; he was able to move, but could not get about. On admission he was unconscious, his breathing was

stertorous, he was quite flaccid, and his pupils were much contracted. His arteries were tortuous and thickened, and his pulse tension was increased. He rapidly sank and died.

Post-mortem.—His vessels were bad; his kidneys were granular; and his left cardiac ventricle was hypertrophied. There was an old hæmorrhagic cyst in the dura mater on the left side, which may have been the cause of his attacks seven years before. There was a hæmorrhage into the left lower posterior part of the pons the size of an acorn; the blood had ruptured into the fourth ventricle, and from thence had escaped under the cerebellum more on the left side than the right. Weights: brain, 1,648 gms.; heart, 555 gms.; kidneys, 215 gms.

CASE 66. Male, aged 46, admitted and died April 18th, 1905 (P.-m. 186).—Three months before he had been brought home dazed. He recovered, but a fortnight later he had an unexplained attack of hæmatemesis. The day before his attack he spat up some blood, and the next day he went to pass his water when he suddenly felt giddy. On admission he was comatose and flaccid, and his knee-jerks were exaggerated. His pulse rate was 60 per minute, and the tension was increased. There was exophthalmos on the right side, and the right pupil was dilated, whilst the left was constricted. Later on both pupils were dilated and fixed. A large quantity of albumen was present in the urine. He very quickly died.

Post-mortem.—His vessels were bad; his kidneys were not granular; but the left side of his heart was much hypertrophied. There was a large hæmorrhage into the upper dorsal pontine region, which had practically destroyed the pons and had ruptured into the submembranous space from the fourth ventricle, and had tracked forward and compressed the cavernous sinus on the right side. Weights: heart, 25 oz.

CASE 67. Female, aged 40, admitted and died September 16th, 1906 (P.-m. 440).—She had been admitted in December, 1904, for what was diagnosed as hydronephrosis and left cerebral hæmorrhage with right hemiplegia. She became suddenly comatose, with contracted pupils, and died in half an hour.

Post-mortem.—The heart was hypertrophied on the left side; and the left kidney was destroyed by a hydatid cyst. There were two patches of softening in the caudate nucleus and optic thalamus on the left side, which were the causes of her old trouble. There was a large hæmorrhage into the pons rupturing into the fourth ventricle, and a secondary hæmorrhage into each crus. Weights: heart, 369 gms.

LIST

OF

GENTLEMEN EDUCATED AT GUY'S HOSPITAL

WHO HAVE PASSED THE

EXAMINATIONS OF THE SEVERAL UNIVERSITIES, OR OBTAINED

OTHER DISTINCTIONS, DURING THE YEAR 1910.

University of London.

Examination for the Degree of Doctor of Medicine.

Branch I.—*Medicine.*

H. S. Brown

Branch III.—*Mental Diseases and Psychology.*

J. G. P. Phillips

Branch IV.—*Midwifery and Gynæcology.*

H. O. Brookhouse

Branch V.—*State Medicine.*

A. H. G. Burton | F. A. Sharpe

Branch VI.—*Tropical Medicine.*

H. C. Keates | J. M. W. Pollard

Third (M.B., B.S.) Examination for Medical Degrees.

May.

Honours.

T. D. M. Stout (Distinguished in Medicine).

Pass.

E. L. Elliott
H. Gardiner
G. Maxted
N. L. M. Reader
T. Stansfield
C. C. Tudge

October.

Pass.

A. N. Cox
F. A. Dick
G. Dunderdale
A. H. Gool
W. S. Kidd
A. E. Lees
R. Montgomery
G. T. Mullally
H. F. Renton
R. Stout
G. Y. Thomson
A. D. Vazquez

Supplementary Pass List.

Group I.—*Medicine.*

W. E. Fox | J. T. Montgomery

Group II.—*Surgery and Midwifery.*

M. M. Cowasjee | J. A. Edmond
E. A. Penny

Second Examination for Medical Degrees.

Part I.

March.

F. V. Bevan-Brown	H. W. Evans	A. N. Minns
F. C. S. Broome	*C. H. Gould	J. Y. Moore
F. Collar	A. C. Hancock	L. Muir Smith
W. L. G. Davies	*S. S. B. Harrison	J. Stephenson
F. H. Dodd	M. D. McManus	

**Awarded a mark of distinction.*

Part II.

T. I. Bennett	W. Robinson	H. Webb
S. Keith	H. C. Rook	O. R. L. Wilson
*G. S. Miller	A. L. Shearwood	
J. F. G. Richards	P. Smith	

**Distinguished in Physiology.*

Part I.

July.

Organic and Applied Chemistry.

W. L. E. Reynolds	H. Q. F. Thompson	H. P. Whitworth
P. D. Scott	W. L. Webb	

Part II.

Anatomy, Physiology, and Pharmacology.

V. Atienza	H. L. Meyer	A. J. E. Smith
R. Creasy	A. H. G. Moore	J. L. Stewart
A. S. Erulkar	R. D. Passey	A. Wills
J. M. Joly	J. A. Ryle	W. A. Young
W. Matthews	C. Sherris	

First Examination for Medical Degrees.

July.

J. E. Clark	J. Kyle	B. Sampson
A. W. A. Davies	W. M. Lansdale	A. G. Simmins
R. W. D. C. Easom	E. A. Leviseur	J. F. H. Stallman
D. H. A. Galbraith	H. J. Leviseur	J. G. Stevens
H. F. T. Hogben	A. L. Punch	*W. E. Tanner
N. E. Kendall	K. N. Purkiss	

**Awarded a mark of distinction in Inorganic Chemistry.*

December.

E. Biddle | G. B. Dowling

University of Oxford.

Second Examination for M.B. and B.Ch.

Medicine, Surgery and Midwifery.

G. H. Hunt (Christchurch).

Pathology.

T. B. Heaton (Christchurch).

Forensic Medicine and Hygiene.

E. P. Poulton (Balliol).

University of Cambridge.

Degree of Doctor in Medicine.

H. Ackroyd (Caius)
H. C. Cameron (St. John's)
H. B. Carlyll (St. John's)
C. D. Edwards (St. John's)
W. Ledlie (Christ's)
A. H. Miller (Trinity)
A. S. M. Palmer (Jesus)
F. Shufflebotham (Trinity)

Degree of Master in Surgery.

C. W. Greene (Emm.)
A. S. B. Bankart (Trinity)

Third Examination for the Medical and Surgical Degrees.

Part II.

L. Bromley (Caius)
A. B. Carter (Jesus)
H. L. Duke (Caius)
K. T. Khong (St. John's)
W. Ledlie (Christ's)
H. Lee (St. John's)
H. G. Rice (St. John's)
J. G. Saner (Caius)
C. S. E. Wright (Emm.)

Part I.

H. B. Barber (Clare)
J. B. Hance (Christ's)
H. Lee (St. John's)
A. J. McNair (Emm.)
W. C. D. Maile (Pemb.)
F. D. Saner (Christ's)
A. M. Zamora (Christ's)

Examination for Diploma of Public Health.

H. P. W. Barrow
A. H. G. Burton

Examination for Diploma in Tropical Medicine and Hygiene.

E. P. Minett

University of Durham.

Third Examination for the Degrees of M.B. and B.S.

B. G. H. Connolly

Third Examination for the Degree of M.B.

G. E. W. Lacey

Second Examination for the Degree of M.B.

Anatomy and Physiology.

H. G. Dodd

Royal College of Physicians of London.

Examination for the Membership.

C. H. Rippmann | E. B. Smith

Final Examination for the Licence.

January.

F. S. Adams	H. G. Rice	C. Weller
W. H. Catto	J. G. Saner	J. W. Williams
T. J. Killard-Leavey	V. T. P. Webster	

April.

F. D. Berry	P. V. G. Pedrick	N. A. Dyce Sharp
W. T. Clarke	E. P. Poulton	T. D. M. Stout
G. Dunderdale	A. E. Rayner	G. Y. Thomson
F. Kahlenberg	N. L. M. Reader	C. C. Tudge
G. Maxted	F. D. Saner	C. Witts
F. Morres	H. I. Shaheen	

July.

J. G. Blecksmidt	W. E. Fox	A. L. Saul
F. A. Dick	A. L. George	R. Stout
H. W. Doll	K. T. Khong	A. D. J. B. Williams
J. A. Edmond	E. A. Penny	
F. C. Endean	A. S. Roe	

October.

G. B. Cockrem	R. Montgomery	Q. H. Richardson
A. N. Cox	G. T. Mullally	A. D. Vazquez
W. H. Talfourd Jones	H. T. Renton	
C. D. Killpack	W. Reynolds	

Royal College of Surgeons of England.

Final Examination for the Fellowship.

H. Chapple | K. H. Digby

E. L. M. Lobb

Primary Examination for the Fellowship.

G. E. Genge-Andrews
G. S. Miller
C. H. G. Pochin
A. J. Hull
D. W. Smith
J. F. G. Richards
W. Robinson

Final Examination for the Membership.

January.

F. S. Adams
W. H. Catto
T. J. Killard-Leavey
H. G. Rice
J. G. Saner
V. T. P. Webster
C. Weller
J. W. Williams

April.

F. D. Berry
W. T. Clarke
G. Dunderdale
F. Kahlenberg
G. Maxted
F. Morres
P. V. G. Pedrick
E. P. Poulton
A. E. Rayner
N. L. M. Reader
F. D. Saner
H. I. Shaheen
N. A. Dyce Sharp
T. D. M. Stout
G. Y. Thomson
C. C. Tudge
C. Witts

July.

J. G. Blecksmidt
F. A. Dick
H. W. Doll
J. A. Edmond
F. C. Endean
W. E. Fox
A. L. George
K. T. Khong
A. D. J. B. Williams
E. A. Penny
A. S. Roe
A. L. Saul
R. Stout

October.

G. B. Cockrem
A. N. Cox
W. H. Talfourd Jones
C. D. Killpack
R. Montgomery
G. T. Mullally
A. D. Vazquez
H. T. Renton
W. Reynolds
Q. H. Richardson

Final Examination for the Licence in Dental Surgery.

May.

H. Harrison
E. P. Hudson
S. W. Ingram
A. E. F. Peaty
K. G. Hoby
F. A. Lowe
H. S. Morris
A. G. Poock
C. F. Snow
G. V. Dymott
N. Edgar
H. H. Glover
A. J. Reynolds
C. F. L. Ruck
A. J. Schaefer
H. Sturton

October.

H. F. Barge
C. H. Barnett
R. N. Curnow
F. S. Glover
C. J. Henry
A. P. L. Johnson
W. J. Kennealy
E. A. C. Knox-Davies
S. Lawson
S. Morgan
C. H. G. Penny
C. E. Rice
G. E. Rowstron
A. T. Rycroft
P. B. Stoner
E. S. Tail
W. H. Wotton
E. O. Yerbury

Medical Department, Royal Navy.

D. A. Mitchell

MEDALLISTS AND PRIZEMEN,

JULY, 1911.

Open Scholarships in Arts.

Alexander Beckett Bond, Bradfield College, £100.
John Arnold Molony Alcock, Radley College, £50.
Samuel Vidot, S. Louis College, Seychelles, Certificate.

Open Scholarships in Science.

Arthur Lisle Punch, Preliminary Science Class, Guy's Hospital, £150.
Alfred George Simmins, Preliminary Science Class, Guy's Hospital, £60.
John Frank Herbert Stallman, Dulwich College and Preliminary Science Class, Guy's Hospital, Certificate.

Scholarship for University Students.

Ronald Cathcart Ozanne, B.A., Hertford College, Oxford, £50.

Open Scholarships in Dental Mechanics.

October, 1910, Montague Fred. Hopson, £20.
Max. Schneider, Certificate.
May, 1911, Arthur James Barber, £20.

Junior Proficiency Prizes.

Arthur Joseph Eagleton Smith, £20.
Frederick Charles Sedgwick Broome, £15.

The Beaney Prize for Pathology.

Nathan Mutch, £34.

The Michael Harris Prize for Anatomy.

Arthur Joseph Eagleton Smith, £10.
Frederick Vivian Bevan-Brown, Certificate.

The Wooldridge Memorial Prize for Physiology.

Arthur Joseph Eagleton Smith } equal,
Frederick Vivian Bevan-Brown } £5 each.
Charles Hamilton Gould, Certificate.

Dental Prizes.

First Year's Prize in Dental Subjects.

Thomas Eric Henderson, £10.
Thomas Bernice Tustian, Certificate.
John William Mayer, Certificate.

Second Year's Prize in Dental Subjects (1910).

Wilfred Stephen Ollis, £10.
William Hector Wotton, Certificate.

Second Year's Prize in General Subjects.

Guy William Enston Holloway, £10.

Prize for Operative Dental Surgery.

Douglas Wain, £10.

Newland-Pedley Gold Medal for Practical Dentistry.

Guy William Enston Holloway.
Stanley Joseph Frederick Webb, Certificate.

Golding-Bird Gold Medal & Scholarship in Bacteriology.

Frank Cook, £20.

The Oldham Prize in Ophthalmology.

Alan Herapath Todd, £30.

Treasurer's Gold Medal for Clinical Medicine.

Edward Palmer Poulton.

Treasurer's Gold Medal for Clinical Surgery.

Gerald Thomas Mullally.

THE PHYSICAL SOCIETY.

Honorary President.—

Honorary Vice-Presidents.—
G. H. Savage, M.D., Sir James Goodhart, Bart., M.D., LL.D., Frederick Taylor, M.D.

Presidents.—G. W. Goodhart, M.B., B.C., A. H. Todd, B.Sc., M.B., B.S., A. Neville Cox, M.B., B.S., F. Cook, B.Sc., M.B., B.S., G. Marshall, G. T. Mullally, M.B., B.S., N. Mutch, M.B., B.C., E. P. Poulton, M.B., B.Ch., A. Sandison, M.B., B.C., J. G. Saner, M.B., B.C., T. I. Bennett, J. A. Edmond, J. B. Hance, H. L. James, A. J. MacNair, E. G. Schlesinger, B.Sc., M.B., B.S.

Hon. Secretaries.—C. H. Rippmann, M.D., K. H. Digby, M.B., F.R.C.S.

Session 1910–1911.—The Society's prize of £10 for the best essay read during the Session was awarded to Mr. A. H. Todd for his paper on "Parotid Tumours."

Mr. A. Sandison gained the Treasurer's prize of £5 for his paper on "Rheumatic Fever in the Last Decade."

Messrs. T. I. Bennett and W. T. Chaning-Pearce were presented by the Chairman with a book-prize each for the high standard of their papers submitted.

Mr. E. P. Poulton gained the Society's prize of £5 for showing the best specimens of scientific interest during the Session.

The prize of £5 for the Member who most distinguished himself in the discussions was divided between Messrs. F. Cook and E. G. Schlesinger.

CLINICAL APPOINTMENTS HELD DURING THE YEAR 1910.

HOUSE PHYSICIANS.

C. A. Basker	A. A. Greenwood	S. J. Darke
A. E. Lees	A. L. Fitzmaurice	H. L. Attwater
E. L. Elliott	V. T. P. Webster	

HOUSE SURGEONS.

H. R. Mullins	H. C. Lucey	T. F. Brown
T. Evans	C. H. Mills	J. L. Johnston
R. C. H. Francis	L. Bromley	

ASSISTANT HOUSE SURGEONS.

C. H. Mills	H. Gardiner	T. D. M. Stout
A. E. Duvivier	A. L. Fitzmaurice	J. L. Johnston
E. L. Elliott	V. T. P. Webster	R. C. H. Francis
J. G. Saner	L. Bromley	N. A. D. Sharp
E. P. Poulton	G. H. Peall	F. Kahlenberg
	W. T. Clarke	

OUT-PATIENT OFFICERS.

T. F. Brown	N. A. D. Sharp	F. Kahlenberg
A. E. Lees	S. J. Darke	I. Evans
J. L. Johnston	H. L. Attwater	A. L. Fitzmaurice
E. L. Elliott	C. H. Mills	L. Bromley
G. H. Hunt	R. C. H. Francis	V. T. P. Webster
	J. G. Saner	

OBSTETRIC RESIDENTS.

G. Dunderdale	F. S. D. Berry	C. Witts
V. Townrow	W. Johnson	A. H. Crook

CLINICAL ASSISTANTS.

F. S. Adams	H. L. Attwater	L. Bromley
R. C. H. Francis	N. A. D. Sharp	V. T. P. Webster
F. D. Saner	J. G. Saner	F. S. D. Berry
F. Kahlenberg	G. H. Peall	A. E. Rayner
W. T. Clarke	H. Gardiner	G. H. Hunt
W. S. Kidd	E. P. Poulton	T. D. M. Stout
G. Y. Thomson	C. C. Tudge	A. Neville Cox
F. A. Dick	H. W. Doll	G. Maxted

CLINICAL ASSISTANTS IN THE MEDICAL WARDS.

W. S. Kidd	N. L. M. Reader	C. C. Tudge
J. Pryce Davies	H. W. Doll	W. E. Fox
E. Billing	L. K. Edmeades	G. C. Lowe
G. B. Cockrem	E. P. Poulton	A. D. J. B. Williams
A. Neville Cox	J. M. Jarvie	A. M. Bodkin
A. E. Rayner	R. Stout	G. R. Hind
H. G. B. Blackman	M. M. Munden	A. J. McNair
N. Mutch	A. Sandison	H. V. Leigh

CLINICAL ASSISTANTS IN THE SURGICAL WARDS.

H. Shaheen	F. D. Saner	H. L. Duke
N. A. D. Sharp	W. H. T. Jones	T. S. Allen
P. J. Watkin	A. D. Vernon Taylor	J. A. Delmege
	H. N. Eccles	

CLINICAL ASSISTANTS IN THE MEDICAL OUT-PATIENTS.

L. Mandel	A. D. J. B. Williams	W. T. Clarke
L. C. D. Irvine	J. H. Campain	A. L. Gardner

SURGEONS' DRESSERS.

H. L. James	H. H. Davis	N. Mutch
A. J. McNair	A. H. Todd	H. L. S. Griffiths
A. C. Jepson	R. Heaton	H. Daw
M. C. Wall	G. L. Preston	H. P. Warner
G. Marshall	F. G. Lloyd	N. S. Carruthers
A. Seabrooke	A. H. Birks	O. E. Williams
P. J. Monaghan	A. J. Fradersdorff	G. W. M. Andrew
J. B. Hance	A. Sandison	J. L. M. Symns
L. Milton	R. S. Bennett	W. E. S. Digby
G. Covell	E. W. Blake	W. S. Lacey
H. G. Crawford	T. E. Roberts	B. R. Parmiter
P. J. Watkin	T. S. Allen	E. R. Hart
G. T. Foster Smith	F. Cook	E. G. Schlesinger
C. A. R. Gatley	C. Aldis	A. C. L. D'Arifat
S. S. Crosse	V. Glendining	W. J. D. Smyth
G. B. H. Jones	H. L. Hopkins	P. Smith
W. M. Langdon	R. C. Poyser	J. L. Stewart
H. N. Eccles	F. N. Doubleday	Jap Ah Chit
C. F. Constant	W. S. Hyde	T. B. Heaton
F. Tooth	J. Eaves	T. B. Cole
G. W. B. Garrett	M. Pern	E. C. Peers
W. S. George	D. A. Davies	

OPHTHALMIC HOUSE-SURGEONS.

C. H. Crump | H. G. Rice | H. C. Lucey

OPHTHALMIC DRESSERS.

B. T. Verver
G. Maxted
J. A. Edmond
G. Y. Thomson
R. Stout
E. A. Penny
W. P. Vicary
G. C. Lowe
C. D. Killpack
A. H. Todd

G. E. W. Lacey
T. D. M. Stout
H. W. Barber
J. Pryce Davies
W. E. Levinson
A. H. Birks
L. Milton
T. S. Sharpley
N. S. Carruthers
A. M. Bodkin
W. H. Langdon

E. P. Poulton
G. Dunderdale
R. Montgomery
F. A. Dick
W. Reynolds
G. T. Mullally
R. Heaton
J. M. Jarvie
W. T. Chaning Pearce
J. L. Stewart

DRESSERS IN THE THROAT DEPARTMENT.

E. L. Elliott
F. S. D. Berry
A. Neville Cox
W. S. Kidd
T. Lewis Jones
J. A. Edmond
H. W. Barber
A. L. Gardner

W. T. Clarke
H. W. Doll
H. Gardiner
R. Stout
W. E. Fox
N. S. Carruthers
A. M. Bodkin
H. L. S. Griffiths

H. Steinbach
H. F. Percival
G. H. Hunt
C. C. Tudge
G. E. W. Lacey
A. S. Roe
H. T. Depree
R. Montgomery

ASSISTANT SURGEONS' DRESSERS.

F. Cook
E. G. Schlesinger
J. L. Stewart
T. P. Cole
F. C. Newman
G. W. B. Garrett
C. Warner
H. C. Godding
G. W. King
A. L. Shearwood
T. I. Bennett
J. L. D. Lewis
M. Scott
E. C. Cline

C. Aldis
A. C. L. D'Arifat
H. N. Eccles
M. Pern
V. F. Soothill
D. A. Davies
R. S. Kennedy
F. C. Hunot
E. White
W. Matthews
K. B. Clarke
O. R. L. Wilson
R. D. Passey
W. C. Whitworth

H. L. Hopkins
V. Glendining
J. M. J. Menage
E. C. Peers
W. S. George
C. Worster Drought
T. B. Heaton
J. P. Jones
E. G. Reeve
H. J. Hoby
S. Wickenden
L. B. Stringer
H. Webb

ASSISTANT SURGEONS' CLERKS.

H. J. Hoby | F. C. Newman

DENTAL SURGEONS' DRESSERS.

F. A. Dick
A. H. G. Burton
J. M. Jarvie
A. Seabrooke

R. Stout
A. M. Bodkin
N. Mutch
H. L. Hopkins

G. Mandel
W. E. Fox
F. G. Lloyd
N. S. Carruthers

CLERKS IN THE SKIN DEPARTMENT.

J. A. Edmond
V. Glendining
H. C. Godding

A. Sandison
T. P. Cole
G. Marshall

F. Cook
A. J. McNair

AURAL SURGEONS' DRESSERS.

E. L. Elliott
R. Stout
L. Mandel
N. S. Carruthers
W. T. Chaning Pearce
W. H. T. Jones
H. V. Leigh
G. Dunderdale
B. Blackwood
J. Pryce Davies
H. Steinbach
W. T. Clarke
J. A. Edmond
G. A. Blake

MEDICAL WARD CLERKS.

T. S. Allen
G. T. Foster Smith
R. C. Poyser
B. R. Parmiter
J. L. M. Symns
W. S. Lacey
D. A. Davies
J. M. Joly
C. A. R. Gatley
M. Pern
T. B. Heaton
E. G. Schlesinger
A. Samuel
F. N. Doubleday
A. C. L. D'Arifat
J. P. Hunot
H. C. Godding
L. B. Stringer
T. I. Bennett
J. L. D. Lewis
H. J. Hoby
F. C. Newman
C. Worster Drought
S. Wickenden
G. E. Genge-Andrews
J. S. Lauder
A. B. Danby
H. C. Rook
J. F. G. Richards
W. C. D. Maile
E. R. Hart
W. E. S. Digby
W. S. Hyde
T. E. Roberts
G. Covell
E. C. Peers
T. P. Cole
G. B. H. Jones
W. S. George
S. S. Crosse
W. J. D. Smyth
P. Smith
F. Cook
H. L. Hopkins
V. A. Luna
E. C. Cline
E. L. Jones
M. Scott
R. D. Passey
W. C. Whitworth
J. M. Joly
V. F. Soothill
T. Hampson
A. G. H. Moore
S. Keith
C. H. G. Pochin
G. S. Miller
A. L. Shearwood
L. P. Harris
W. K. Fry
H. G. Crawford
E. W. Blake
A. Sandison
L. Milton
W. M. Langdon
C. F. Constant
Jap Ah Chit
H. Sharpe
V. A. Luna
G. W. B. Garrett
P. J. Watkin
H. N. Eccles
V. Glendining
C. Aldis
J. P. Jones
A. Tilbury
F. Tooth
W. Matthews
H. Webb
K. B. Clarke
R. S. Kennedy
C. Warner
O. R. Wilson
J. L. Perceval
G. W. King
G. A. Pratt
W. Robinson
W. L. Webb

SURGICAL WARD CLERKS.

R. S. Kennedy
C. Warner
F. C. Hunot
G. W. King
T. Hampson
L. B. Stringer
L. P. Harris
W. C. Whitworth
J. L. Perceval
G. S. Miller
J. F. G. Richards
A. G. H. Moore
G. A. Pratt
R. Creasy
R. Sherris
A. C. Clifford
F. A. Hampton
J. A. Martin
D. P. Pickering
O. P. Morgan
D. W. Jones
V. F. Soothill
A. Tilbury
E. L. Jones
K. B. Clarke
O. R. Wilson
H. Webb
S. Wickenden
W. Matthews
E. M. Mahon
W. Robinson
T. A. Townsend
A. B. Danby
A. S. Erulkar
G. D. Eccles
A. J. E. Smith
R. A. Fawcus
D. W. John
W. H. Ogilvie
W. R. Reynell
F. Collar
K. J. Keer
C. Worster Drought
E. C. Cline
H. C. Godding
H. J. Hoby
A. L. Shearwood
J. L. D. Lewis
W. K. Fry
G. E. Genge-Andrews
C. H. G. Pochin
H. C. Rook
W. C. D. Maile
J. S. Lauder
V. Atienza
J. A. Ryle
A. M. Zamora
N. Garrard
E. G. Martin
R. C. Ozanne
A. Wills

POST-MORTEM CLERKS.

E. A. Penny	G. Dunderdale	G. Maxted
R. Stout	T. D. M. Stout	J. A. Edmond
J. Pryce Davies	G. Cockrem	W. E. Fox
G. T. Mullally	G. Y. Thomson	T. B. Heaton
H. W. Barber	E. Billing	A. D. Vazquez
L. C. D. Irvine	J. B. Hance	A. L. Gardner
B. Blackwood	N. Mutch	A. H. Todd
A. J. McNair	C. D. Killpack	H. H. Davis
G. R. Hind	H. G. B. Blackman	H. F. Renton
H. P. Warner	H. T. Depree	A. H. Gool
G. A. Blake	F. G. Lloyd	G. Marshall
T. S. Allen	G. W. M. Andrew	O. E. Williams
H. L. James	A. C. Jepson	G. Covell
P. J. Monaghan	C. Aldis	A. S. Seabrooke
H. L. Hopkins	F. Cook	E. G. Schlesinger
A. H. Birks	P. Smith	J. L. M. Symns

OBSTETRIC DRESSERS.

A. D. Vazquez	R. Montgomery	H. Platts
T. O'Callaghan	W. T. Chaning Pearce	G. H. Hunt
H. F. Stephens	J. M. Jarvie	G. T. Mullally
G. R. Hind	J. H. Campain	F. S. Adams
A. S. Roe	F. A. Dick	A. M. Bodkin
T. S. Sharpley	A. H. Gool	G. A. Blake
H. Daw	P. J. Monaghan	B. Blackwood
N. Mutch	A. J. McNair	H. L. James
A. L. Gardner	A. H. Todd	C. D. Killpack
H. H. Davis	J. B. Hance	E. R. Hart
H. P. Warner	G. Marshall	E. W. Blake
C. M. Ryley	G. W. M. Andrew	L. C. D. Irvine
G. Foster Smith	F. G. Lloyd	B. R. Parmiter
H. T. Depree	T. E. Roberts	

EXTERN OBSTETRIC ATTENDANTS.

G. B. Cockrem	W. E. Fox	E. P. Poulton
A. S. Roe	G. Y. Thomson	F. A. Dick
E. Billing	T. Lewis Jones	M. C. Thavara
G. R. Hind	A. L. Gardner	E. A. Penny
T. S. Sharpley	R. Stout	G. C. Lowe
H. F. Renton	C. D. Killpack	B. Blackwood
J. A. Delmege	W. P. Vicary	H. Platts
L. C. W. Cane	W. E. Levinson	H. T. Depree
L. C. D. Irvine	N. S. Carruthers	H. L. James
O. E. Williams	H. G. B. Blackman	A. J. Fradersdorff
G. T. Mullally	A. H. Gool	G. A. Blake
A. M. Bodkin	J. M. Jarvie	H. W. Barber
A. S. Seabrooke	R. Heaton	J. H. Campain
H. V. Leigh	A. Sandison	H. L. S. Griffiths
A. C. Jepson	H. Daw	C. M. Ryley
N. Mutch	A. J. McNair	E. C. Peers
E. G. Reeve	H. H. Davis	P. J. Monaghan
A. H. Todd	W. M. Langdon	R. S. Bennett
W. S. Hyde	T. S. Allen	E. R. Hart
V. Glendining	W. S. Lacey	J. B. Hance

DENTAL APPOINTMENTS HELD DURING THE YEAR 1910.

DENTAL HOUSE SURGEONS.

F. B. Bull
N. Edgar
C. H. Bradnam
S. J. Reynolds
R. W. Powell
A. L. Saul

ASSISTANT DENTAL HOUSE SURGEONS.

C. H. Barnett
E. O. Yerbury
H. E. Elwood
W. H. Wotton
C. J. Henry
H. F. Barge
F. W. Paul
E. A. C. Knox-Davies
E. P. Hudson
A. G. Poock
C. H. G. Penny
G. W. E. Holloway

ASSISTANT DEMONSTRATORS IN DENTAL MECHANICS.

H. L. Meyer
G. W. E. Holloway
G. B. Pritchard
W. H. Wotton

ASSISTANT DEMONSTRATORS IN DENTAL METALLURGY.

E. O. Yerbury
J. H. Rhodes
P. B. Stoner
H. F. Barge

ASSISTANT DEMONSTRATORS IN DENTAL MICROSCOPY.

H. O. Salt
C. H. G. Penny

DRESSERS IN THE GAS ROOM.

A. J. Reynolds
A. T. Rycroft
G. W. E. Holloway
S. Lawson
H. H. Glover
F. A. Jaques
J. E. R. Evans
W. H. Wotton
R. R. Adams
A. J. Percy
G. B. Pritchard
C. E. Rice
W. A. Thompson
G. H. H. Phillips
A. Stanley Morgan
C. J. Henry
F. W. Paul
H. D. Shore
I. G. Samuels
P. B. Stoner
F. S. Glover
C. H. G. Penny
H. O. Dumayne
W. J. Kennealey
C. F. L. Ruck
E. S. Tait
W. S. Lakeman
W. S. Ollis
R. N. Curnow
P. V. G. Pedrick
G. E. Rowstron
A. S. Morgan
C. Wade
S. Lawson
C. T. Watson
E. L. Fraser
R. G. Farrington
G. Matthews
W. H. Wotton
H. Harrison
E. J. M. Charles
J. H. Rhodes
H. E. Elwood
H. O. Salt
R. B. Campion
G. H. Warner
V. E. D. Bergh
J. Benson
H. J. Burch
L. E. Messinier
R. Neft
H. L. Messenger
R. Orozco-Casorla
L. S. Langley
J. F. Patel
S. J. F. Webb
D. Wain

DRESSERS IN THE EXTRACTION ROOM.

F. G. Farrington
P. J. Peatfield
F. B. Stradling
A. J. Percy
E. L. Fraser
D. Wain
P. B. Stoner
J. E. R. Evans
R. G. Farrington
W. S. Ollis
J. S. Cocks
H. D. Shore
C. H. Housden
C. H. Stainer
H. N. Purdom
C. M. Desai
G. L. Pemberton
J. E. Davies
L. R. Pickett
W. R. Morris
A. F. Salsbury

R. R. Steele
W. S. Lakeman
F. J. Tipper
E. W. Bacon
F. Wisher
F. R. Wallis
H. O. Salt
J. H. Rhodes
C. D. Neale
E. R. Bailey
J. H. Ross
E. H. Huckett
R. M Veale
E. R. Williams
V. F. H. Golledge
A. C. Achner
J. S. Sutton
J. H. H. Griffin
W. T. Flooks
M. Schneider
C. D. Neale

H. G. Elliott
A. J. Chapman
V. E. D. Bergh
S. W. Bevis
L. S. Langley
W. C. Wade
H. O. Dumayne
E. S. Tait
E. J. M. Charter
T. R. Trounce
R. Rodgers
L. D. Wright
R. Neft
D. H. Barr
C. J. Phillips
W. L. Stranach
C. H. Medlock
T. B. Tustian
W. L. Partridge
E. W. Bacon
C. Glover

CASUALTY DRESSERS.

E. J. M. Charter
H. C. Corke
R. G. Farrington
V. E. D. Bergh
L. S. Langley
E. L. Fraser
E. W. Bacon
R. Orozco-Casorla
C. D. Neale
H. G. Elliott
A. F. Camp
C. H. Stainer
H. N. Purdom
R. Rodgers

C. M. Desai
G. Matthews
W. S. Lakeman
H. D. Shore
A. J. Percy
H. L. Messenger
L. E. Messinier
D. Wain
S. J. Webb
S. W. Bevis
T. R. Trounce
E. S. Huckett
F. J. Tipper
F. B. Stradling
C. A. Achner

F. Wisher
F. S. Cooper
G. H. Warner
J. S. Cocks
C. T. Watson
G. B. Pritchard
J. F. Patel
A. J. Chapman
C. Wade
R. Neft
H. L. Bailey
I. G. Samuels
A. D. Tanner
F. R. Wallis

LIST OF ORIGINAL PAPERS BY MEMBERS OF GUY'S STAFF

CONTRIBUTED TO THE MEDICAL PRESS DURING THE YEAR.

RICHARD ASSHETON, M.A. Cantab. Professor Hubrecht's Paper on the Early Ontogenetro Phenomena in Mammals: an Appreciation and a Criticism, *The Quarterly Journal of Microscopical Science*, vol. liv., 1909.

Tropidonotus and the "Archenteric Knot" of Ornithorhynchus, *The Quarterly Journal of Microscopical Science*, vol. liv., 1910.

The Geometrical Relation of the Nuclei in an Invaginating Gastrula (*e.g.*, Amphioxus) considered in connection with cell rhythm, and Driesch's conception of Entelechy, Archiv. fur Entwickelungsmechanik der Organismen, bd. xxix., 1910.

A. P. BEDDARD, M.A., M.D. Camb., F.R.C.P. Lond. Secondary Constipation. *The Practitioner*, May, 1910.

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A. E. BOYCOTT, M.A., M.D. Oxon. Peritoneal Blood Transfusion. *British Medical Journal*, March 5th, 1910.

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A Case of Unilateral Aplasia of the Kidney in a Rabbit. *Journal of Anatomy and Physiology*, October, 1910.

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A. E. BOYCOTT, M.A., M.D. Oxon., and C. GORDON DOUGLAS, M.A., M.B., B.Ch. Oxon. Further Observations on Transfusion. *The Journal of Pathology and Bacteriology*, January, 1910.

R. DAVIES-COLLEY, M.A., M.B., F.R.C.S. The Association of Toxæmia of Pregnancy with Hæmorrhage, *The British Medical Journal*, 1911, vol. i., p. 1418.

KENELM H. DIGBY, M.B., B.S., F.R.C.S. Displacements of the Semilunar Cartilages, *The Lancet*, January 15th, 1910, p. 165, No. 3 of vol. i.

Rigors, *Guy's Hospital Gazette*, July 9th, 1910, vol. xxiv., No. 575, page 275.

Subepithelial Lymphatic Glands, *Guy's Hospital Gazette*, May 13th, 1911, vol. xxv., No. 597.

C. H. FAGGE, M.S. Lond., F.R.C.S. A Lecture on the Complications of Gall-stones. *The Clinical Journal,* November 2nd, 1910.

HERBERT FRENCH, M.D. Oxon., F.R.C.P. Lond. Bronzed Diabetes, with Cirrhosis of both Liver and Pancreas, and Pigmentary Deposits in those Organs. *Proceedings of the Royal Society of Medicine,* February, 1910.

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Some Forms of not very Obvious Pyuria, *Guy's Hospital Gazette,* May 14th, 1910.

A Case of Exostosis of the Os Calcis, *The Practitioner,* July, 1910.
Materia Medica for Nurses, *The Nursing Mirror,* 1910.

A Note on the Abuse of Purgatives. *The Lancet,* August 20th, 1910.

A Case of Spondylitis Deformans, *Guy's Hospital Gazette,* October 1st, 1910.

Two Cases of Locomotor Ataxy, with absence of the knee-jerk upon the right side, but with a knee-jerk of normal briskness upon the left, *Guy's Hospital Gazette,* November 26th, 1910.

Bilateral Paralysis of the Sixth Cranial Nerve after Fractured Base of the Skull, *Guy's Hospital Gazette,* December 24th, 1910.

Sir J. F. GOODHART, Bart., LL.D., M.D. Aberd., F.R.C.P. Lond. The Treatment of Chronic Constipation. *The Lancet,* August 13th, 1910.

Note on the Central Origin of some Cases of so-called Heart-block. *The Lancet,* September 10th, 1910.

Chronic Constipation and its Treatment. *The British Medical Journal,* October 8th, 1910.

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G. W. GOODHART, M.B., B.C. Cantab. Chloroform Necrosis of the Liver, *The Lancet,* September 10th, 1910, and *The British Medical Journal,* November 5th, 1910.

ARTHUR F. HERTZ, M.A., M.D. Oxon., B.Ch., F.R.C.P. Lond. Duodenal Ulcer, *The Medical Chronicle,* February, 1910.

The Investigation of Constipation by the X-rays (illustrated), *The Practitioner,* May, 1910.

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Asthma, *The Clinical Journal,* July, 1910.

A Clinical Lecture on Muco-membranous Colitis, *The Clinical Journal,* August 3rd, 1910.

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Address on Dilated Stomach, *The British Medical Journal,* March 4th, 1911.

Goulstonian Lecture on the Sensibility of the Alimentary Canal in Health and Disease, *The Lancet,* April and May, 1911.

MONTAGUE F. HOPSON, L.D.S. Eng., F.L.S. A Review of some Modern Theories of Variation and Heredity, and some Suggestions as to their Application to the Study of Orthodontia, *The Dental Record*, January, 1910.

A. C. JORDAN, M.D., B.C. Cantab. Types of Phthisis from the Radiographer's Point of View, *The Lancet*, September 10th, 1910.

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E. L. KENNAWAY and another. Uber Nitroclupein, Zeitschrift fur Physiologische Chemic, bd. 72, 486, 1911.

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The Operative Treatment of Chronic Constipation (illustrated), *The Practitioner*, May, 1910.

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Influence of Water on the Boiling Point of Ethyl Alcohol at Pressures above and below the Atmospheric Pressure, *Transactions of the Chemical Society*, 1911, vol. 99, p. 997.

A. W. ORMOND, F.R.C.S. Eng. Sympathetic Ophthalmia, *The Clinical Journal*, May 11th, 1910.

A. W. ORMOND, F.R.C.S. Eng., with R. A. RANKINE and Another. Notes on Twenty-eight Cases of Mongolian Imbeciles, with Special Reference to their Ocular Condition (illustrated), *The British Medical Journal*, July 23rd, 1910.

A. MORTON PALMER. Thesis on Human Temperatures, Surface and Internal.

F. W. PAVY, M.D. Lond., F.R.S. (and Another). On the Presence of Sugar in Healthy Urine as a Source of the Osazone Reaction, *The British Medical Journal*, July 9th, 1910.

On the Governing Influence of Environment on Enzymic Action, *The Journal of Physiology*, vol. xli., Nos. 3 and 4.

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Observations upon Disordered Action of the Heart, so-called "Soldier's Heart," *Journal of the Royal Army Medical Corps*, December, 1910.

T. REED. On the Anatomy of some Tubers, *Annals of Botany,* vol. xxiv., No. xcv., pp. 537—548, July, 1910.

R. P. ROWLANDS, M.S. Lond., F.R.C.S. A Clinical Lecture on when to Operate for Appendicitis, *The British Medical Journal,* January 29th, 1910.

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The Prevention and Correction of Deformity following Arthritis of the Hip-joint, *The Lancet,* July 30th, 1910, vol. ii., p. 307.

Hour-glass Contraction of the Stomach, *The British Medical Journal,* March 25th, 1911, p. 669.

Fracture-Dislocations of the Ankle, *Guy's Hospital Gazette,* 1911.

Operations for Pott's and Dupuytren's Fractures, *The Clinical Journal,* May 3rd, 1911, p. 61, vol. xxxviii., No. 4.

J. H. RYFFEL, M.A., M.B., B.C. Cantab. Critical Review: Lactic Acid in Metabolism, part ii., *The Quarterly Journal of Medicine,* July, 1910.

G. H. SAVAGE, M.D. Lond. Marriage and Insanity, *The Lancet,* August 6th, 1910.

Insanity and Marriage, *The British Medical Journal,* October 22nd, 1910.

LAURISTON E. SHAW, M.D. Lond., F.R.C.P. Lond. The True Aim of a United Medical Profession and the Handicap of the Trade Union Bogey, *The British Medical Journal,* July 16th, 1910.

CHARTERS J. SYMONDS, M.S., F.R.C.S. The Treatment of Central Osteitis by Metal Drains (Presidential Address delivered before the Medical Society of London), *The Clinical Journal,* November 16th, 1910.

FREDERICK TAYLOR, M.D., F.R.C.P. The Diagnosis of Prolonged Pyrexia, *The Medical Press and Circular,* November 30th and December 7th, 1910.

Clinical Lecture on Adams—Stokes' Disease, *The Clinical Journal,* January 4th, 1911.

W. HALE WHITE, M.D. Lond., F.R.C.P. Lond. A Clinical Lecture on a Case of Subphrenic Abscess, *The Clinical Journal,* February 9th, 1910.

Constipation in Adults, *The Practitioner,* May, 1910.

Gastrotaxis, *The British Medical Journal,* June 4th, 1910.

A Clinical Lecture on a Case of Pernicious Anæmia having changes in the Spinal Cord.

The Outlook of Sufferers from Exophthalmic Goitre, *The Quarterly Journal of Medicine,* October, 1910.

Two Clinical Lectures on Typhoid Fever delivered at Guy's Hospital, *The Clinical Journal,* November 23rd and December 7th, 1910.

On the Treatment and Prognosis of Exophthalmic Goitre. The Purvis Oration delivered before the West Kent Medico-Chirurgical Society on December 2nd, 1910, *The Lancet,* December 3rd, 1910.

GUY'S HOSPITAL.

MEDICAL AND SURGICAL STAFF.

1911.

Consulting Physicians.—Sir Samuel Wilks, Bart., M.D., LL.D., F.R.S.; F. W. Pavy, M.D., LL.D., F.R.S.; P. H. Pye-Smith, M.D., F.R.S.; Sir James Goodhart, Bart., M.D., LL.D.; F. Taylor, M.D.

Consulting Surgeons.—Thomas Bryant, M.Ch.; Sir H. G. Howse, M.S.; W. H. A. Jacobson, M.Ch.; R. Clement Lucas, B.S.; C. H. Golding-Bird, M.B.

Consulting Obstetric Physician.—A. L. Galabin, M.D.

Consulting Physician for Mental Diseases.—G. H. Savage, M.D.

Consulting Ophthalmic Surgeons.—C. Higgens, Esq.; W. A. Brailey, M.D.

Consulting Aural Surgeon.—W. Laidlaw Purves, M.D.

Consulting Dental Surgeons.—F. Newland-Pedley, Esq.; W. A. Maggs, Esq.

Consulting Anæsthetist.—Tom Bird, Esq.

Physicians and Assistant Physicians.

W. Hale White, M.D.
G. Newton Pitt, M.D.
Sir E. Cooper Perry, M.D.
L. E. Shaw, M.D.
J. Fawcett, M.D.
A. P. Beddard, M.D.
H. S. French, M.D.
A. F. Hertz, M.D.
H. C. Cameron, M.D.

Surgeons and Assistant Surgeons.

Charters J. Symonds, M.S.
W. Arbuthnot Lane, M.S.
L. A. Dunn, M.S.
Sir Alfred Fripp, M.S., C.B., K.C.V.O.
F. J. Steward, M.S.
C. H. Fagge, M.S.
R. P. Rowlands, M.S.
P. Turner, M.S.
E. C. Hughes, M.C.

Obstetric Surgeons.

J. H. Targett, M.S.
G. Bellingham Smith, B.S.

Ophthalmic Surgeons.

H. L. Eason, M.S., M.D.
A. W. Ormond, Esq.

Surgeon in Charge of Throat Department.

F. J. Steward, M.S.

Surgeon in Charge of Aural Department.

W. M. Mollison, M.C.

Surgeon in Charge of Actino-Therapeutic Department.

C. E. Iredell, M.D.

Surgeon in Charge of the Orthopædic Department.

R. P. Rowlands, M.S.

Surgeon in Charge of the Genito-Urinary Department.

A. R. Thompson, Ch.M.

Physician for Mental Diseases.

Maurice Craig, M.D.

Physician in Charge of Skin Department.
SIR E. COOPER PERRY, M.D.

Physician in Charge of the Department for Nervous Diseases.
A. F. HERTZ, M.D.

Physician in Charge of the Department for Diseases of Children.
H. C. CAMERON, M.D.

Dental Surgeons.

R. WYNNE ROUW, ESQ.	M. F. HOPSON, ESQ.
H. L. PILLIN, ESQ.	J. B. PARFITT, ESQ.

Assistant Dental Surgeons.

J. L. PAYNE, ESQ.	F. J. PEARCE, ESQ.
E. B. DOWSETT, ESQ.	H. P. AUBREY, ESQ.

Anæsthetists.

G. ROWELL, ESQ.	R. DAVIES-COLLEY, M.C.
H. F. LANCASTER, M.D.	T. B. LAYTON, M.S.
C. J. OGLE, ESQ.	V. TOWNROW, M.B., B.S.
H. M. PAGE, ESQ.	L. Bromley, M.B., B.C.
F. E. SHIPWAY, M.D.	J. GODFREY SANER, M.B., B.C.

H. GARDINER, M.B., B.S.

Bacteriologist.
J. W. H. EYRE, M.D.

Radiographers.
E. W. H. SHENTON, ESQ. | A. C. JORDAN, M.D.
C. J. MORTON, M.D.

Medical Registrars and Tutors.
C. H. RIPPMANN, M.D. | G. H. HUNT, M.B., B.Ch.

Obstetric Assistant and Registrar.
H. CHAPPLE, M.C.

Surgical Registrars and Tutors.
V. TOWNROW, M.B., B.S. | L. BROMLEY, M.B., B.C.

Ophthalmic Registrars and Clinical Assistants.
W. ANDERSON, M.B. | H. LEE, M.B., B.C.

Resident Surgical Officer.
W. H. TRETHOWAN, M.B., B.S.

Curator of the Museum.
J. FAWCETT, M.D.

Warden of the College.
W. M. MOLLISON, M.C.

Lying-in Charity.
Mr. TARGETT AND Mr. BELLINGHAM SMITH.

Dean of the Medical School.
H. L. EASON, M.D., M.S.

Sub-Dean of the Medical School
H. C. Cameron, M.D.

MEDICAL SCHOOL STAFF.

Medicine.

Clinical Medicine ... ... THE PHYSICIANS AND ASSISTANT PHYSICIANS.

Principles and Practice of Medicine (Lectures) W. HALE WHITE, M.D., G. NEWTON PITT, M.D., SIR E. COOPER PERRY, M.D., AND L. E. SHAW, M.D.

Practical Medicine ... ... C. H. RIPPMANN, M.D., AND G. H. HUNT, M.B., B.Ch.

Medical Revision Classes ... ... H. C. CAMERON, M.D.

Surgery.

Clinical Surgery ... ... THE SURGEONS AND ASSISTANT SURGEONS.

Principles and Practice of Surgery (Lectures) CHARTERS J. SYMONDS, M.S., W. ARBUTHNOT LANE, M.S., L. A. DUNN, M.S., AND SIR ALFRED FRIPP.

Operative Surgery ... ... R. P. ROWLANDS, M.S., P. TURNER, M.S. AND T. B. LAYTON, M.S.

Practical Surgery ... ... V. TOWNROW, M.B., B.S., AND L. BROMLEY, M.B., B.C.

Surgical Revision Classes ... ... P. TURNER, M.S.

Obstetrics and Gynaecology.

Clinical Gynæcology ... ... THE OBSTETRIC PHYSICIANS.

Obstetrics and Gynæcology (Lectures) J. H. TARGETT, M.S., AND G. BELLINGHAM SMITH, M.B., B.S.

Practical Obstetrics ... ... H. CHAPPLE, M.C.

Obstetric Revision Classes ... ... G. BELLINGHAM SMITH, M.B., B.S.

Pathology.

Pathology (Lectures) ... ... A. E. BOYCOTT, M.D.

Morbid Histology ... ... A. E. BOYCOTT, M.D.

Morbid Anatomy (Demonstrations) in Post-mortem Room J. FAWCETT, M.D., H. S. FRENCH, M.D. AND A. F. HERTZ, M.D.

Surgical Pathology (Demonstrations) R. P. ROWLANDS, M.S.

Medical Pathology (Demonstrations) J. FAWCETT, M.D.

General Pathology (Demonstrations) A. E. BOYCOTT, M.D.

Ophthalmology.

Clinical Ophthalmology ... ... THE OPHTHALMIC SURGEONS.

Ophthalmology (Lectures) ... ... H. L. EASON, M.S., M.D.

Diseases of the Throat and Nose.

F. J. STEWARD, M.S.

Diseases of the Ear.

W. M. MOLLISON, M.C.

Diseases of the Skin.

SIR E. COOPER PERRY, M.D.

Diseases of the Nervous System.

A. F. HERTZ, M.D.

Diseases of Children.

H. C. CAMERON, M.D.

Diseases of the Genito-urinary System.
A. R. THOMPSON, Ch.M.

Dental Surgery.
R. WYNNE ROUW, ESQ.

Mental Diseases.
MAURICE CRAIG, M.D.

Materia Medica and Pharmacology.

Materia Medica (*Lectures*) ... ... A. P. BEDDARD, M.D.
Practical Pharmacology ... ... M. S. PEMBREY, M.D., AND H. GARDINER, M.B., B.S.
Practical Pharmacy ... ... THE HOSPITAL PHARMACIST.

Forensic Medicine.
J. H. RYFFEL, B.C.

Hygiene and Public Health.
R. KING BROWN, M.D.

Anaesthetics.
G. ROWELL, ESQ.

Bacteriology.
J. W. H. EYRE, M.D.

Anatomy.

Systematic Anatomy (*Lectures*) ... F. J. STEWARD, M.S., AND C. H. FAGGE, M.S.
Practical Anatomy ... ... T. B. LAYTON, M.S., R. DAVIES-COLLEY, M.C., AND J. G. SANER, M.B., B.C.

Physiology.

Physiology (*Lectures*) ... ... M. S. PEMBREY, M.D.
Practical Physiology... ... ... M. S. PEMBREY, M.D., J. H. RYFFEL, M.A., B.C., E. L. KENNAWAY, M.B., B.Ch., AND H. GARDINER, M.B., B.S.

Chemistry.

Chemistry (*Lectures*)... ... ... JOHN WADE, D.Sc.
Practical Chemistry ... ... W. C. BALL, M.A., AND R. W. MERRIMAN, M.A., B.Sc.

Physics.

Physics (*Lectures*) ... ... A. H. FISON, D.Sc.
Practical Physics ... ... H. H. ABRAM, M.Sc.

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