TRANSACTIONS

OF THE

PATHOLOGICAL SOCIETY OF LONDON.

VOLUME THE FORTY-SIXTH.

COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE SESSION 1894-95.

LONDON:
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1895.

The present publication, being the Forty-sixth Volume of Transactions, constitutes the Forty-ninth published Annual Report of the Pathological Society's Proceedings.

The Council think it right to repeat that the exhibitors are alone responsible for the descriptions given of the Specimens exhibited by them, the only change made in the Reports furnished by the authors being such verbal alterations as were absolutely necessary.

20, Hanover Square, W.;
August, 1895.

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OF VOLUME XLVI.

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1846	CHARLES J. B. WILLIAMS, M.D., F.R.S.
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1891	Sir GEORGE MURRAY HUMPHRY, M.D., LL.D., F.R.S.
1893	FREDERICK WILLIAM PAVY, M.D., LL.D., F.R.S.
1895	HENRY TRENTHAM BUTLIN, D.C.L.

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OF THE

Pathological Society of London,

ELECTED AT

THE GENERAL MEETING, MAY 21st, 1895,

For the Session 1895-96.

President.

HENRY TRENTHAM BUTLIN, D.C.L., F.R.C.S.

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*** *Members are requested to inform the Secretaries of any corrections which may be necessary.*

LIST OF MEMBERS OF THE SOCIETY.

Honorary Members.

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Metchnikoff, E., M.D., Directeur de l'Institut Pasteur, Paris.

Pasteur, Professor L., Member of the Institute, Paris.

Rindfleisch, Edouard, M.D., Professor of Pathological Anatomy in the University of Bonn.

Simon, Sir John, K.C.B., D.C.L., LL.D., F.R.S., 40, Kensington-square, W.

Virchow, Rudolf, M.D., Professor of Pathological Anatomy in the University of Berlin.

EXPLANATION OF ABBREVIATIONS.

O.M.—Original Member.
Pres.—President.
T.—Treasurer.
V.-P.—Vice-President.
S.—Secretary.
C.—Member of Council.

Those marked thus (L) have paid Composition Fee for Annual Subscription.
Those marked thus (‡) have paid Composition Fee for Transactions.

GENERAL LIST OF MEMBERS.

Elected

1891 Abbott, Francis Charles, M.D., St. Thomas's Hospital Medical School, S.E.

1879 Abercrombie, John, M.D., 23, Upper Wimpole-street, W.

1885 Abraham, Phineas S., M.A., M.D., 2, Henrietta Street, W.

1858 Acland, Sir Henry Wentworth, Bart., K.C.B., M.D., F.R.S., Broad-street, Oxford.

1883 Acland, Theodore Dyke, M.D., 74, Brook-street, W. (C. 1892-4.)

1891 Adami, J. George, M.A., M.D., Montreal, Canada.

‡1866 Adams, Arthur Bayley.

1890 Adams, James, 4, Chiswick-place, Eastbourne.

LO.M. Adams, William, 5, Henrietta-street, Cavendish-square, W. (C. 1851-4. V.-P. 1867-9.)

L1848 Aikin, Charles A., 12, Ladbroke-terrace, W. (C. 1864-6.)

1872 Aikin, Charles Edmund, 12, Ladbroke-terrace, W.

L1882 Allchin, William Henry, M.D., 5, Chandos-street, W.

1884 Anderson, Alexander Richard, 5, East Circus-street, Nottingham.

1871 Anderson, William, 2, Harley-street, W. (C. 1888-90.)

L1863 Andrew, James, M.D., Sunnycote, Emery Down, Lyndhurst, Hants. (C. 1868-70. V.-P. 1889-90.)

1887 Arkle, Charles, M.D., 66, Wimpole-street, W.

1883 Ashby, Henry, M.D., 13, St. John-street, Manchester.

1882 Axe, J. Wortley, 1a, Lower Sloane-street, Sloane-square, S.W.

1863 Bagshawe, Frederick, M.A., M.D., 16, Warrior-square, Hastings.

‡1856 Balding, Daniel Barley, Royston, Herts.

1881 Ballance, Charles A., M.S., 106, Harley-street, W. (C. 1890-2.)

1875 Barker, Arthur E. J., 87, Harley-street, W. (C. 1884-6.)

1885 Barling, Gilbert, M.B., 85, Edmund-street, Birmingham. (C. 1894-5.)

L1874 Barlow, Thomas, M.D., B.S., 10, Wimpole-street, W. (C. 1879-81. V.-P. 1894-5.)

1862 Barratt, Joseph Gillman, M.D.

1877 Barrow, A. Boyce, 37, Wimpole-street, W.

1881 Barrs, Alfred George, M.D., 22, Park-place, Leeds.

L1853 Barwell, Richard, 55, Wimpole-street, W. (C. 1862-4. V.-P. 1889-90.)

L1861 Bastian, H. Charlton, M.A., M.D., F.R.S., 8a, Manchester-square, W. (C. 1869-71. V.-P. 1885-7.)

1877 Bateman, Arthur W., B.A., Tenterfield, New South Wales.

Elected

L1876 Batteson, John, 26, Windsor-road, Forest-gate, E.

1882 Battle, William Henry, 2, Mansfield-street, W.

1870 Bäumler, Christian G. H., M.D., University of Erlangen.

1874 Beach, Fletcher, M.B., 64, Welbeck-street, W., and Winchester House, Kingston Hill, Surrey.

1892 Beadles, Cecil F., Colney Hatch Lunatic Asylum, N.

1879 Beale, Edwin Clifford, M.B., 23, Upper Berkeley-street, W.

L1852 Beale, Lionel S., M.B., F.R.S., 61, Grosvenor-street, W. (C. 1858-9· V.-P. 1874-5.)

1856 Bealey, Adam, M.D., M.A., Felsham Lodge, Hollington-park, St. Leonard's-on-Sea.

1865 Beeby, Walter, M.D., Bromley, Kent.

L1880 Beevor, Charles Edward, M.D., 33, Harley-street, W. (C. 1888-90.)

1883 Benham, Robert Fitzroy, Abercorn House, Castletown-road, West Kensington, W.

1886 Bennett, Frederick Joseph, 24, George-street, Hanover-square, W.

1877 Bennett, William Henry, 1, Chesterfield-street, W. (C. 1891-93.)

1889 Bentley, Arthur, J.M., M.D.

1878 Bernard, Francis R., M.D., 45, Warwick-street, Worthing.

1882 Berridge, William Alfred, Redhill, Surrey.

1886 Berry, James, 60, Welbeck-street, W. (C. 1895).

1891 Beville, Frederick Wells, The Firs, Palace-road, East Molesey.

‡1856 Bickersteth, Edward R., 2, Rodney-street, Liverpool.

1889 Bidwell, Leonard Arthur, 54, Harley-street, W.

1882 Bindley, Philip Henry, M.B., Branksome-road, St. Leonard's-on-Sea.

1890 Bindley, Robert Alfred, M.B., Westbury House, Harlesden, N.W.

1878 Bindon, William John Vereker, M.D., 18, St. Ann's-street, Manchester.

L1850 Birkett, Edmund Lloyd, M.D., Westbourne Rectory, Emsworth, Hampshire. (C. 1856-7.)

1881 Biss, Cecil Yates, M.D., 135, Harley-street, W.

1865 Bisshopp, James, Bedford-place, Tunbridge Wells.

1889 Black, Robert, M.D., 6, Pavilion Parade, Brighton.

1850 Blagden, Robert, Stroud, Gloucestershire.

1863 Blanchet, Jean B., M.D., M.S., Montreal, Quebec, Canada.

1879 Boileau, J. P. H., M.D., Brigade-Surgeon, Army.

1876 Bond, Thomas, M.B., 7, Broad Sanctuary, Westminster, S.W.

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

1861 Bower, Richard Norris (Travelling).

1881 Bowlby, Anthony A., 24, Manchester-square, W. (C. 1886-8, 1895. S. 1893-4.)

1892 Boyce, Rubert William, M.B., University College, Liverpool.

1882 Boyd, Stanley, M.B., 134, Harley-street, W. (C. 1893-5.)

1889 Bradford, John Rose, M.D., F.R.S., 52, Upper Berkeley-street, W.

1880 Bramwell, Byrom, M.D., 23, Drumsheugh-gardens West, Edinburgh.

1889 Bredin, J. Noble, 1, Norton Folgate, N.E.

Elected

1877 Bridges, Robert, M.B., M.A., Manor House, Yattendon, Berks.

‡1867 Bridgewater, Thomas, LL.D. Glas., M.B. Lond., Harrow-on-the-Hill, Middlesex.

1873 Briggs, Jacob Myers, M.D., Coeymans, New York, U.S.

1868 Bright, George Charles, M.D., Cannes, Alpes Maritimes, France.

1857 Briscoe, John, 5, Broad-street, Oxford.

1885 Briscoe, John F., Rawdon House, Alton, Hants.

L1851 Bristowe, John S., M.D., F.R.S., 13, Old Burlington-street, W. (C. 1854-8. S. 1861-4. C. 1865-7. V.-P. 1868-76, 1887. P. 1885-6.)

1860 Broadbent, Sir William Henry, Bart., M.D., 84, Brook-street, W. (C. 1871-3. V.P. 1882-4.)

1886 Brockatt, Andrew Alexander, St. Cuthbert's, Malvern.

L1852 Brodhurst, Bernard E., 20, Grosvenor-street, W. (C. 1862-4.)

1884 Brodie, Charles Gordon, 30, Harley-street, W.

1863 Brodie, George Bernard, M.D., 3, Chesterfield-street, Mayfair, W.

L1865 Brown, Augustus, M.D., Felsberg, Wilton Road, Shanklin, I.W.

1871 Brown, Frederick Gordon, 17, Finsbury-circus, E.C.

L1866 Browne, Lennox, 15, Mansfield-street, W.

1877 Bruce, J. Mitchell, M.D., 23, Harley-street, W.

1890 Brunton, T. Lauder, M.D., D.Sc., LL.D., F.R.S., 10, Stratford-place, W.

L1855 Bryant, Thomas, 65, Grosvenor-street, W. (C. 1863-6. V.-P. 1877-9.)

1894 Buchanan, George Seaton, M.D., 27, Woburn-square, W.C.

1890 Buckland, Francis O., M.A., M.B., C.M., 6, Lower Sloane-street, S.W.

1894 Bunch, Frank Vigers, 6, Gordon Place, W.C.

1891 Burghard, Frederic François, M.D., M.S., 46, Weymouth-street, W.

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1887 Butler-Smythe, Albert Charles, 76, Brook-street, W.

1872 Butlin, Henry Trentham (President), 82, Harley-street, W. (C. 1876-8, 1887-9. S. 1884-6. V.-P. 1891-2.)

1866 Butt, William Frederick.

L1883 Buxton, Dudley W., M.D., 82, Mortimer-street, W.

L1856 Buzzard, Thomas, M.D., 74, Grosvenor-street, W. (C. 1869-70. V.-P. 1881-3.)

1893 Caddy, Duncan James, M.D., 4, Earl's Court-gardens, S.W.

1885 Cahill, John, 12, Seville-street, Lowndes-square, S.W.

1893 Caley, Henry Albert, M.D., 24, Upper Berkeley-street, W.

1892 Campbell, Henry Johnstone, M.D., 54, Welbeck-street, W.

1891 Carless, Albert, M.S., 10, Welbeck-street, W.

1891 Carr, John Walter, M.D., 19, Cavendish-place, W.

1855 Carter, H. Vandyke, M.D., Scarborough.

1876 Carter, Robert Brudenell, 31, Harley-street, W.

1879 Cassidy, Joseph Lamont, M.D., 44, Harley-street, W.

Elected

1877 Casson, John Hornsey, Teheran, Persia.

L1868 Cavafy, John, M.D., 2, Upper Berkeley-street, W. (C. 1881-3.)

1864 Cay, Charles Vidler, Deputy Surgeon-General, Army.

1863 Cayley, William, M.D., 27, Wimpole-street, W. (C. 1870-1, 1875-8. S. 1872-4. V.-P. 1884-6. T. 1888-93.)

1869 Chaffers, Edward, Keighley, Yorkshire.

1884 Chaffey, Wayland Charles, M.D., 13, Montpellier-road, Brighton.

1891 Chaplin, Arnold, M.D., 24, Finsbury-circus, E.C.

1884 Chavasse, Thomas Frederick, M.D., C.M., 24, Temple-row, Birmingham.

1879 Cheyne, William Watson, M.B., C.M., 75, Harley-street, W. (C. 1885-7. V.-P. 1892-3.)

1858 Child, Gilbert W., Cowley House, Oxford.

1873 Chisholm, Edwin, M.D., Abergeldie, Ashfield, near Sydney, New South Wales [care of Messrs. Dawson, 121, Cannon-street, E.C.].

L1865 Church, William Selby, M.D., 130, Harley-street, W. (C. 1871-3. V.-P. 1894-5.)

L1868 Churchill, Frederick, M.D., 4, Cranley-gardens, Queen's-gate, S.W.

L1861 Clapton, Edward, M.D., 22, St. Thomas's-street, Southwark, S.E.

1872 Clark, Andrew, 71, Harley-street, W.

1886 Clark, Francis William, The Dispensary, Newcastle-on-Tyne.

1891 Clarke, J. Jackson, M.B., 9, Old Cavendish-street, W.

1885 Clarke, John Michell, M.D., 28, Pembroke-road, Clifton, Bristol.

1881 Clarke, W. Bruce, M.B., 51, Harley-street, W. (C. 1892-4.)

L1875 Clutton, Henry Hugh, M.A., 2, Portland-place, W. (C. 1884-6. V.-P. 1892-3.)

‡1865 Coates, Charles, M.D., 10, Circus, Bath.

1885 Coats, Joseph, M.D., 31, Lynedoch-street, Glasgow.

1856 Cockle, John, M.D., M.A., The Lodge, West Molesey.

1892 Cole, Robert Henry, Moorcroft, Hillingdon, Uxbridge.

1886 Collier, William, M.D., 62, High-street, Oxford.

1891 Collins, Edward Treacher, 84, Wimpole-street, W.

1888 Collins, William Job, M.D., M.S., 1, Albert-terrace, Regent's-park, N.W.

1878 Collyns, R. T. Poole, 20, Lingfield-road, Wimbledon.

1888 Colman, Walter Stacy, M.B., 22, Wimpole-street, W.

1882 Colquhoun, Daniel, M.D., Dunedin, New Zealand.

1891 Cook, Herbert G. Graham, M.D., University College, Cardiff.

1858 Cooke, R. T. E. Barrington, 15, St. Nicholas-cliff, Scarborough, Yorkshire.

1871 Cooke, Thomas, 40, Brunswick-square, W.C.

1866 Coombs, Rowland Hill, Mill-street, Bedford.

1892 Cooper, C. Dudley, London County Lunatic Asylum, Claybury, Woodford, Essex.

Elected

1875 Cory, Robert, M.D., 73, Lambeth Palace-road, S.E.
1892 Cotterell, Edward, 5, West Halkin-street, S.W.
1876 Cottle, Wyndham, M.D., 3, Savile-row, W.
L1861 Couper, John, 80, Grosvenor-street, W. (C. 1870-2.)
1873 Coupland, Sidney, M.D. (Treasurer), 16, Queen Anne-street, W. (C. 1878-81, 1889-91. S. 1886-8. V.-P. 1892-3. T. 1894.)
1884 Crichton, George, M.D., 3, Cambridge-villas, Twickenham.
1873 Cripps, William Harrison, 2, Stratford-place, W. (C. 1883-5. V.-P. 1893-4.)
L1877 Crocker, Henry Radcliffe, M.D., 121, Harley-street, W. (C. 1887-9.)
1856 Croft, John, 6, Mansfield-street, W. (C. 1870-2. V.-P. 1882-4.)
1879 Crooke, George Frederick, M.D., 2, Edmund-street, Birmingham.
1886 Crookshank, Edgar, M.B., Saint Hill, near East Grinstead, Sussex. (C. 1890-3.)
1875 Cross, Francis Richardson, 5, The Mall, Clifton, Bristol.
1890 Crowle, Thomas H. Rickard, 3, Campden Hill-road, W.
1889 Cuff, Robert, M.B., 1, The Crescent, Scarborough.
1885 Cullingworth, Charles James, M.D., 46, Brook-street, W.
1871 Cumberbatch, A. Elkin, 80, Portland-place, W.
1873 Curnow, John, M.D., 11, Wimpole-street, Cavendish-square, W. (C. 1882-4.)
1893 Curtis, Henry Jones, M.D., 41, Torrington-square, W.C.

1884 Dakin, W. Radford, M.D., B.S., 57, Welbeck-street, W.
1884 Dallaway, Dennis, 5, Duchess-street, W.
1883 Dalton, Norman, M.D., 4, Mansfield-street, W.
1873 Davidson, Alexander, M.D., 2, Gambier-terrace, Liverpool.
1885 Davies, Arthur, M.D., 23, Finsbury-square, E.C.
L1869 Davies-Colley, J. Neville C., M.C., 36, Harley-street, W. (C. 1886-2. V.-P. 1890-1.)
1883 Davis, Edwin Harry, West Hartlepool.
‡1859 Davis, Francis William, R.N.
1879 Davy, Henry, M.D., 29, Southernhay, Exeter.
1894 Dawson, Bertrand, M.D., 46, Finsbury-pavement, E.C.
1889 Dean, Henry Percy, M.B., B.S., 84, Wimpole-street, W.
1887 Delépine, Sheridan, M.B., C.M., 258, Oxford-road, Manchester.
1880 Dent, Clinton T., 61, Brook-street, W.
1856 Dick, H., M.D.
1871 Dickinson, Edward Harriman, M.A., M.D., 162, Bedford-street, Liverpool.
L1858 Dickinson, William Howship, M.D., 9, Chesterfield-street, W. (C. 1866-8. S. 1869-71. V.-P. 1872-4. P. 1889-90.)
L1890 Dickinson, William Lee, M.D., 9, Chesterfield-street, W.
1872 Diver, Ebenezer, M.D., Kenley, Caterham-valley, Surrey.
1872 Doran, Alban Henry Griffiths, 9, Granville-place, W. (C. 1882-4. V.-P. 1894-5.)

Elected

L1866 Down, John Langdon H., M.D., 81, Harley-street, W. (C. 1872-4.)
1893 Dowson, Walter, M.D., 9, Great George-street, Bristol.
1877 Drake-Brockman, E. F., Madras Medical Service [care of Mr. Lewis, Gower-street, W.C.].
1880 Dreschfeld, Julius, M.D., 325, Oxford-road, Manchester.
1879 Drewitt, F. G. Dawtrey, M.D., 2, Manchester-square, W. (C. 1890-2.)
1893 Drysdale, John Hannah, M.B., Rodney-street, Liverpool.
L1865 Duckworth, Sir Dyce, M.D., LL.D., 11, Grafton-street, Bond-street, W. (C. 1877.)
L1847 Dudgeon, Robert E., M.D., 53, Montagu-square, W.
1868 Duke, Oliver Thomas, M.B., India.
1871 Dukes, Clement, M.D., B.S., Sunnyside, Rugby.
1877 Dunbar, J. J. MacWhirter, M.D., Hedingham House, Clapham-common, S.W.
1877 Duncan, Andrew, M.D., 8, Henrietta-street, Covent-garden, W.C.
1889 Duncan, John, M.D., St. Petersburg.
1884 Dunn, Louis Albert, M.B., M.S., 10, St. Thomas's-street, S.E.
1879 Durham, Frederic, M.B., 82, Brook-street, W.

1893 Eccles, William McAdam, 10, Welbeck-street, W.
1892 Eddowes, Alfred, M.D., 25, Old Burlington-street, W.
L1880 Edmunds, Walter, M.C., 75, Lambeth Palace-road, S.E. (C. 1892-4.)
1882 Edwards, F. Swinford, 55, Harley-street, W.
1889 Elam, William Henry, New Barnet, Herts.
1883 Elder, George, M.D., 17, Regent-street, Nottingham.
1867 Ellis, James, M.D., California.
1873 Engelmann, George Julius, M.D., A.M., 3003, Locust-street, St. Louis, Miss., U.S.
L1846 Erichsen, Sir John Eric, Bart., LL.D., F.R.S., 6, Cavendish-place, W. (C. 1849-51. V.-P. 1863-4.)
1875 Evans, Julian, A.M., M.D., Marwood House, Honiton, Devon.
1894 Evans, Willmott H., 6, Gower-street, W.C.
1879 Eve, Frederic S., 125, Harley-street, W. (C. 1885-7. V.-P. 1895.)
1876 Ewart, James Cossar, M.B., C.M., F.R.S., School of Medicine, Edinburgh.
1881 Ewart, Joseph, M.D., Montpellier Terrace, Brighton.
L1877 Ewart, William, M.D., 33, Curzon-street, W. (C. 1889-1.)
‡1859 Ewens, John, The Elms, Cotham-hill, Bristol.
1887 Eyles, Charles Henry, Gold Coast Colony.

1889 Fairbank, Frederick Royston, M.D., 16, Eversfield-place, St. Leonard's-on-Sea.
1894 Fawcett, John, M.D., The College, Guy's Hospital, S.E.

Elected

1872 Fayrer, Sir Joseph, K.C.S.I., M.D. LL.D., F.R.S., 53, Wimpole-street, W. (C. 1880-2. V.-P. 1890-1.)

1872 Fenn, Edward L., M.D., Grey Friars, Colchester.

1883 Fenwick, E. Hurry, 14, Savile-row, W. (C. 1894-5.)

1872 Fenwick, John C. J., M.D., 25, North-road, Durham.

L1863 Fenwick, Samuel, M.D., 29, Harley-street, W.

1892 Fenwick, W. Soltau, M.D., 10, Devonshire-street, W.

1885 Féré, Charles, M.D., Médecin de Bicêtre; Boulevard St. Michel, 37, Paris.

1859 Fisher, Alexander, M.D., 2, Bruntsfield Gardens, Edinburgh.

1882 Fleming, George, C.B., LL.D., Higher Leigh, Combe Martin, North Devon.

1893 Fletcher, H. Morley, M.A., M.D., B.C., 98, Harley-street, W.

1872 Forbes, Daniel Mackay, Shoreditch Infirmary, 204, Hoxton-street, N.

‡1866 Foster, Sir Balthazar Walter, M.D., M.P., 11, George-street, Hanover-square, W.

1872 Fotherby, Henry I., M.D., Woodthorpe Cote, Reigate.

1891 Foulerton, Alexander Grant Russell, 22, Ovington-gardens, S.W.

1880 Fowler, James Kingston, M.A., M.D., 35, Clarges-street, W. (C. 1887-8.)

1878 Fox, Thomas Colcott, M.B., B.A., 14, Harley-street, W. (C. 1892-4.)

1858 Francis, Charles Richard, M.B., Bengal Medical Establishment, Indian Army.

1892 Frederick, Herbert J., St. Thomas's Hospital, S.E.

1886 Freeman, Henry William, 24, Circus, Bath.

O.M. Frere, J. C.

1891 Fripp, Alfred Downing, M.S., 65, Harley-street, W.

1864 Frodsham, John Mill, M.D., Streatham, S.W.

1894 Furnivall, Percy, 34, Adelaide-road, N.W.

1893 Fyffe, William Kington, M.B., 19, Duke-street, W.

1880 Gabbett, Henry Singer, M.D., 20, Burlington-place, Eastbourne.

‡1858 Gairdner, William Tennant, M.D., LL.D.Edin., F.R.S., 225, St. Vincent-street, Glasgow. (V.-P. 1891-2.)

1890 Galloway, James, M.A., M.D., 21, Queen Ann-street, W.

1870 Galton, John H., M.D., Sylvan-road, Upper Norwood, S.E.

1855 Gamgee, J.

L1846 Garrod, Sir Alfred Baring, M.D., F.R.S., 10, Harley-street, W. (C. 1851. V.-P. 1863-5.)

1892 Garrod, Archibald Edward, M.D., 9, Chandos-street, W.

1879 Garstang, Thomas Walter Harropp, Headingley House, Knutsford, Cheshire.

1872 Garton, William, M.D., Inglewood, Aughton, near Ormskirk, Lancashire.

1891 Gaster, Aughel, M.D., 224, Belsize-road, N.W.

Elected

1880 Gibbes, Heneage, M.B., University of Michigan, Ann Arbor, Michigan, U.S.A.

L1853 Gibbon, Septimus, M.D., 39, Oxford-terrace, Hyde-park, W.

1878 Gibbons, R. A., M.D., 29, Cadogan-place, S.W.

1893 Gibbs, Charles, Charing-cross Hospital, W.C.

1876 Gill, John, M.D., 31, Apsley-road, Clifton, Bristol.

1881 Glynn, Thomas Robinson, M.D., 62, Rodney-street, Liverpool.

1873 Godlee, Rickman John, M.B., M.S., 19, Wimpole-street, W. (C. 1877-80. 1891-2. S. 1887-9. V.-P. 1893-4.)

1878 Golding-Bird, Cuthbert H., M.B., B.S., 12, Queen Anne-street, W. (C. 1885-7. V.-P. 1894-5.)

1890 Goodall, E. Wilberforce, M.D., The Eastern Hospital, Homerton, N.E.

1871 Goodhart, James Frederic, M.D., 25, Portland-place, W. (C. 1876-8. 1886-8. S. 1883-5. V.-P. 1892-3.)

1894 Gossage, Alfred Milner, M.B., B.Ch., 54, Upper Berkeley-street, W.

1875 Gould, Alfred Pearce, M.S., 10, Queen Anne-street, W. (C. 1883-5.)

1870 Gowers, William Richard, M.D., F.R.S., 50, Queen Anne-street, W. (C. 1878-9.)

L1858 Gowland, Peter Y., 82, Gloucester-terrace, Hyde-park, W.

1888 Grant, J. Dundas, M.A., M.D., C.M., 8, Upper Wimpole-street, W.

1867 Green, T. Henry, M.D., 74, Wimpole-street, W. (C. 1871-3, 1878-9. S. 1875-6. V.-P. 1886-8.)

1895 Green, Charles David, M.D., Addison House, Upper Edmonton.

1873 Greenfield, William Smith, M.D., B.S., 7, Heriot-row, Edinburgh. (C. 1877-80. V.-P. 1893-4.)

1886 Greves, Edwin Hyla, M.D., Rodney House, Suffolk-road, Bournemouth.

1885 Griffith, Walter Spencer Anderson, M.D., 96, Harley-street, W.

1892 Griffith, William Stokes, M.B., B.C., 4, Bramham-gardens, S.W.

1887 Griffiths, Joseph, M.B., C.M., 16, Panton-street, Cambridge.

1876 Griffiths, Thomas D., M.D., Hearne Lodge, Swansea.

1882 Gross, Charles, M.D., M.S., 112, Westbourne-grove, W.

1876 Gwyther, James, M.B.

1887 Habershon, Samuel Herbert, M.D., 70, Brook-street, W.

L1851 Hacon, E. Dennis, 269, Mare-street, Hackney, N.E. (C. 1872.)

1892 Hadley, Wilfred James, M.D., 11, Wimpole-street, W.

1882 Haig, A., M.D., 7, Brook-street, W.

1894 Hallidie, Andrew Hallidie Smith, M.B., 6, West-street, Finsbury-circus, E.C.

1877 Hallowes, Frederick Blackwood, Redhill, Surrey.

1886 Hamilton, David James, M.B., 1, Albyn-place, Aberdeen.

1890 Handfield-Jones, Montagu, M.D., 35, Cavendish-square, W.

1886 Handford, Henry, M.D., 14, Regent-street, Nottingham.

1891 Hankin, E. H., St. John's College, Cambridge.

Elected

1882 Harbinson, Alexander, M.D., County Lunatic Asylum, Lancaster.

L1848 Hare, Charles John, M.D., Berkeley House, 15, Manchester-square, W. (C. 1852-4. V.-P.1874-7.)

L1856 Harley, George, M.D., F.R.S., 25, Harley-street, W. (C. 1862-5. V.-P. 1878-80.)

1893 Harley, Vaughan, M.D., 25, Harley-street, W.

1872 Harris, Henry, M.D., Trengweath-place, Redruth, Cornwall.

1879 Harris, Vincent Dormer, M.D., 31, Wimpole-street, W.

L1858 Hart, Ernest, 38, Wimpole-street, W. (C. 1867-8.)

1891 Haslam, William F., 33, Paradise-street, Birmingham.

1870 Haward, John Warrington, 16, Savile-row, W. (C. 1879-81. V.-P. 1890-1.)

1886 Hawkins, Francis Henry, M.B., 26, Portland-place, Reading.

1890 Hawkins, Herbert Pennell, M.D., 109, Harley-street, W.

L1856 Heath, Christopher, 36, Cavendish-square, W. (C. 1866-7. V.-P. 1879-81.)

1892 Heaton, George, M.B., B.Ch., 33, Temple-row, Birmingham.

1881 Hebb, Richard G., M.D., 9, Suffolk-street, S.W. (C. 1891-3.)

1884 Hebbert, Charles Alfred.

1878 Hellier, John B., M.D., Headingley, Leeds.

1879 Henderson, George Courtenay, M.D., Kingston, Jamaica, West Indies.

1892 Henry, Robert, Moorcroft, Hillingdon, Uxbridge.

1869 Hensley, Philip J., M.D., 4, Henrietta-street, W.

1884 Herringham, Wilmot Parker, M.D., 13, Upper Wimpole-street, W. (C. 1894-5.)

1892 Hewlett, Richard Tanner, M.D., King's College, Strand, W.C.

1864 Hickman, William, M.B., 5, Harley-street, W. (C. 1890-2.)

1880 Hobson, John Morrison, M.D., Glendalough, Morland-road, Croydon.

L1854 Holmes, Timothy, 6, Sussex-place, Hyde-park, W. (C. 1862-3. S. 1864-7. C. 1868. V.-P. 1869-71.)

O.M. Holthouse, Carsten. (C. 1852-4, V.-P. 1874-5.)

1878 Hood, Donald William Charles, M.D., 43, Green-street.

1864 Hood, Wharton P., M.D., 11, Seymour-street, W.

1882 Hopkins, John, Central London Sick Asylum, Cleveland-street, W.

1879 Horrocks, Peter, M.D., 26, St. Thomas's-street, S.E.

1883 Horsley, Victor, M.B., B.S., F.R.S., 25, Cavendish-square, W. (C. 1888-9.)

L1880 Hovell, T. Mark, 105, Harley-street, W.

1893 Howard, Robert James Bliss, M.D., 31, Queen Anne-street, W.

1875 Howse, Henry Greenway, M.S., 59, Brook-street, W. (C. 1878-81.)

1884 Hudson, Charles Elliott Leopold Barton, 16, Harley-street, W.

L1856 Hudson, John, M.D., 11, Cork-street, W.

1874 Humphreys, Henry, M.D., Victoria-road, Fleet, Hants.

1883 Humphry, Sir George Murray, M.D., LL.D., F.R.S., University of Cambridge. (P. 1891-2.)

Elected

1888 Hunter, William, M.D., 54, Harley-street, W.

1852 Hutchinson, Jonathan, F.R.S., 15, Cavendish-square, W. (C. 1856-9. V.-P. 1872-3, 1881-3. P. 1879-80.)

1882 Hutchinson, Jonathan, jun., 1, Park-crescent, W. (C 1889-91.)

1884 Hutton, Henry Richmond, M.B., 8a, St. John-street, Manchester.

1889 Hyslop, Theophilus Bulkeley, M.D., C.M., Bethlem Convalescent Hospital, Witley, Surrey.

1880 Ingram, Ernest Fortescue, Newcastle, Natal, S. Africa.

1886 Jackson, Arthur Molyneux, M.D., Kent County Asylum, Barming Heath, Maidstone.

1865 Jackson, J. Hughlings, M.D., F.R.S., 3, Manchester-square, W. (C. 1872-3. V.-P. 1888-9.)

1886 Jackson, Philip J., 216, Great Dover-street, S.E.

1875 Jalland, William Hamerton, St. Leonard's House, Museum-street, York.

1888 James, James Thomas, M.D., 30, Harley-street, W.

‡1853 Jardine, John Lee, Capel, near Dorking, Surrey.

1881 Jennings, William Oscar, M.D., 8, Rue Roy, Paris.

1879 Jessop, Charles Moore, Clare Lodge, Redhill.

1866 Jessop, Thomas Richard, 31, Park-square, Leeds.

1878 Johnson, Arthur Jukes, Yorkville, Ontario, Canada.

1876 Johnson, Charles Henry, Winton House, Basingstoke, Hants.

LO.M. Johnson, Sir George, M.D., F.R.S., 11, Savile-row, W. (C. 1846-50. V.-P. 1863-4, 1884-6. T. 1880-3.)

1888 Johnson, Raymond, M.B., B.S., 20, Weymouth-street, Portland-place, W.

1881 Johnston, Joseph, M.D., 24, St. John's Wood-park, N.W.

1854 Johnstone, Athol A. W., St. Moritz House, 61, Dyke-road, Brighton.

L1853 Jones, Sydney, M.B., 18, Wimpole-street, W. (C. 1864-6. V.-P. 1886-7.)

1888 Jones, Talfourd, M.B., Eastbourne.

L1862 Jones, Thomas Ridge, M.D., 4, Chesham-place, S.W. (C. 1882-4.)

1886 Juler, Henry Edward, 23, Cavendish-square, W.

1890 Kanthack, A. A., M.D., B.S., St. Bartholomew's Hospital, E.C. (C. 1894-5.)

1867 Kelly, Charles, M.D., Broadwater-road, Worthing, Sussex. (C. 1874.)

L1846 Kent, Thomas J., 89, Piccadilly, W.

1879 Kesteven, William Henry, Hillwood, Waverley-grove, Hendon, N.W

1859 Kiallmark, Henry Walter, 5, Pembridge-gardens, W. (C. 1875-6.)

1882 Kidd, Percy, M.D., 60, Brook-street, W. (C. 1889-91.)

1867 King, Edwin Holborow Netley Court, Southampton.

1871 King, Robert, M.B., Boyfield House, Moulton, Spalding, Lincolnshire.

L1852 Kingdon, J. Abernethy, 2, Bank-buildings, E.C.

Elected

1888 Kynsey, William Raymond, C.M.G., Colombo, Ceylon.

1878 Lancereaux, Etienne, M.D., 44, Rue de la Bienfaisance, Paris.
1882 Lane, William Arbuthnot, M.B., M.S., 8, St. Thomas's-street, S.E. (C. 1891-3.)
1865 Langton, John, 62, Harley-street, W. (C. 1882-4.)
1869 Larcher, O., M.D.Par., 97, Rue de Passy, Paris. [M. Kliensieck, Libraire, Rue de Lille, 11, Paris, per Messrs. Longmans.]
1884 Larder, Herbert, Whitechapel Infirmary, Baker's-row, N.E.
1873 Latham, Peter Wallwork, M.D., 17, Trumpington-street, Cambridge.
1876 Law, William Thomas, M.D., 9, Norfolk-crescent, W.
1883 Lawford, John Bowring, M.D., C.M., 55, Queen Anne-street, W.
1853 Lawrence, Henry John Hughes, Picton House, Llandowror, St. Clears. (C. 1873-5.)
1892 Lawrence, Turner William Pelham, M.B., 46, Maida-vale, W.
1893 Lawson, Arnold, 12, Harley-street, W.
1859 Lawson, George, 12, Harley-street, W. (C. 1870-1. V.-P. 1884-5.)
1879 Laycock, George Lockwood, M.B., Melbourne, Victoria, Australia.
1891 Lazarus-Barlow, Walter S., M.B.(Sydney), The Acacias, Chesterton, Cambridge.
1875 Lediard, Henry Ambrose, M.D., 41, Lowther-street, Carlisle.
L1852 Lee, Henry, 9, Savile-row, W. (C. 1860-2. V.-P. 1875-6.)
1879 Leech, Daniel John, M.D., 96, Mosley-street, Manchester.
L1877 Lees, David B., M.D., 22, Weymouth-street, W. (C. 1890-2.)
1867 Lees, Joseph, M.D., 21, Brixton-road, S.W.
1877 Leeson, John Rudd, M.D., C.M., 6, Clifden-road, Twickenham.
1868 Legg, John Wickham, M.D. (C. 1874-5.)
1892 Leith, Robert Fraser Caldie, M.B., C.M., B.Sc., 20, Merchiston-terrace, Edinburgh.
‡1892 Leudet, Robert, 16, Rue du Contrat-Social, Rouen, France.
1861 Lichtenberg, George, M.D., 47, Finsbury-square, E.C.
1889 Light, Edwin Mellor, M.B., B.C., 2, Wilton-place, Belgrave-square, S.W.
1877 Lister, Sir Joseph, Bart., D.C.L., LL.D., F.R.S., 12, Park-crescent, W. (C. 1880-2. V.-P. 1887-8, 1891-2.)
1895 Little, Ernest Graham Gordon, M.D., 50, Alderney-street, Eccleston-square, S.W.
1889 Little, John Fletcher, M.B., 32, Harley-street, W.
L1862 Little, Louis S., China.
1874 Liveing, Edward, M.D., 52, Queen Anne-street, W.
L1863 Liveing, Robert, M.D., 11, Manchester-square, W. (C. 1876.)
1882 Lockwood, C. B., 19, Upper Berkeley-street, W. (C. 1893-5.)
1876 Longhurst, Arthur Edwin Temple, M.D., 4, Eaton Square, S.W. (C. 1885-7.)
1892 Lovell, C., M.B., Wimbledon.
1881 Lubbock, Montagu, M.D., 19, Grosvenor-street, W.
1873 Lucas, R. Clement, M.B., B.S., 50, Wimpole-street, W. (C. 1883-5.)

Elected

1880 Lund, Edward, 22, St. John-street, Manchester.

1879 Lunn, John Reuben, St. Marylebone Infirmary; Rackham-street, Ladbroke-grove-road, W.

1887 Lyon, Thomas Glover, M.D., 8, Finsbury-circus, E.C.

1873 McConnell, J. F.

1871 Mac Cormac, Sir William, 13, Harley-street, W. (C. 1878-80.)

1893 McFadyean, John, Royal Veterinary College, Great College-street, N.W.

1882 Mackenzie, Frederic Morell, 29, Hans-place, S.W.

1885 Mackenzie, Hector William Gavin, M.A., M.D., 59, Welbeck-street, W. (C. 1895.)

1870 Mackenzie, John T., Bombay, India.

1878 Mackenzie, Stephen, M.D., 18, Cavendish-square, W. (C. 1888-90.)

1879 Maclagan, Thomas John, M.D., 9, Cadogan-place, S.W.

1865 MacLaurin, Henry Normand, M.D., 187, Macquarie-street, Sydney, New South Wales.

1879 Macready, Jonathan Forster, 51, Queen Anne-street, W.

1885 Maguire, Robert, M.D., 4, Seymour-street, W.

1877 Makins, George Henry, 47, Charles-street, Berkeley-square, W. (C. 1889-91.)

1887 Malcolm, John David, M.B., C.M., 13, Portman-street, W.

1892 Mann, Harold Edward, Alderney.

1890 Manson, Patrick, M.D., C.M., 21, Queen Anne-street, W.

1876 Maples, Reginald, Kingsclere, near Newbury.

1868 Marsh, F. Howard, 30, Bruton-street, W. (C. 1876-7.) (V.-P. 1889-90.)

1887 Martin, Sidney, M.D., B.S., 10, Mansfield-street, W. (C. 1893-5.)

1889 Mason, David James, M.D., Rosemont, Maidenhead.

1867 Mason, Philip Brookes, Burton-on-Trent.

1892 Masters, John Alfred, M.D., 57, Lexham-gardens, Kensington, W.

1884 Maudsley, Henry Carr, M.D., 11, Spring-street, Melbourne, Victoria.

L1852 May, George, jun., M.B., Reading.

1888 May, William Page, M.D., B.Sc., 38, Weymouth-street, W.

1881 Maylard, Alfred Ernest, M.B., 4, Berkeley-terrace, Glasgow.

1874 Meredith, William Appleton, C.M., 21, Manchester-square, W.

1859 Messer, John Cockburn, M.D., Assistant Surgeon, R.N.

1894 Michels, Ernst, 6, West-street, Finsbury-circus, E.C.

1866 Mickley, George, M.A., M.B., St. Luke's Hospital, Old-street, E.C.

1882 Money, Angel, M.D.

1879 Moore, Norman, M.D., 94, Gloucester-place, Portman-square, W. (C. 1885-7. V.-P. 1895.)

1881 Moore, Thomas, 6, Lee-terrace, Blackheath, S.E.

1875 Morgan, John H., 68, Grosvenor-street, W. (C. 1886-8.)

1874 Morison, Alexander, M.D., C.M., 14, Upper Berkeley-street, W.

1880 Morison, Basil Gordon, M.B.

Elected

1869 Morris, Henry, M.A., 8, Cavendish-square, W. (C. 1877-9, 1884-6· S. 1881-3. V.-P. 1888-9.)

1879 Morris, Malcolm Alexander, 8, Harley-street, W.

1894 Morrice, George Gavin, M.D., Crown-chambers, Salisbury.

1891 Morton, Charles A., 24, St. Paul's-road, Clifton, Bristol.

1875 Morton, John, M.B., Guildford.

1884 Mott, Frederick Walker, M.D., 84, Wimpole-street, W. (C. 1891-3.)

1879 Moullin, Charles W. Mansell, 69, Wimpole-street, W.

1893 Mummery, John Howard, L.D.S.Eng., 10, Cavendish-place, W.

1876 Munro, William, M.D., C.M., Clarkefield, Fountain-street, Cheetham Hill, Manchester.

1885 Murray, Hubert Montague, M.D., 27, Savile-row, W.

1894 Murray, John, M.B., B.C., 133, Harley-street, W.

1864 Myers, Arthur B. R., 43, Gloucester-street, Warwick-square, S.W. (C. 1872-3.)

1887 Myers, W. H., Fort Wayne, Indiana, U.S.A.

1887 Nason, Edward Noel, M.B., 80, Abbey-street, Nuneaton.

1873 Nettleship, Edward, 5, Wimpole-street, W. (C. 1882-4.)

1875 Newby, Charles Henry, 15, Landport-terrace, Southsea, Hants.

1884 Newland-Pedley, F., 32, Devonshire-place, Portland-place, W.

1865 Newman, William, M.D., Stamford, Lincolnshire.

1895 Nias, J. Baldwin, M.D., 40, Brook-street, W.

1868 Nicholls, James, M.D., Trenarren, Newquay, Cornwall.

1876 Nicholson, John Francis, M.D., 29, Albion-street, Hull.

1878 Nootт, William Mathias, 8, Kensington-park-road, W.

L1864 Norton, Arthur T., 101, Harley-street, W. (C. 1877-9.)

1883 Norvill, Frederic Harvey, M.B., Summerland, Yeovil, Somersetshire.

1856 Nunn, Thomas William, 8, Stratford-place, W. (C. 1864-6. V.-P. 1878-80.)

1880 O'Connor, Bernard, M.D., 25, Hamilton-road, Ealing.

1873 O'Farrell, George Plunkett, M.D., 19, Fitzwilliam-square, Dublin.

1880 Ogilvie, George, M.B., C.M., 22, Welbeck-street, W.

1880 Ogilvie, Leslie, M.B., C.M., 46, Welbeck-street, W.

1894 Ogle, Cyril, M.B., 30, Cavendish-square, W.

1850 Ogle, John W., M.D., 30, Cavendish-square, W. (C. 1855-6. S. 1857-60. C. 1861-3. V.-P. 1865-8.)

1876 Oliver, John Ferens, M.D., 12, Old Elvet, Durham.

1888 Openshaw, Thomas Horrocks, M.S., 16, Wimpole-street, W.

1860 Orange, William, M.D., C.B., 12, Lexham-gardens, W.

1875 Ord, William Miller, M.D., 37, Upper Brook-street, W. (C. 1880-2. V.-P. 1893-4.)

1892 Ord, William Wallis, M.D., 2, Queen-street, Mayfair, W.

1875 Osborn, Samuel C., Maisonnette, Datchet, Bucks.

Elected

1879 Ormerod, J. A., M.D., 25, Upper Wimpole-street, W. (C. 1887-9.)
1881 Owen, Isambard, M.D., 40, Curzon-street, W.
1865 Owles, James Allden, M.D., Hill View, Woking, Surrey.

1870 Paget, Sir James, Bart., D.C.L., LL.D., F.R.S., 5, Park-square west, Regent's-park, W.
1884 Paget, Stephen, 57, Wimpole-street, W. (C. 1894-5.)
1872 Parker, Robert William, 13, Welbeck-street, W. (C. 1881-3.)
1874 Parker, Rushton, M.B., B.S., 59, Rodney-street, Liverpool.
L1853 Parkinson, George, 50, Brook-street, W.
1882 Pasteur, William, M.D., 4, Chandos-street, W. (C. 1893-5.)
1885 Paul, Frank Thomas, 38, Rodney-street, Liverpool.
1895 Paul, J. E., 43, Queensborough Terrace, W.
L1865 Pavy, Frederick William, M.D., LL.D., F.R.S., 35, Grosvenor-street, W. (C. 1872-4. V.-P. 1891-2. P. 1893-4.)
1868 Payne, Joseph Frank, M.D., 78, Wimpole-street, W. (C. 1873-5, 1883-5. S. 1880-2. V.-P. 1888-9.)
1872 Pearce, Joseph Chaning, M.D., C.M., Montague House, St. Lawrence-on-Sea, Kent.
1863 Pearson, David R., M.D., 23, Upper Phillimore-place, W.
1879 Peel, Robert, 130, Collins-street East, Melbourne, Victoria.
1889 Penberthy, John, Royal Veterinary College, Camden Town, N.W.
1887 Penrose, Francis George, M.D., 4, Harley-street, W.
1884 Pepper, Augustus Joseph, M.B., C.M., 13, Wimpole-street, W.
1888 Perry, Edwin Cooper, M.D., Superintendent's House, Guy's Hospital, S.E.
1878 Philipps, Sutherland Rees, M.D., St. Ann's-heath, Virginia Water, Chertsey.
1871 Phillips, Charles Douglas F., M.D., 10, Henrietta-street, W.
1878 Phillips, John Walter, 30, Stanley-street, West Melbourne, Victoria.
1863 Pick, Thomas Pickering, 18, Portman-street, W. (C. 1870-1. V.-P. 1885-7.)
1893 Pinkerton, Robert A., M.A., M.D., 71, Craven-park, Harlesden, N.W.
1867 Pitt, Edward G., M.D.
1884 Pitt, George Newton, M.D. (Hon. Secretary), 24, St. Thomas's-street, S.E. (C. 1890-2.)
1876 Pitts, Bernard, M.A., M.C., 109, Harley-street, W. (C. 1888-90.)
1887 Pitts, Robert Zaccheus, Springfield, Chelmsford.
1883 Poland, John, 4, St. Thomas's-street, Southwark, S.E.
1882 Pollard, Bilton, M.B., B.S., 24, Harley-street, W. (C. 1895).
L1846 Pollock, George D. (Trustee), 35, Chester-square, S.W. (S. 1850-3. C. 1854-6. V.-P. 1863-5. P. 1875-6.)
1850 Pollock, James Edward, M.D., 52, Upper Brook-street, W. (C. 1862-4. V.-P. 1879-81.)
1870 Poore, George Vivian, M.D., 30, Wimpole-street, W. (C. 1883-5.)
1876 Port, Heinrich, M.D., 48, Finsbury-square, E.C.

Elected

L1879 Potter, Henry Percy, St. Mary Abbotts' Infirmary, Marloes-road, Kensington, W.

1866 Powell, Richard Douglas, M.D., 62, Wimpole-street, W. (C. 1873-5, 1881-3. S. 1877-9. V.-P. 1887-8.)

1884 Power, D'Arcy, M.A., M.B., 26, Bloomsbury-square, W.C. (C. 1891-3.)

1865 Power, Henry, 37a, Great Cumberland-place, W. (C. 1876-7.)

1887 Pratt, William Sutton, Weedon, Northamptonshire.

1884 Price, J. A. P., M.D., 41, Castle-street, Reading.

L1856 Priestley, Sir William Overend, M.D., 17, Hertford-street, W.

1888 Primrose, Alexander, M.B., C.M. 196, Simcoe-street, Toronto, Canada.

1882 Pringle, J. J., M.B., C.M., 23, Lower Seymour-street, W.

L1848 Purnell, John James, Woodlands, Streatham-hill, S.W. (C. 1858-61.)

1865 Pye-Smith, Philip Henry, M.D., F.R.S., 48, Brook-street, W. (C. 1874-7. V.-P. 1890-1.)

LO.M. Quain, Sir Richard, Bart., M.D., LL.D., F.R.S. (Trustee), 67, Harley-street, W. (C. 1846-51. S. 1852-6. T. 1857-68. *Pres.* 1869-70. V.-P. 1871-3.)

1872 Ralfe, Charles Henry, M.D., M.A., 26, Queen Anne-street, W. (C. 1877-9.)

1857 Ranke, Henry, M.D., Munich.

‡1890 Ransom, William Bramwell, M.D., The Pavement, Nottingham.

1891 Ratcliffe, Joseph Riley, M.B., C.M., The General Hospital, Birmingham.

1887 Raven, Thomas Francis, Broadstairs, Kent.

1870 Ray, Edward Reynolds, Dulwich Village, S.E.

1875 Reid, Robert William, M.D., C.M., 8, Queen's-gardens, Aberdeen.

1881 Renner, William, M.R.C.S., Wilberforce-street, Free Town, Sierra Leone.

1893 Rennie, George Edward, 16, College-street, Hyde-park, Sydney, N.S.W.

1854 Reynolds, J. Russell. M.D., F.R.S., 38, Grosvenor-street, W. (C. 1868-9.)

1866 Rivington, Walter, M.S., 95, Wimpole-street, W.

‡1865 Roberts, David Lloyd, M.D., 11, St. John's-street, Manchester.

1871 Roberts, Frederick Thomas, M.D., 102, Harley-street, W. (C. 1883-5.)

1878 Roberts, William Howland, M.D., Surgeon, Madras Army.

1888 Robertson, Robert, M.D., The Bungalow, Ventnor, Isle of Wight.

1885 Robinson, Arthur Henry, M.D., Mile End Infirmary, Bancroft-road, N.E.

1887 Robinson, Henry Betham, M.D., 1, Upper Wimpole-street, W.

1882 Robinson, Tom, M.D., 9, Princes-street, Cavendish-Square, W.

1888 Rolleston, H. D., M.D., M.A., 13, Upper Wimpole-street, W. (C. 1894-5.)

L1858 Rose, Henry Cooper, M.D., Penrose House, Hampstead, N.W. (C. 1873-4.)

1876 Rose, William, M.B., B.S., 17, Harley-st., W.

1875 Rossiter, George Frederick, Cairo Lodge, Weston-super-Mare.

Elected

L1877 Roth, Bernard, 29, Queen Anne-street.

1888 Roughton, Edmund Wilkinson, 33, Westbourne-terrace, W.

1891 Rouillard, Laurent Antoine John, M.B., St. Thomas's Hospital, S.E.

1887 Roy, Charles Smart, F.R.S., M.D., M.A., University of Cambridge.

1891 Ruffer, Marc Armand, M.D., 5, York-terrace, Regent's-park, N.W.

1891 Russell, William, M.D., 46, Albany-street, Edinburgh.

1869 Rutherford, William, M.D., F.R.S., 14, Douglas-crescent, Edinburgh.

1853 Salter, S. James A., M.B., F.R.S., Basingfield, near Basingstoke, Hants. (C. 1861-3. V.-P. 1880-2.)

1854 Sanderson, John Burdon, M.D., D.C.L.Durham, F.R.S., 50, Banbury-road, Oxford. (C. 1864-7. V.-P. 1873-4.)

1875 Sangster, Charles, 148, Lambeth-road, S.E.

1886 Saundby, Robert, M.D., 83A, Edmund-street, Birmingham.

1871 Saunders, Charles Edward, M.D., Sussex County Lunatic Asylum, Hayward's Heath.

1890 Saunders, Frederick William, M.B., B.C., Chieveley House, Newbury.

1873 Savage, George Henry, M.D., 3, Henrietta-street, Cavendish-square, W. (C. 1881-3.)

1882 Savill, Thomas Dixon, M.D., 12, Upper Berkeley-street, W.

1891 Schoerstein, Gustave Isidore, M.B., B.S., 11, Portland-place, W.

1894 Scholefield, Robert Ernest, M.B., Westwood, Lee, S.E.

1877 Semon, Felix, M.D., 39, Wimpole-street, W. (C. 1885-7.)

1894 Sequeira, James Harry, M.D., 6, West-street, Finsbury-circus, E.C.

1872 Sergeant, Edward, Town Hall, Bolton, Lancashire.

1876 Sharkey, Seymour J., M.D., 2, Portland-place, W. (C. 1884-6. V.-P. 1895.)

1880 Shattock, Samuel G., 4, Crescent-road, The Downs, Wimbledon. (C. 1885-7, 1893-5. S. 1890-2.)

1885 Shaw, Lauriston Elgie, M.D., 10, St. Thomas's-street, S.E.

L1886 Sherrington, Charles Scott, M.D., F.R.S., 27, St. George's-square, S.W. (C. 1894-5.)

L1856 Shillitoe, Buxton, 2, Frederick's-place, E.C.

1875 Siddall, Joseph Bower, M.D., C.M., Conybeare, Northam, Bideford.

1880 Silcock, A. Quarry, M.D., B.S., 52, Harley-street, W. (C. 1888-90.)

1866 Sims, Francis Manley Boldero, 12, Hertford-street, W.

1892 Slater, Charles, M.B., 16, Northwick-terrace, N.W.

1887 Smallpeice, William Donald, 42, Queen Anne's-gate, S.W.

‡1875 Smee, Alfred Hutchinson, The Grange, Hackbridge, Carshalton, Surrey.

1879 Smith, E. Noble, 24, Queen Anne-street, W.

1887 Smith, Frederick John, M.D., 4, Christopher-street, Finsbury-square, E.C.

1875 Smith, George John Malcolm, M.D., Hurstpierpoint, Sussex.

1894 Smith, Guy Bellingham, M.B., B.S., Guy's Hospital, S.E.

1872 Smith, Thomas Gilbart, M.D., 68, Harley-street, W.

Elected

1878 Smith, Herbert Urmson, M.B., Cape Colony.

1873 Smith, Richard T., M.D., 117, Haverstock-hill, N.W.

1883 Smith, Robert Percy, M.D., Bethlem Royal Hospital, St. George's-road, S.E.

1869 Smith, Robert Shingleton, M.D., Deepholm, Clifton Park, Bristol.

1892 Smith, Solomon Charles, M.D., 4, Portman Mansions, Baker-street, W.

1856 Smith, Thomas, 5, Stratford-place, W. (C. 1867-9. V.-P. 1877-8.)

1866 Smith, William, Melbourne, Australia.

1870 Smith, William Johnson, Seamen's Hospital, Greenwich, S.E. (C. 1879-81.)

L1869 Smith, William Wilberforce, M.D., 14, Stratford-place, W.

1894 Snow, Herbert, M.D., 6, Gloucester-place, Portman-square, W.

1870 Snow, William Vicary, M.D., Richmond Gardens, Bournemouth.

1888 Solly, Ernest, M.B., Strathlea, Harrogate, Yorks.

1868 Southey, Reginald, M.D., M.S., 32, Grosvenor-road, Pimlico. (C. 1882-4.)

1887 Spencer, Walter George, M.B., 35, Brook-street, W.

1888 Spicer, Robert Henry Scanes, M.D., 28, Welbeck-street, W.

1861 Squire, Alexander Balmanno, 24, Weymouth-street, W.

1885 Squire, John Edward, M.D., 53, Harley-street, W.

1890 Stabb, Ewen Carthew, St. Thomas's Hospital, Albert-embankment, S.E.

1895 Starling, Ernest Henry, M.D., Guy's Hospital, S.E.

1889 Stewart, Edward, M.D., Brook House, East Grinstead.

L1854 Stewart, William Edward, 42, Devonshire Street, W.

1891 Stiles, Harold Jalland, M.B., C.M., 5, Castle-terrace, Edinburgh.

1879 Stirling, Edward Charles, Adelaide, South Australia [care of Messrs. Elder & Co., 7, St. Helen's Place, E.C.].

1883 Stoker, George, 14, Hertford-street, W.

1881 Stokes, Henry Fraser, 2, Highbury-crescent, N.

1884 Stonham, Charles, 4, Harley-street, W. (C. 1893-5.)

1875 Sturge, W. A., M.D., 29, Boulevard Dubouchage, Nice.

L1871 Sutherland, Henry, M.D., 6, Richmond-terrace, Whitehall, S.W.

1882 Sutton, John Bland, 48, Queen Anne-street, W. (C. 1887-90.)

‡1867 Swain, William Paul, 17, The Crescent, Plymouth.

1881 Symonds, Charters James, M.S., 26, Weymouth-street, Portland-place, W. (C. 1886-8.)

1870 Tait, Robert Lawson, 7, The Crescent, Birmingham.

1886 Targett, James Henry, M.B., M.S. (Hon. Secretary), 6, St. Thomas's-street, S.E. (C. 1894.)

1891 Tate, Walter William Hunt, 4, Queen Anne-street, W.

1870 Tay, Waren, 4, Finsbury-square, E.C. (C. 1881-2.)

L1871 Taylor, Frederick, M.D., 20, Wimpole-street, W. (C. 1879-81.)

1885 Taylor, Henry H., 10, Brunswick-place, Brighton.

Elected

1892 Taylor, James, M.D.Edin., 34, Welbeck-street, W.
1880 Taylor, Seymour, M.D., M.C., 16, Seymour-street, W.
1879 Thin, George, M.D., 22, Queen Anne-street, W. (C. 1889-90.)
L1852 Thompson, Sir Henry, 35, Wimpole-street, W. (S. 1859-63. C. 1865-7. V.-P. 1868-70.)
1891 Thomson, Henry Alexis, M.D., 2, Coates-crescent, Edinburgh.
1884 Thomson, John, M.B., C.M., 18, Walker-street, Edinburgh.
1894 Thomson, St. Clair, M.D., 28, Queen Anne-street, W.
1892 Thorburn, William, B.S., 96, Mosley-street, Manchester.
1874 Thornton, John Knowsley, M.B., 22, Portman-street, W.
1872 Thornton, William Pugin, 35, St. George's-road, Canterbury.
1880 Tirard, Nestor Isidore, M.D., 28, Weymouth-street, W.
1884 Tivy, William James, 8, Lansdowne-place, Clifton, Bristol.
1856 Tomes, Sir John, F.R.S., Upwood Gorse, Caterham, Surrey. (C. 1867-9.)
1882 Tooth, H. H., M.D., 34, Harley-street, W. (C. 1892-4.)
1886 Totsuka, Kankai.
L1872 Townsend, Thomas Sutton, 68, Queen's Gate, S.W.
1888 Trevelyan, E. F., M.D.
1881 Treves, Frederick, 6, Wimpole-street, W. (C. 1887-90. V.-P. 1895.)
1851 Trotter, John W., Bossall Vicarage, York. (C. 1865-9.)
1895 Troutbeck, Henry, M.B., B.C., 148, Ashley-gardens, S.W.
1859 Truman, Edwin Thomas, 23, Old Burlington-street, W.
1888 Tubby, Alfred Herbert, M.S., 39, Finsbury-circus, E.C.
1867 Tuckwell, Henry Matthews, M.D., 64, High-street, Oxford.
1858 Tudor, John, Dorchester, Dorset.
L1875 Turner, Francis Charlewood, M.D., 15, Finsbury-square, E.C. (C. 1884-6, 1895. S. 1891-3.)
1882 Turner, George Robertson, 49, Green-street, W.
1863 Turner, James Smith, 12, George-street, Hanover-square, W.
1890 Turner, William Aldren, M.D., 13, Queen Anne-street, W.
1893 Turney, Horace George, M.B., M.Ch., 28, Wimpole-street, W.
L1858 Turtle, Frederick, Clifton Lodge, Woodford, Essex.
1880 Tyson, William Joseph, M.D., 10, Langhorne-gardens, Folkestone.

1867 Venning, Edgcombe, 30, Cadogan-place, S.W.
1889 Voelcker, Arthur Francis, M.D., B.S., 31, Harley-street, W. (C. 1895.)

L1867 Wagstaffe, William Warwick, B.A., Purleigh, St. John's-hill, Sevenoaks. (C. 1874, 1878-80. S. 1875-7.)
1885 Wakley, Thomas, jun., 5, Queen's-gate, S.W.
1893 Walker, Norman Purvis, M.D., 7, Manor-place, Edinburgh.
1881 Waller, Bryan Charles, M.D., Masongill House, Cowan-bridge, Kirkby-Lonsdale.
1890 Wallis, Frederick Charles, M.B., M.S. 26, Welbeck-street, W.
1888 Walsham, Hugh, M.A., M.B., B.C., 32, New Cavendish-street, W.

Elected

1873 Walsham, William Johnson, M.B., C.M., 77, Harley-street, W. (C. 1881-3.)

1859 Walters, John, M.B., Reigate, Surrey.

1892 Ward, Allan Ogier, M.D.Edin., Lansdowne House, Tottenham.

1892 Waring, Holburt Jacob, M.B., M.S., 15, Upper Brook-street, W.

1889 Washbourn, John Wychenford, M.D., Guy's Hospital, S.E.

1877 Waterhouse, Charles, M.B., M.C., Carl Ludwigstrasse, Währing, Vienna.

1891 Waterhouse, Herbert Furnivall, M.D., C.M., 81, Wimpole-street, W.

1892 Weaver, Frederick Poynton, M.D., Cedar Lawn, Hampstead Heath, N.W.

1890 Webb, Charles Frere, M.D., New-street House, Basingstoke.

1894 Weber, Frederick Parkes, M.D., 19, Harley-street, W.

L1858 Weber, Hermann, M.D., 10, Grosvenor-street, W. (C. 1867-70. V.-P. 1878-80.)

1876 Weir, Archibald, M.D., St. Mungho's, Great Malvern.

1864 Welch, Thomas Davies, M.D., Fairmount, Frith-hill, Godalming, Surrey.

1894 Wells, Sydney Russell, M.B., 14, Girdler's-road, West Kensington, W.

1853 Wells, Sir Thomas Spencer, Bart., 3, Upper Grosvenor-street, W. (C. 1865-8. V.-P. 1876-7.)

1892 Wesbrook, Frank F., M.D.(Winnipeg), Cambridge.

L1851 West, Charles, M.D., 4, Evelyn Mansions, Carlyle-place, Victoria-street, S.W. (C. 1856-7.)

1877 West, Samuel, M.D., 15, Wimpole-street, W. (C.1884-6, 1891-3. S. 1889-90.)

1888 Wethered, Frank J., M.D., 34, Queen Anne-street, W.

1891 Wheaton, Samuel Walton, M.D., 76, The Chase, Clapham Common, S.W.

1867 Whipham, Thomas Tillyer, M.D., 11, Grosvenor-street, W. (C. 1880-2.)

1869 Whipple, John H. C., M.D., Army Medical Staff.

1877 White, Charles Haydon, 20, Shakespeare-street, Nottingham.

1894 White, Charles Powell, 67, Queen-street, E.C.

1891 White, Gilbert B. Mower, M.B., B.S., 105, Gower-street, W.C.

1881 White, William Hale, M.D., 65, Harley-street, W. (C. 1888-90.)

1886 White, William Henry, M.D., 43, Weymouth-street, W.

‡1868 Whitehead, Walter, 24, St. Ann's-square, Manchester.

1877 Whitmore, William Tickle, 7, Arlington-street, S.W.

1870 Wicksteed, Francis William, Chester House, Weston-super-Mare.

1869 Wilkin, John F., M.D., M.C., New Beckenham, Kent.

1871 Wilkinson, J. Sebastian, New Zealand.

1855 Wilks, Samuel, M.D., F.R.S. (Trustee), 72, Grosvenor-street, W. (C. 1857-60. V.-P. 1869-72, 1883-5. P. 1881-2.)

1879 Willcocks, Frederick, M.D., 14, Mandeville-place, W.

Elected

1886 Willett, Edgar William, M.B., 25, Welbeck-street, W.

1869 Williams, Albert, M.D. (Travelling).

‡1858 Williams, Charles, 48, Prince of Wales-road, Norwich.

1866 Williams, Charles Theodore, M.D., 2, Upper Brook-street, W. (C. 1875-8.)

1881 Williams, Dawson, M.D., B.S., 25, Old Burlington-street, W. (C. 1893-5.)

1872 Williams, Sir John, Bart., M.D., 63, Brook-street, W. (C. 1878-80.)

1881 Williams, W. Roger, 28, Winckley-square, Preston.

1876 Williamson, James Mann, M.D., Ventnor, Isle of Wight.

1863 Willis, Francis, M.D., The Spa, Braceborough, Stamford.

1889 Wilson, Albert, Leytonstone, Essex.

1888 Wilson, Claude, M.D., C.M., 6, York-road, Tunbridge Wells.

1859 Wilson, Edward Thomas, M.B., Montpelier-terrace, Cheltenham.

1859 Wilson, Robert James, 7, Warrior-square, St. Leonards-on-Sea.

1891 Wilson, Theodore Stacey, M.B., C.M., 65, Temple-row, Birmingham.

‡1861 Windsor, Thomas, Medical Library, Boston, Mass., U.S. [care of B. F. Stevens, 4, Trafalgar-square, W.].

1889 Wingrave, V. Harold Wyatt, 7, Taviton-street, Gordon-square, W.C.

1874 Wiseman, John Greaves, Dearden-street, Ossett, Yorkshire.

1865 Witherby, William H., M.D., Pitt-place, Coombe, Croydon.

1876 Wood, William Edward Ramsden, M.A., M.D., The Priory, Rochampton, S.W.

1883 Woodcock, John Rostron, 155, Hagley-road, Birmingham.

1883 Woodhead, German Sims, M.D., Beverley, I, Nightingale-lane, Balham, S.W. (C. 1891-3.)

1879 Woodward, G. P. M., M.D., Deputy Surgeon-General; Sydney, New South Wales.

1884 Worts, Edwin, 6, Trinity Street, Colchester.

1869 Wyman, William S., M.D., Red Brae, 18, Putney-hill, S.W.

1890 Wynne, Edward T., M.B., 7, Rochester-gardens, Hove, Brighton.

1884 Wynter, Walter Essex, M.D., 30, Upper Berkeley-street, W.

1894 Yearsley, Percival Macleod, 11, Wimpole-street, W.

1872 Young, Henry, M.B., Monte Video, South America.

ANNUAL REPORT OF COUNCIL,

1894-95.

PRESENTED AT THE ANNUAL MEETING, MAY 21ST, 1895.

Your Council has to report that fifteen new members have been elected during the past session.

Dr. C. Thiersch and Dr. C. Ludwig, both of the University of Leipzig and honorary members of the Society, have died during the past year.

The Society has lost by death comparatively few of its members, although it has to deplore the loss of some of its most illustrious workers. The members who have died are Sir George Buchanan, Mr. Arthur Durham, Mr. Hulke, and Dr. Bevan Rake. Mr. Hulke joined the Society in 1854, and held the offices of Hon. Sec., Treasurer, Vice-President, and President, whilst Mr. Durham and Sir George Buchanan had each filled the office of Vice-President.

Eight members have resigned.

The Council note with much satisfaction the steady increase of the experimental work brought before the meetings, and trusts that members of the Society engaged in research work at the various laboratories recently equipped in London will continue to bring their results to enrich the 'Transactions' and add to the interest of the meetings.

The finances of the Society continue in a very satisfactory condition. The income of the current year was £497 6*s.* 11*d.*; the expenditure, after investing the life composition fees, £511 13*s.* 5*d.*, the small deficit being due to the inclusion in the current expenditure of the sum of £34 7*s.* 6*d.*, which, as will be seen on reference to the balance-sheet, is a special charge, which will not recur in

future years, and is due to the fact that in respect of the items marked with an asterisk in the balance-sheet the payments are for a year and a half instead of for the current year. In the absence of this charge there would be a balance to the good on the year's working of £20 1*s.* 0*d.*

The amount of money invested in Consols has increased from £1184 11*s.* 2*d.* to £1214 3*s.* 2*d.*, whilst the present balance in hand is £139 18*s.* 2*d.*

F. W. Pavy.

Statement of Receipts and Payments for the Year ending 30th April, 1895.

SIDNEY COUPLAND, Esq., M.D., *Treasurer.*

RECEIPTS.	£	s.	d.	£	s.	d.
Balance in hand, 1st May, 1894				154	4	8
Subscriptions:						
232 paid direct	388	10	0			
138 „ through Bank						
370						
13 Admissions at 21*s.*	13	13	0			
2 Non-Resident Admissions at £3 3*s.*	6	6	0			
3 Life Compositions	31	10	0			
				439	19	0
Sale of 'Transactions':						
Per Publisher				25	18	3
Dividends				31	9	8
				£651	11	7

PAYMENTS.	£	s.	d.	£	s.	d.
Meetings:						
Rent to Christmas, 1894	105	0	0			
Refreshments, waiters, &c., do.	26	15	0			
Do. for half Session from Christmas, 1894, to end of Session 1894–5	13	7	6*			
Microscopes	23	9	0			
				168	11	6
'Transactions,' &c.:						
Printing, Binding, &c., of Vol. XLV	142	7	9			
Illustrations	76	17	0			
Index	3	3	0			
				222	7	9
Secretariat and Treasury:						
Assistant Secretary to Christmas, 1894	42	0	0			
Do. for half Session from Christmas, 1894, to end of Session 1894–5	21	0	0*			
Addressing Circulars, &c.	2	9	0			
Bank Charges	2	2	0			
Stationery and Sundry Printing	15	7	0			
Petty Cash, &c.	6	6	2			
				89	4	2
				480	3	5
Investment of Life Compositions in Consols (£29 12*s.*)				31	10	0
				511	13	5
Balance at Bank	135	9	8			
Petty Cash in hand	4	8	6			
				139	18	2
				£651	11	7

Amount Invested in Consols, 30th April, 1895—£1214 3*s.* 2*d.*

Audited and found correct, 6th May, 1895.

ARTHUR FRANCIS VOELCKER, J. HUTCHINSON, JUN., *Auditors.*

SIDNEY COUPLAND, *Treasurer.* F. W. PAVY, *President.* ANTHONY A. BOWLBY, *Hon. Sec.*

* These payments are brought into this Account in order to make it include all expenses of the Session.

LIST OF SPECIMENS AND REPORTS

BROUGHT BEFORE THE SOCIETY DURING THE SESSION 1894–5.

I. DISEASES, ETC., OF THE NERVOUS SYSTEM.

II. DISEASES, ETC., OF THE ORGANS OF RESPIRATION.

III. DISEASES, ETC., OF THE ORGANS OF CIRCULATION.

IV. DISEASES, ETC., OF THE ORGANS OF DIGESTION.

V. DISEASES, ETC., OF THE GENITO-URINARY ORGANS.

VI. DISEASES, ETC., OF THE ORGANS OF MOTION.

X. MISCELLANEOUS COMMUNICATIONS.

XI. SPECIAL COMMUNICATIONS.

XII. DISEASES, ETC., OF THE LOWER ANIMALS.

REPORTS OF THE COMMITTEE ON MORBID GROWTHS.

LIST OF PLATES.

LIST OF FIGURES IN THE TEXT.

REPORT.

SESSION 1894-1895.

I. DISEASES, ETC., OF THE NERVOUS SYSTEM.

1. *Case of serous pachymeningitis with atrophy of the cerebral convolutions in a syphilitic child.* (*Card specimen.*)

By J. Walter Carr, M.D.

The specimen consists of the calvarium and brain of a female child aged 19 months.

The birth of the child was natural and easy, no instruments being used, and no history could be obtained of any subsequent injury.

There was a strong syphilitic history; the father had had syphilis when in the army; the mother had had four miscarriages, and this was her first living child. When seven weeks old the child came under treatment at the Victoria Hospital for Children, Chelsea, for well-marked congenital syphilis; she was very anæmic, and for many months had snuffles and nasal discharge. Despite continuous mercurial treatment she had, a few weeks before death, signs of slight epiphysitis of the lower end of each femur, which subsided in two or three weeks.

The mother stated that from two weeks old she was liable at frequent intervals to convulsive attacks, which were sometimes very severe; that she never took much notice, never sat up alone, and at the time of her death was like an infant three months old; no rigidity was ever noticed.

Death occurred rather suddenly on December 31st, 1894, and at the autopsy was found to be due to diffuse pneumonia affecting both lungs; all other organs in the chest and abdomen were normal.

There were very slight rachitic changes in the bones; the fontanelle was not quite closed.

The head was not enlarged, but the bones were slightly thickened.

The dura mater appeared normal externally, but was lined on its inner side by a thin membrane, thickest over the vertex, and becoming gradually thinner towards the base; it could be stripped off the dura fairly readily; on its inner aspect it presented a peculiar gelatinous appearance and consistence. There was also a good deal of thick gelatinous material over the convolutions and at the base of the brain, with slight excess of subarachnoid fluid. Under the microscope the membrane was found to consist of a finely fibrillated connective tissue, with no evidence of any recent hæmorrhage.

Pia mater and vessels normal; no sign of any gummata at base of brain.

Weight of brain 18 oz. (the normal weight in a child of eighteen months being about 30 oz.).

There was very marked pallor, depression, and hardening of the convolutions on each side in the region of the Sylvian fissures; on the right side the affected area reached upwards from the posterior limb of the Sylvian fissure to the upper limit of the mid-frontal convolution, and backwards almost to the angular gyrus. On the left side the convolutions involved were those more immediately surrounding the posterior limb of the Sylvian fissure—viz. the superior temporo-sphenoidal, angular, supra-marginal, the lower ends of the ascending parietal and ascending frontal, and the convolutions of the island of Reil. The convolutions elsewhere were pale, but otherwise natural.

On cutting into the brain the lateral ventricles were not dilated, but on the left side the upper part of the island of Reil was occupied by a cavity of irregular shape about three quarters of an inch long by half an inch from above down, and extending into the convolutions above and overhanging the insula. This cavity was occupied by a network of very thin membranous connective tissue, and did not contain any fluid or show any sign of hæmorrhage.

The spinal cord and its membranes appeared normal.

The case was probably one of serous pachymeningitis, described by Dr. Gowers ('Diseases of the Nervous System,' vol. ii, p. 328) as a very rare condition, met with in young children and

general paralytics, in which a membranous layer lines the dura mater and is continuous at the base with a thinner layer that covers the arachnoid, with more or less fluid between the two, constituting external hydrocephalus, and with or without compression atrophy of the brain.

I can find no description of a precisely similar case. In vol. xlii of the 'Transactions' of this Society Dr. Wheaton records the case of an infant, aged seven months, with a similar membrane beneath the dura mater, but also sixteen ounces of fluid, and the hemispheres were uniformly shrunken. There was an enlarged spleen, but no other distinct evidence of syphilis.

Several cases of cerebral atrophy in children have also been described; in vol. xl of the 'Transactions' Dr. Angel Money records one in a child aged four years. There was syphilitic meningitis, both the dura mater and the pia arachnoid being thickened and adherent to each other; there was disease of the arteries and wasting and sclerosis of the right motor area. Ashby and Wright ('Diseases of Children,' p. 423) describe sclerosis of the brain as "more often local than general, and mostly secondary to some inflammatory lesion or softening. . . . In rare cases the whole or greater part of the brain is shrunken and indurated, as the result of a meningo-encephalitis occurring during intra-uterine life, or shortly after birth; such cases are probably syphilitic." They mention one case, that of an idiot aged twenty months, who had suffered from convulsions, and in whom the entire convex surface of the brain was hard and shrunken.

In my case the meningitis was probably specific, and the cerebral atrophy and sclerosis secondary; the cavity in the left hemisphere might have been due to softening.

Congenital syphilis is usually supposed to be a rare cause of idiocy, but the case illustrates the possibility of its being so, and also at least one way in which the mental impairment may be produced. *January* 15*th*, 1895.

2. *Hæmatoma of the dura mater.*

By W. P. Herringham, M.D.

A. E. T—, a boy aged 2, was admitted to St. Bartholomew's Hospital, under Dr. Hensley, for anæmia and an enlarged spleen, and died four months later with the same symptoms. The liver, treated with ferrocyanide of potassium and hydrochloric acid, gave in an extreme form the blue reaction characteristic of pernicious anæmia. The skull shows the bones described by Parrot as characteristic of syphilis. No other sign of this disease was present. The dura mater shows two conditions:

1. Blood adherent to its inner surface, both in small flecks, and also in two large patches in the frontal regions symmetrically placed, and lying immediately internal to the frontal bosses before mentioned. Since, however, the internal table of the skull and the external layer of the dura mater are both natural, it appears improbable that the hæmorrhage is dependent upon the existence of the nodes.

2. Hæmorrhage in the tissue of the dura mater itself, both near the aforesaid hæmatomata and also in other parts, especially in the falx cerebri. The arachnoid membrane was natural and quite free from blood.

These hæmatomata have been amply treated of late by Dr. Wynne ('Trans. Path. Soc.,' vol. xliii), Dr. Newton Pitt (ibid.), and Dr. Wilson (ibid., vol. xlv). More than one source has been assigned to the hæmorrhage, but the mode of their production still remains doubtful. This specimen is shown because, in this instance, the condition of the dura mater points clearly to that membrane as the origin of the hæmorrhage.

December 4th, 1894.

3. *A large subdural hæmorrhage occurring in a case of infantile scurvy.*

By William Wallis Ord, M.D.

W. B—, a male infant aged 11 months, was brought to my out-patients at the Victoria Hospital, Chelsea, on October 29th, 1894. The family history was good; there was no evidence to be obtained of syphilis, tubercle, or hæmophilia. The boy was a twin; there was one elder child, who was in good health. The twins had been brought up on a proprietary food from their birth, and the mother stated that she had prepared it conscientiously according to the directions, *i. e.* with a small quantity of milk, not more than half-pint in twenty-four hours. The only difference that was noted in the behaviour of the twins was that the patient often vomited his food, while his brother never did. The latter was subsequently brought up to the hospital, and was found to be markedly rachitic, but showed no sign of scurvy.

On examining the patient there was apparent a marked ricketty deformity of the skull, there being four well-marked cranial bosses surrounding a widely open fontanelle; the head was not tender, and there was no craniotabes. The bones of the extremities were unaffected, and no history could be elicited of the child ever having screamed when being washed or handled. Scattered over the trunk and limbs were bluish-purple subcutaneous hæmorrhages, varying in size from a pin-point to a shilling; they were irregularly distributed, and not very numerous. These had been first noticed in August, and had been increasing lately in number; there were a few raised ulcerated nodules around the anus. There were two lower incisors cut; the gum around these was swollen, rather bluish in appearance, and bled easily. At the margin of the upper gum were two or three slightly raised bluish prominences. This gum also was apt to bleed when the child was fed. There was a slight bulging of the right upper eyelid, with a bluish stain showing through the skin, but no real proptosis.

The child was at once admitted, and put on a diet of peptonised

milk and fresh meat juice, with lemon juice. There was found a slight enlargement of both liver and spleen, with great general anæmia; otherwise the physical signs were normal, and the urine contained neither blood nor albumen.

The child at first improved in condition, and began to be bright and lively. The hæmorrhages were practically all absorbed by November 12th, and no fresh ones made their appearance. During November there were irregular rises of temperature, as high as 103·2°, without obvious cause. There was occasional vomiting, and towards the middle of the month a very obstinate and intractable diarrhœa made its appearance. The rash around the anus disappeared without any specific treatment; the anæmia increased, and the child began to lose flesh. An examination of the blood was made on November 28th, which showed that there were 1,420,000 red corpuscles and 20,000 white corpuscles to the cubic millimetre, with only 10 per cent. of normal hæmoglobin. On December 2nd, the second of two days of intense fog, the temperature rose to 104°, and there were marked signs of bronchitis in the right lung. He became rapidly worse, and died at 8 p.m. on December 3rd.

The medicinal treatment adopted consisted in the administration of the citrate of iron and quinine whenever the diarrhœa allowed; arsenic was only given for a few doses towards the end of November.

Autopsy (December 5th, 3.30 p.m.).—Body extremely pallid; no *post-mortem* staining; no rigor mortis; a few faint traces of subcutaneous hæmorrhages on the abdomen. On opening the body there was a considerable amount of subcutaneous fat of normal appearance.

Right lung: the upper and lower lobes were solid and airless, sinking in water; the middle lobe was œdematous.

Left lung: there was a large number of subpleural hemorrhages scattered over the surface, not extending deeply into the lung tissue; there was one deep-seated hæmorrhage of recent date in the lower lobe; both lobes showed signs of bronchitis.

Heart: considerable hypertrophy of left ventricle; no valvular lesion; decolourised clot in right ventricle; muscle very pale.

Liver: large and anæmic.

Spleen: weight 2 oz.; perhaps a little pale, but otherwise normal.

Kidneys: large and pale; capsule easily detachable.

Stomach: studded internally with numerous small submucous hæmorrhages of various dates; no ulceration.

Intestines: normal; no hæmorrhages or ulceration.

The mesenteric glands, especially those of the sigmoid mesocolon, were enlarged and fleshy, and showed on section central hæmorrhages; no other hæmorrhages were found in the abdomen.

On removing the skull-cap a large quantity of clear slightly stained fluid escaped; the calvaria was found lined throughout by a bright red subdural blood-clot, thicker on the right side, and not descending lower than the incision in the skull except for a short distance over the right orbit, and also over the left squamous bone; save at these points the clot was entire; there was no sign of hæmorrhage at the base of the skull. The brain was distorted, and the cerebral hemispheres deeply cupped, especially the right.

The orbital hæmatoma had disappeared except for a slight staining of the tissues above the eye.

The long bones were unaffected; epiphyses normal in size, and not soft or spongy on section; no hæmorrhages.

There was well-marked beading of the ribs, but no marked deformity of chest; the rib cartilages on section were gelatinous and vascular.

There are several points of great interest in this case. First as regards the history, the patient having been brought up on a food that was not, as Dr. Barlow happily taught us to say the other day, a "living food," the amount of milk used in its preparation being small, and its benefit often lost on account of the vomiting. In the second place, the large size of the hæmatoma, without any symptom pointing to intra-cranial pressure arising during life. Third, the freedom from trouble of the long bones, a circumstance which, as Dr. Barlow pointed out in his recent Bradshaw Lecture, would at one time have militated against the diagnosis of scurvy. Undoubtedly the limbs are first, and chiefly, affected in the majority of cases; but, as both Dr. Barlow and Dr. Sutherland have pointed out, extensive hæmorrhages may take place in connection with the cranial bones, the bones of the extremities being unaffected. Finally, the fact that of twin brothers, brought up quite identically in the matter of care and nourishment, one should develop scurvy and rickets, the other even more marked rickets but no

scurvy, affords another proof, if one were wanted, of the non-epidemic nature of this disease. *December 18th*, 1894.

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4. *Case of cerebro-spinal meningitis.* (*Card specimen.*)

By R. G. Hebb, M.D.

H. W—, male aged 9 months, was admitted under Dr. Donkin on November 6th, 1894.

The child was quite well up to the evening of October 27th, when at 10 p.m. it was suddenly seized with vomiting and diarrhœa; the motions were yellow and offensive. On October 29th there was severe general tenderness, so that the child screamed when touched; there was pain at the back of the head and retraction. It had frequent sweatings and was very restless at nights. On November 3rd the mother noticed that the right elbow was swollen and shiny; it was not red, nor did it pit on pressure. There was no cough and no dyspnœa.

The child had been fed from the breast only. The parents live in Chapel Street, Brixton, where during the past twelve months "the drains have been bad," but have recently been relaid. During the past year cases of diphtheria and scarlet fever have occurred in the house. The child's brother is well and the parents quite healthy.

On admission the child was found to be well nourished. Temperature 103°. Heart and lungs normal. There was considerable general tenderness, the child screaming when touched. This was more marked about the right elbow than elsewhere, and the right arm seemed more helpless than the left. There was at this time no noticeable swelling of the joints. The anterior fontanelle was widely open, bulging and tense. After admission the temperature became intermittent, varying from between 99° and 104°. There was occasional vomiting, and the bowels were freely open. No optic neuritis. On November 12th general rigidity set in; left pupil larger than right; the child is apathetic and drowsy; does not scream or object when examined. 14th.—The rigidity has

increased, and there is well-marked opisthotonos; external strabismus. Pulse rapid, regular. Respirations regular. 16th.—Extensive stomatitis. Child more drowsy; swallowing much impaired. 17th.—General convulsions.

Died 8.35 p.m. Temperature during last three days descended to 97°—100°. Urine acid; no albumen.

Post-mortem examination made forty-two hours after death. Body emaciated. *Post-mortem* decomposition just commencing. Body flaccid. Testicles in canals. Bulgings, size of pigeon's egg, on inner side of both elbow-joints. Fluctuation in both swellings with grating in joints on rotation. On opening these joints about three quarters of an ounce of thick, slightly sanious pus was evacuated from each. In both part of the coronoid and olecranon processes are necrosed. The left foot is swollen and boggy, both on the plantar and dorsal aspects, and the skin around the big toe-joint is thin and bluish. There is fluctuation and grating in this joint; and the ends of the metatarsal and phalangeal bones are bare and rough. There is about half an ounce of sanious pus in the joint, and a diffuse abscess of the sole and dorsum of the foot. Other joints *nil.*

Anterior fontanelle large, but no evidence of rickets. Cranial bones dry and white. Brain 32 oz.; convolutions flattened. Fluctuation marked. Almost the whole of the cerebral and cerebellar surfaces are covered with yellow purulent lymph, which is thickest about the middle line of base and vertex. The purulent lymph, which is subarachnoid in distribution, spreads also all the way down the spinal cord on the posterior aspect, of which there is quite a large collection. There is much turbid and purulent fluid in the lateral ventricles, and in the wall of the right descending cornu there is a large area of septic hæmorrhagic inflammation. Both middle ears are filled with greenish-yellow pus. Tonsils *nil.* Whole of the lower lobe of left lung is purple and consolidated (recent broncho-pneumonia). Rest of lungs and pleuræ normal. In front of thymus there is a diffuse collection of pus.

Heart 1½ oz., and pericardium normal. Abdominal viscera febrile, otherwise *nil.*

Microscopical examination of the pus (subarachnoid and from joints) showed, when stained with alkaline methylene blue, large numbers of very small cocci, ovalish, often in pairs, free in the plasma; arrangement diffuse and scattered; no clumps or chains.

Many are surrounded by a halo, but a definite capsule is uncertain. The cocci are quite decolourised by Gram's method.

From the ordinary cocci of suppuration the microbe of this case is distinguished by its arrangement, size, and colour reaction. From the *Diplococcus pneumoniæ*, Fraenkel, by its shape and colour reaction. From *Diplococcus intracellularis*, Weichselbaum, in that this latter usually occurs in pairs (though it is seen in clumps and solitary); it is almost invariably within the cells. From the microbe of suppurative meningitis, described by Neumann and Schiffe, in that this latter is really a bacillus 2 μ long.

Neither of the last two organisms stains with Gram's method. It is quite different from the *Streptococcus meningitis* described by me in volume xlv, p. 10, of these 'Transactions.'

December 18*th*, 1894.

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5. *Some gross lesions in the brains of lunatics, with remarks upon the frequency with which the two sides of the brain are affected.*

By Cecil F. Beadles.

These five brains are shown as illustrating some of the grosser lesions that are to be met with in the brain of the insane after death. The relation which they bear to the mental aberration is often anything but clear, for more or less similar lesions may at times be found in persons dying non-insane, and who during life may not have exhibited any cerebral symptoms. They show, too, an advanced degree of some of the most common morbid changes that are almost invariably found in asylum patients.

Most of these are undoubtedly the result of vascular lesions, and I shall refer to the frequency with which such lesions occur in various parts of the central nervous system.

Cerebellar lesions.—Specimen 1.—The first specimen is a cerebellum into the right hemisphere of which an extensive hæmorrhage has taken place. The right lobe has been almost completely ploughed up by blood from a ruptured vessel in its substance, and converted into a large cyst filled with clotted and fluid blood,

which communicated with the exterior. The left lobe and pons are somewhat softened. The cerebral hemispheres are fairly developed, and present no signs of hæmorrhage, but are likewise rather softer than natural. The arteries at the base presented atheromatous changes.

This brain was from a man aged sixty-five, whose insanity was of four years' duration, having been admitted into Colney Hatch Asylum in March, 1890. He was greatly depressed and suicidal, and was continually rubbing himself, from a delusion that hundreds of living creatures existed under his skin and were eating up his body, and under the idea of allowing them to escape he had cut himself about in numerous places. He complained of a constant dragging sensation in the right loin, which he believed due to cancer of the kidney. Tactile sensation was impaired, gait slow and crouching, and knee-jerks increased. He continued very desponding, apathetic, and hypochondriacal; took no interest in his surroundings, and remained unoccupied. He was always complaining of constipation without cause, and had the belief that no passage existed through his body. Habits were cleanly. Continuing in the same state, with the same delusions of insects, &c., remaining unoccupied, he became more feeble, and died suddenly in June, 1894. Getting out of bed during the night and commencing to dress, he suddenly fell on his head and expired in a few minutes. In this case the heart was hypertrophied, and the aorta with its valve was atheromatous; the kidneys were large, and their capsules adherent in places, leaving a granular surface on removal.

Death from hæmorrhage into the cerebellum is very rare both in lunatic asylums and elsewhere. In the *post-mortem* records of Colney Hatch I have only been able to discover nine cases in which this had happened; three of these were men and six were women.

Small hæmorrhages, which were not themselves fatal, and indications of old blood extravasations, as shown by patches of softening in this region of the brain proper, are also by no means frequent. There were three of the former and eleven of the latter. In addition to these there were seven cases in which one of the cerebellar hemispheres was replaced to a considerable extent, or almost entirely, by a large cyst, much of whose wall was formed merely by the thickened pia-arachnoid membrane, and whose con-

tents consisted of clear fluid. It is probable that most of such cases are hæmorrhagic in origin.

Thus we have a total of thirty cases in which presumably vascular lesions had occurred in the cerebellum, as disclosed by an examination of 3,300 brains.

In a few of these cases similar lesions existed elsewhere in the brain. For instance, in a female where the left lobe of the cerebellum was converted into a shell filled with recently shed blood, there co-existed a small hæmorrhage of old date in the left corpus striatum, with flattening of the central ganglia, and in another case a large cavity below the left hemisphere was associated with a cyst of smaller size in the left side of the pons.

General shrinking and hardening of one lobe of the cerebellum is now and then come upon. The second specimen is an instance in point.

Specimen 2.—The right cerebellar lobe is considerably reduced in size, and the vacant space in the recent state occupied by a large collection of fluid within the thickened pia arachnoid. The arteries at the base of the brain were much diseased, and the right internal carotid at its entrance into the cranial cavity was occluded by a calcareous mass. There was also atrophy of some of the cerebral convolutions with some dilatation of the ventricles.

The patient was a female aged 56, whose insanity was of only four months' duration. With an attack of two weeks' existence she was admitted into the asylum on May 11th, 1888, in greatly impaired health. She had a wild excited look, had delusions of persecution, and was subject to epileptic fits, of dirty habits, and refused food. She rapidly developed into dementia, and became progressively weaker. On August 25th she had a series of severe fits accompanied with left hemiplegia, which, increasing in severity, left her comatose. At the end of forty-eight hours, however, she rallied for a short time, became brighter though restless; but deglutition had become difficult, and she sank and died on September 4th. All the viscera except the brain were fairly healthy, and no special lesion was found after death to account for the final attack. It may have been due to an embolus, but more likely was the result of pressure from fluid on the medulla.

Unilateral atrophy of the cerebellum to as great an extent as this has been observed after death in the brain of sane persons

who presented no symptoms during life. The cause of this atrophy is not always clear. It may be a secondary degeneration, but there is often no lesion elsewhere noticeable to the naked eye throughout the entire brain. In the case just described it would seem that defective blood-supply was the exciting cause, but in some cases it doubtless is due to the contraction that follows an old extravasation of blood into its substance, while in others it may result from old inflammatory processes in its neighbourhood. It may be congenital.

Sometimes the reduction in size of one of the cerebellar lobes is definitely associated with signs of an old vascular lesion in one of the cerebral hemispheres, as in a female, where shrinking and hardening of the left lobe, with gelatinous fluid contained in a sac formed externally by thickened pia mater, co-existed with an old clot the size of a bean in the second middle frontal gyrus of the left side. The cerebellum as a whole weighed 4 oz.

Another case is that of a police constable, aged 37, whose illness had existed for eight months before admission, and dated from a fall. He had been an excessive whisky drinker, and although mental symptoms had manifested themselves many years before, he continued on duty up to a few days before certification. Melancholia, with aural hallucinations and delusions of suspicion with suicidal tendency, were the main features. His father died of softening of the brain. The state of the patient varied from time to time, but apparently without any of the special signs of cerebellar disease. At the close of two months he became very excited and violent, after which he relapsed into a helpless paralysed condition, confused and unable to answer any questions, destructive and dirty in his habits and sleepless at night, and he died after three months' residence in the asylum, having been comatose for forty-eight hours. The whole brain was smaller than normal, with great atrophy of the cortex along several convolutions, especially the left ascending frontal at the apex. The left side of the cerebellum was atrophied and softened, the medulla shrunken in appearance. In addition, the more common lesions of ventricular dilatation, flattening of the central ganglia, excess of fluid, and thickening of the membranes were present. Hypertrophy of the left cardiac ventricle, slight thickening of the mitral flaps, and some incompetence of the aortic valve, with small fibrotic kidneys, completed the points of importance. These cases where the wasting

in the two situations is on the same side do not fall in with the statement made by Gowers,[1] that "atrophy of the whole of one cerebral hemisphere is associated with atrophy of the opposite cerebellar hemisphere," and that the latter may be associated with atrophy of the opposite corpus striatum alone.

In a female with the optic thalamus and cerebellar hemisphere both smaller on the left side, the left communicating artery of the circle of Willis was very small, but the vertebral on that side was larger than on the right. Moreover all the basal vessels were very atheromatous. A fatal case of hæmorrhage into the left side of the pons, which was associated with reduction in size of the right cerebellar lobe, I shall shortly refer to more fully.

Seldom in the asylum do we get cases exhibiting the characteristic symptoms of cerebellar disease, such as vertigo, staggering gait, vomiting, &c. This, in view of Nothnagel's researches, is doubtless because in asylum patients, when the hind brain shows signs of disease, it is almost invariably one of its lobes that is affected, and not its central portion. Moreover it is probable that hæmorrhage into the middle region of the cerebellum, when it does occur, is usually at once fatal, so that indications of old blood extravasations we could scarcely expect to find. I have found no cases of associated paralysis agitans to support the theory put forward by Hughlings Jackson.

This want of signs was especially mentioned in the case of a female where the right side was absorbed, and a large cyst, the size of a green walnut, filled with clear fluid, pressed upon the surface and flattened the convolutions around. It was separated from the fourth ventricle by a thin membrane only. The middle lobe was not affected. The heart showed hypertrophy of the left ventricle with mitral stenosis, and the kidneys were cirrhosed. The patient was admitted in November, 1878, with insanity of three weeks' duration. She was thin and ill-nourished, melancholic, and had great dread without apparent cause: delusions that her face was being burnt to pieces, that her flesh was falling off and her eyes dropping out, were prominent and persistent. She died in May, 1880, from exhaustion following great excitement, with dread and despair and a strong wish to die, having several times attempted to strangle herself. Death took place in a semi-comatose state at the age of forty-eight.

[1] 'Diseases of the Nervous System,' vol. ii, p. 580.

I have already spoken of the rarity of central lesions, it may therefore be worth while to mention the few of which I have found reference. Amongst the males, hæmorrhage is reported twice and softening once, as occurring in the central portion of the cerebellum.

The first case of hæmorrhage was in a patient who had been a seaman, and died at the age of fifty-six, having been the subject of mania with delusions for over fourteen years. The day before he died he had a severe apoplectic seizure, accompanied with left hemiplegia. In addition to the above lesion there was general wasting and softening of the cerebrum and hypertrophy of the heart.

The second is a patient admitted in a state of imbecility with repeated epileptic fits. His occupation had been a carman, and his whole manner had changed of late, having become so for over a month, the cause of which was unknown. The total duration of his insanity was little more than $3\frac{1}{2}$ months. He was forty-eight when he died. The heart was fatty with hypertrophy of the left ventricle and valvular disease, in addition to marked arterial degeneration.

The case of softening which is recorded was in a male patient, who died at the age of sixty-three, having had mania with epilepsy for close on three years. On admission his illness was only of two weeks' duration. He was subject to epileptic attacks, which had greatly impaired his memory. Frequent outbreaks of violence occurred, when he committed extravagant acts, such as wandering into the street in almost a nude condition. Nearly a year passed before he had his first fit in the asylum, during which his left side was chiefly implicated. After this he remained quiet, was fond of reading, and only rarely had fits. There is no mention of any cerebellar symptoms. At the autopsy there was found on the upper surface of the cerebellum, in the middle line, an area of red softening about the size and shape of an almond, which extended only a short distance from the surface, and was covered by thickened pia mater and arachnoid. Besides this the membranes were thickened and adherent in patches over the convex surface of the cerebral hemispheres, and were with difficulty removed, tearing away some of the grey cortex in the attempt. The ventricles were greatly dilated with clear fluid, and there was slight granulation of the ependyma. The white substance of the fornix and commissures was very softened and friable. The arteries at the base were atheromatous; great hypertrophy of the left side of the heart, with advanced

fatty change but without valvular disease, was also present, as well as granular kidneys, with narrowed cortices containing small cysts.

The only case that I have been able to discover, where cerebellar symptoms are distinctly stated as existing, was in a female, where a sanguineous clot was found in the anterior part of the cerebellum pressing upon the medulla oblongata. Here there was atheroma of the arteries and of the aortic valve. The patient was an inmate of the asylum from September, 1851, to November, 1870. During the greater portion of this time she had been in a state of despondency and melancholia, and at one period was considered strongly suicidal in tendency. She was incoherent and timid in nature. On the date of death it is noted that for some little time past she had frequently complained of feeling suddenly giddy, and had the impression that she would fall down suddenly and die. Her health had been declining for the last six years; she was of very quiet demeanour, very cleanly in habits, and very retiring. On the morning on which she died she had a swoon, but rapidly recovered, and made preparations for breakfast; shortly after, however, she was found dead with her head reclining on her bed. Her age was sixty-five.

Before we leave the subject of the small brain it is worth while to observe the frequency with which the two hemispheres are implicated. Of the cases referred to, it will already have been noticed that the left side was most frequently mentioned. They are included in the following table:

Table showing the distribution of thirty-four cases of gross lesions of the cerebellum.[1]

Form of Lesion.	Total.				Male.				Female.			
	R.	L.	B.	C.	R.	L.	B.	C.	R.	L.	B.	C.
Hæmorrhage	1	4	1	3	1	...	...	2	...	4	1	1
Old hæmorrhage indicated by extravasation	1	2	...	..	...	...	...	...	1	2	...	...
Softening (localised)	3	5	2	1	...	3	2	1	3	2	...	...
Cavity with atrophy	1	4	1	1	...	2	...	...	1	2	1	1
General atrophy (excessive)	...	3	1	...	...	1	...	...	...	2	1	...

[1] For explanation see that of the next table, p. 29. Cases have not been included where general softening of one or both lobes occurred.

In the case where hæmorrhage took place into both lobes, that in the left proved fatal, while that in the right was of small size. There was also an extravasation of blood on the anterior superior frontal gyrus the size of a bean. The female in whom both cerebellar lobes were much reduced in size also had an old blood-clot in the left temporo-sphenoidal lobe, but in the case where a cavity existed on each side no other lesion was present. The centrally situated cyst occurred in a hydrocephalic child, whose case I shall deal with later.

Hæmorrhage into pons and medulla.—Only one case of hæmorrhage is recorded as occurring in the medulla oblongata; this was in a male. In another instance an old hæmorrhage was present in the medulla in the vicinity of the left olivary nucleus of a female, associated with a similar condition in both the right and left lenticular nuclei of the cerebral hemispheres. Two cases of localised softening in the right and one in the left crus cerebri, and one case of hæmorrhage in the left crus are reported in females.

With regard to the pons Varolii, the cases are six of recent hæmorrhage and three of localised softenings or old blood-clots. Two of the former and two of the latter were in females. In one of the male cases of hæmorrhage the extravasation had spread through the peduncle into the left lobe of the cerebellum.

As vascular lesion in either of these situations is, of course, most often at once fatal, we should scarcely expect to find localised softenings or cysts with any frequency in the pons or medulla of lunatics' brains. The degeneration that is secondary to injury or disease of the great brain is naturally not uncommon, but of that I am not now speaking. As a rule, the hæmorrhage that has taken place into one or other of these regions has been the cause of death after the patient has been some years insane, and it is rarely or never the direct cause of the patient becoming certified. But there is no doubt that this was the case with a man who was lately under my care in Colney Hatch. It is the case I have already referred to as one of fatal hæmorrhage into the pons associated with atrophy of one lobe of the cerebellum.

The patient on admission was in an excited state, noisy, and talked incoherently in an extravagant manner. He had a wild expression, no facial paralysis was noticed, but there was continued movement of the head and facial muscles. There was internal strabismus of the left eye; he was continually rolling his eyes about,

and his pupils were somewhat dilated, but equal. Slight general paresis on the right side was present. His attack was said to have existed for fourteen days, during which he had been very violent, necessitating his confinement in a padded room. There had been two epileptiform seizures. He was fifty years of age, had never been insane before, and had no hereditary taint. For the past two years he had been a private attendant upon an insane gentleman. After admission here he continued excited and noisy, striking the wall with both hands, and died about ten hours later during a paralytic seizure. In the lower and anterior part of the left side of the pons was a hæmorrhage of comparatively recent date; it formed a circular mass of about half an inch in diameter, a central black clot, surrounded by softened discoloured brain tissue, pressed upon the pyramidal tract and passed slightly into the medulla. From its appearance it had certainly existed over a week, and probably about a fortnight, and was undoubtedly the cause of the attack in the first instance. Its situation corresponded to the nucleus of the sixth nerve of the left side. Besides this lesion, the right cerebellar lobe was reduced in size to nearly half that of the left, the latter being apparently normal. On section both lobes seemed of natural consistency, and neither contained a hæmorrhage. The membranes and large brain also looked normal, except that the latter was hardened. Cardiac hypertrophy with mitral stenosis and advanced atheroma of the aorta and basal vessels was present. It seems scarcely possible that any relation existed between the condition of the pons and cerebellum, that of the latter having to all appearances been long in existence.

Dilated ventricles.—A slight dilatation of the ventricles of the brain is the usual condition found in all forms of insanity. In this case, however, the dilatation is carried to an unusual degree, and it is rarely that we find the lateral ventricles so greatly distended.

Specimen 3.—Externally the brain appears of fair development, weighing, when fresh, 35½ oz.; it was throughout harder than natural, and there were no signs of old hæmorrhage. The lateral ventricles are enormously dilated, and filled with fluid, lined by a smooth exceedingly thick ependyma, which is slightly detached in places. On the escape of fluid the cerebral hemispheres completely collapsed. The dilatation has taken place more especially outwards, upwards, and backwards at the expense of the brain

substance, and with disappearance of the central grey ganglia. Both hemispheres are equally affected, the frontal lobes in both having least suffered. In the parietal and occipital regions there are places where the nervous structure is less than a quarter of an inch in thickness, the grey matter being exceedingly narrow.

Obtained from a female aged eighty-two, with insanity of thirty-four years' duration, who, on admission in 1858, was an extremely violent, irritable, and jealous imbecile. Her bodily health was good; having been dumb from birth she was uneducated, and her intellectual powers were undeveloped. She quieted down, and was employed in the laundry. In 1864 she was again extremely excitable and dangerous. In 1885 she had developed into a demented state, but was of clean habits, happy, and usefully occupied in the laundry, in which state she continued up to 1890, when her health became more feeble, and she died in February, 1892, from pneumonia following influenza. At no time had she an epileptic fit.

It is possible that in the above case the dilatation of the ventricles was congenital, or that it developed soon after birth; in fact, it is very doubtful whether such extreme cases of uniform bilateral internal hydrocephalus originate in adult life. During life it is practically impossible to diagnose such a condition. The case illustrates how a person, with seemingly little brain substance, may live a prolonged life, and even a useful existence; for this patient was of considerable help in the laundry, where for thirty years she worked with but a few brief intervals.

A similar condition of the brain is at times to be traced to some disease during infancy, usually of an inflammatory nature, such as infantile paralysis. This was so in a man who, although a deaf-mute, had been sufficiently able to look after himself and to follow the occupation of a French polisher until reaching the age of thirty. Not till then was it considered necessary to confine him in an asylum, he having developed paroxysms of great violence, destroying his clothes, and screaming about the streets. There was a history that when five years of age he had a serious illness, "water on the brain," following a fit, subsequently becoming deaf and dumb. His maternal grandfather and uncle were insane. He had been a steady hard-working man until a month before admission to the asylum in December, 1883. While here he was excitable and quarrelsome, made fantastic gesticulations, and was occasionally

destructive. In this condition he continued until his death in March, 1884, from maniacal exhaustion.

At the autopsy the membranes were opaque and slightly adherent to the brain, the convolutions of which were atrophied. The ventricles were enormously dilated, so as to make the brain almost resemble two sacs of fluid. The brain substance was exceedingly soft, flaccid, and wet. Except for hepatisation of the lung apices, the other organs were healthy.

In an imbecile youth aged twenty-eight, where excessive dilatation of the lateral ventricles was found, it is definitely said that the insanity arose from infantile paralysis.

In a lunatic asylum such as Colney Hatch, cases of hydrocephalus are seldom admitted. A particularly interesting case of this kind, however, was a female idiot aged twelve, blind and paraplegic, where the lateral ventricles were dilated to such an extent that the hemispheres were converted into nothing more than cyst walls with flattening and wasting of the convolutions, but which were normally planned. The brain substance was very pale, and the pia mater almost universally adherent. The calvaria was very large, measuring $8\frac{1}{2}$ inches by $6\frac{1}{2}$ inches, and the bone greatly thinned. But the interest of the case lay more especially in the condition of the cerebellum. This contained a cyst as large as an orange, centrally situated, which appeared to have commenced in the roof of the fourth ventricle, and involved both hemispheres. The walls of the cyst were of a reddish-brown colour like old apoplexy, and it contained a clear fluid in communication with the ventricles. Several hæmorrhages had occurred in its walls, and a clot lay on the floor of the fourth ventricle. Round the sides of the medulla, and in the walls of the cerebellar cyst, was heaped up a mass of what appeared to be new growth, pinkish grey in colour, and firmer than the surrounding brain tissue. It was seemingly of a sarcomatous nature, and the recent bleeding had presumably taken place from its substance. The pons was wasted and flattened from pressure. The corpora dentata of cerebellum could not be found.

The history was to the effect that the patient was admitted to the asylum in July, 1878, when she was eight years old, the insanity being then of one year's duration, but the cause is stated as unknown. She was then tall for her age, blind and paraplegic, and unable to walk; her head was large and hydrocephalic, her mental

powers undeveloped, and she was quite unable to do anything. All the special senses were imperfect, and she did not appear to hear distinctly. It was said that she lost her sight gradually about a year before, and that she had healthy brothers and sisters. Previous to admission she had been very spiteful and obscene in language. In 1879 she was quiet, contented, answered questions in a deliberate manner as if weighing their importance, and was continually complaining of headache. It was then suggested that she had a cerebral tumour. In April, 1880, she was quiet and intelligent. Her limbs were wasted, and there was but little muscular power; headache was constant, with frequent vomiting of apparently cerebral origin. In the following December she was bright and cheerful, and answered simple questions fairly well. During the next year she became dirty in habits. After this gradual failure in her health and mental state ensued; she became dull and stupid, rapidly lost flesh, and for three weeks there was persistent vomiting. She then died (March, 1882) with acute tuberculosis of the lungs, which had evidently been lighted up from an old deposit of long standing at one apex. From this history it scarcely seems possible that the intra-cranial condition was wholly congenital, and it is probable that the malignant growth, if such it was, had developed more recently in the wall of the previously existing cyst.

Uniform atrophy of one cerebral hemisphere.—It is not unusual to meet with slight difference in size of the cerebral hemispheres. This may occur with other chronic changes both in the brain and membranes, but sometimes there is little abnormality to be observed with the naked eye on section. No sign of hæmorrhage is present, although it may possibly be due to general shrinking following long antecedent blood extravasation which had slowly become obliterated. The wasting, however, may result from the cutting off of the blood-supply by occluded or thrombosed vessels supplying that side. Where this is the case there is often a preliminary softening and swelling of the hemisphere implicated. In a female with highly diseased arteries at the base, the right hemisphere of the cerebrum was much larger than the left, and on section the ganglia at the base and neighbourhood were found of a dirty yellow appearance with the consistency of gruel. In this case the difference of weight between the two hemispheres was—the right $20\frac{3}{4}$ oz., the left $16\frac{3}{4}$ oz. The left hemisphere seemed

shrunken, but on section appeared normal. The total weight of the encephalon was 42 oz., and the cerebellum $4\frac{3}{4}$ oz.

The same changes in the nervous tissue, in which, however, the sides were reversed and the difference in size less marked, is recorded in a female of forty-two who died with symptoms of paralytic dementia. She had both aortic and mitral disease.

As an instance manifestly due to hæmorrhage, the blood-clot being still visible, was the brain of a man with reduction in size of the left hemisphere. The man had been a painter, and was aged fifty-two on admission to the asylum in 1889, the duration of the mental symptoms having then existed for a year. He was in a state of dementia following hemiplegia. A fairly nourished man, with misshapen lower extremities, vacant expression, the remains of old left facial paralysis, grasp feebler on the left side, and left knee-jerk brisker than the right. Perception much impaired; apparently corresponded only by means of signs, although he could utter words. When given a pencil and paper he wrote some unintelligible words and seemed irritated at the thought of writing. Before admission he had been violent, noisy, shouting incoherently, and wandering vacantly about. His son related that six years before he had an apoplectic stroke, with loss of speech and loss of power on the right side. His speech had been affected since, but he had been able to work till a year ago, when he had another fit. On this occasion he was insensible for twelve hours; there had been none since. He had been a heavy drinker, but had never had lead colic, and there was no insanity in the family. During his stay here the patient was able just at first to do a little work in the ward, but he became very excited, abusive, and threatening when questioned in any way. In May, 1892, he had a number of paralytic seizures, which continued frequent during the following month, leaving the patient in a very low state. From this time he was completely demented and paralysed, only laughing when spoken to. He died in February, 1894, having been insane over five years, the last two of which he spent in bed.

A series of old hæmorrhages were found extending almost throughout the left hemisphere, in consequence of which the whole of that hemisphere was in a state of softening and much reduced in size. The dura mater and pia mater were much thickened.

Apart, however, from any vascular lesion, cerebral atrophy takes place as the result of both chronic alcoholic poisoning and of lead

poisoning, but it is seldom that we find any reference to the latter, although Fagge makes mention of it. The part which lead plays in the production of insanity has never been worked out. It is, moreover, a factor in the pathogenesis of mental aberration that has rarely been taken into account, but is one offering a pregnant field for investigation. From what I have seen in asylum practice I am inclined to believe that lead is a very important element in the production of brain disease, most probably through its effect primarily upon the vessels and kidney.

As a rarer instance of general wasting of the whole of one side of the central nervous system may be mentioned that of a woman who died with senile dementia of not more than eighteen months' duration at the age of seventy-three. The brain was small, weighing $37\frac{3}{4}$ oz. The whole of the left side was appreciably smaller than the right, not only of the cerebral hemisphere, but also of the mesencephalon and medulla, although the frontal and occipital lobes of both sides of the cerebrum were especially small, the convolutions being much atrophied. There was marked deficiency of the third frontal convolution of the left side. On section the brain was harder than natural; the lateral ventricles were considerably dilated, but more particularly the left at its anterior extremity. No distinct hæmorrhage or softenings were discovered. The calvaria was greatly thickened, as were also the dura and pia mater, and a very large amount of fluid was present in the skull and in the ventricles of the brain. The heart was hypertrophied with atheroma of the auriculo-ventricular valves, and to a slight extent of the aorta and the vessels at the base of the brain.

The patient was admitted in feeble health. The onset of the mental state had been gradual during the past six months, and she was now in a demented condition, unable to understand or answer questions, rambling and incoherent, of dirty habits, and wandering about in an aimless manner. She rarely spoke except to repeat what was said to her, and then she would laugh foolishly. She died from pneumonia, which came on suddenly five days previously. A week before this her right arm became much swollen, for which no apparent cause could be found.

Localised atrophy of cerebrum.—We now come to speak of brains where extensive localised wasting exists in portions of one or both of the cerebral hemispheres. The two remaining brains that I

exhibit are instances of this. Such cases are undoubtedly, as a rule, the result of extensive hæmorrhage at some previous period of the patient's existence.

Specimen 4.—In this brain there is great deficiency of substance of the left side. The brain is small, weighs only 37⅓ oz. The lower part of the parietal, upper two thirds of the temporo-sphenoidal, and hinder and lower part of the frontal lobes are absent; in other words, it is the region bordering on the fissure of Sylvius that has principally suffered, and the so-called speech centre has been seriously involved in the destructive lesion. In place of the brain tissue is a deep sulcus occupied by fluid, and covered by thickened membrane. The right hemisphere shows no gross lesion. The membranes are thickened and adherent throughout, and there was a circular thickening on the dura mater the size of a shilling piece lying over the lower end of the left ascending parietal convolution—a small hæmatoma of old date,—thus showing the probable origin of the lesion. Both lateral ventricles are much dilated, but the left to the greatest extent, which is only separated from the exterior at the Sylvian fissure by the thickened membrane already referred to. The consistency of the brain was soft, and it presented signs of old hæmorrhages in the left cerebellar hemisphere and in the right lower part of the pons, with atrophy of the left side. The vessels at the base were atheromatous, and the right vertebral was considerably smaller than the left.

The brain is from a female aged seventy-seven, with insanity of thirty-one years' duration. She was admitted into Colney Hatch in October, 1861, as a case of mania with paralysis, which had existed for eleven months. She was incoherent, mischievous, destructive, and dangerous, and had delusions on religion. Remaining almost throughout maniacal, violent, of dirty habits, and obscene in speech, she had, however, short intervals when she was clean, quiet, and harmless. Death occurred in January, 1892, from pneumonia following influenza.

In another female patient who became aphasic, which lasted till death, no lesion of the third frontal convolution was found, although old hæmorrhagic softening was seen both in the right optic thalamus and in the extra-ventricular portion of the striate body.

Specimen 5.—The other specimen is one of a brain likewise showing great atrophy of the left cerebral hemisphere, but of

somewhat different nature from the last. In this the frontal and parietal lobes are much shrunken, and only the anterior extremity of the temporo-sphenoidal lobe is present. The occipital lobe is entirely absent, its place being taken by a large cavity—a dilatation of the left lateral ventricle—and its walls formed of a blending of the thickened ependyma and pia-arachnoid membrane, with no trace of cerebral tissue between. The right lobe of the cerebellum appears smaller than the left. The pia mater is much thickened, and the basal vessels are very atheromatous.

This brain was obtained from a man aged sixty-six, whose insanity had existed for fourteen years. The notes of this case are interesting.

The patient had been a tailor, with a history of mental symptoms for nine months before admission in 1878. His health was broken down, and he was childish and in a state of dementia, incoherent in speech, and unable to give an intelligible answer to any question that was put to him; for instance, when asked his name, he said, "One pound three shillings." He was noisy and restless. He was said to have been very intemperate in his habits, and to have drunk away all his faculties and energies. In 1883 he had several epileptic fits, his right arm became partially paralysed, and his speech aphasic; he would repeat answers several times over and over again. Previous to this he had remained childish and incoherent, at times being of dirty habits. In 1888 he was quiet, aphasic, and had become more demented. There was no difference between the power of grip in the two arms, and no lameness. He could understand what was said to him, was able to read, but could not write, although he would try with his right hand, but soon shook his head and pointed to his hand. He frequently took up the newspaper, and seemed to enjoy it. His answers to all questions was a smiling "Yes, sir; yes, sir;" his negative was "Yes, sir," with a shake of the head; but the attendant stated that he sometimes made use of the expression "Damn it!" fluently. He could not repeat. Recently he had gained strength, and was now in fair health, of clean habits, and was usefully employed helping the Turkish bath attendant. Up to June, 1891, he remained in the same demented state, with method of communication limited almost entirely to that of gesture, although occasionally he appeared capable of using the right word in the right place. Habits were cleanly. Until lately he had remained in fair physical health, and

was usefully occupied in the ward, although for the past two years the cardiac sounds were feeble, and recently he was generally weaker. Death occurred on August 18th, following exhaustive diarrhœa. There was mitral disease, and much atheroma of the aorta. The kidneys were said to be healthy.

In this patient, with the lesion involving so much of the motor area of the cortex, and the greater part of the temporo-sphenoidal and occipital lobes, it is remarkable that the patient did not suffer from paralysis, that his hearing was apparently good, and that his eyesight seemed unaffected, although there is no record of an ophthalmoscopic examination having been made.

The case was different, however, in a female where the left parietal and both occipital lobes had suffered greatly. This patient had been blind about a year with white atrophy. On dying suddenly, after coma of half an hour's duration, there was found almost complete absence of the left parietal lobe, and partial absence of the occipital lobe of the same side, the vacant space being filled with fluid, continuous with the cavity of the ventricles, and covered only by thickened pia-arachnoid. In addition to this there was a considerable area of yellow softening in the occipital lobe of the right side. The optic nerves and tracts were atrophied and fibrous, and the arteries very atheromatous and much calcified.

Such a degree of wasting or disappearance of brain tissue is unusual, but there are a fair number of cases on record at Colney Hatch, of which the following may be taken as typical examples:

In an imbecile from birth who had been an inmate of Colney Hatch for seven years, and had spent the previous four years in an imbecile asylum, nearly the whole of the left hemisphere was destroyed, and its place taken by a large cyst. A great quantity of fluid was present. He was an ill-developed youth in greatly impaired health, with a paralysed, wasted, and useless right arm. Epileptic fits had occurred during his whole life. These were exceedingly severe, and he was then extremely violent. He became more and more paralysed, and death took place from exhaustion of epilepsy with phthisis at the age of twenty-three after lingering in a semi-comatose condition about three weeks.

In a second patient, who died at the age of twenty-three with epilepsy of twenty-two years' duration, the left side of the brain was replaced by a large cyst, the dura mater being closely applied to the brain and shrunken from the vertex of the skull. The

starting-point in this case was said to date from convulsions when one month old, but there was an hereditary history that his mother's uncle died in an asylum. There were the remains of infantile paralysis of the right side, the forearm and hand being strongly flexed and the leg atrophied and shorter than the other, with considerable arching of the foot. Epileptic fits were frequent and severe. On admission two years before death he answered questions fairly rationally, but he soon developed into a completely demented state with dirty habits.

A third case with great atrophy of the left hemisphere associated with epilepsy was that of a man in whom the cause and duration of insanity were unknown; he had, however, been a labourer. He was violent and outrageous in his conduct, and attempted to strangle the weaker inmates of the workhouse where he had for some time resided. His faculties were impaired, but except for contraction of the right arm, and walking lame from the same cause in his lower limb, he was in good bodily health. Fits were frequent and severe, but gave place after some years to attacks of violent temper. Throughout he remained of clean habits. He died at the age of sixty, the brain disease being over eighteen years in existence, he having been that time in the asylum. The calvaria was much thickened, especially on the left side, the membranes thickened and opaque, also more markedly over the left hemisphere, and there was much subarachnoid fluid. There was a striking want of symmetry between the two cerebral hemispheres, the left weighing 14 oz. and the right 21 oz. The anterior part of the left was hard and fibrous to the touch, the convolutions being atrophied, while other parts of the brain were soft. It is probable that in this case the condition of the brain resulted from a blood effusion or an inflammatory condition set up by an injury.

The following case is of particular interest, for in addition to marked absence of portions of both sides of the brain there existed a single horseshoe-shaped kidney, beyond which no other abnormality was found in the body. The posterior third of each hemisphere was wanting, its place being taken by a large cyst, the right communicating with the right lateral ventricle. The brain substance was hard, but the pia mater and calvaria were normal. This occurred in a man aged thirty-eight, who was subject to epilepsy, but had not previously been in an asylum. He had

had fits since eight years of age, when he had whooping-cough. There was no hereditary insanity. When admitted he was incoherent and unable to answer questions, had no idea of place or time, and was quite unable to take care of himself. He was in poor physical condition, with much-impaired health, and there was evidence of a bromide rash on his body. He died a month later after a succession of fits.

Frequency of vascular lesions on the two sides of the brain.—By far the larger proportion of the cases of marked deficiency of portions of the brain substance are the result of former hæmorrhage into the cerebral tissue, both clot and discoloration having, as a rule, long since disappeared; but as seen from some of the cases mentioned it may be the result of some inflammatory condition within the cranium in early life as a consequence of an acute specific disease. When it is the result of a ruptured blood-vessel the hæmorrhage has been extensive, falling short of an immediate fatal result, it may be, but by a hair's-breadth.

Most often marked localised wasting of regions of the brain is found in persons of advanced years, or in those addicted to alcoholic excess. There is almost invariably an hypertrophied state of the heart associated with advanced atheromatous change in the arteries, and the kidneys are rarely in a healthy condition. Notwithstanding the absence of a large portion of the brain substance in many of the recorded cases, it is strange to note how frequently the patient has been able to live a more or less useful life, though it may be nothing more than an automatic existence. Such patients, it will be seen, have usually been subject to epileptic fits, and that they are very frequently partially paralysed, but this is by no means invariably the case.

A point that is extremely noticeable is the frequency with which this atrophy is confined to the left side of the brain. Of the ten cases mentioned this was so in no less than nine. I have frequently been struck with the fact that both general and marked localised wasting of the brain exists most commonly on the left side. My own experience, agreeing with the general accepted view, is that both meningeal and cerebral hæmorrhage takes place rather more often on the left than on the right side, and the same applies to old vascular lesions as indicated by small foci of softening. With a view of discovering the proportion of the side most constantly affected in the insane I have looked over the records at Colney

Hatch Asylum, and have thought it worth while to give in a table the proportion of the sides affected by vascular lesions within the cranium. This is compiled as a result of the examination of 3300 brains, of which 1835 were from men and 1465 from women.

Table showing the vascular lesions met with in 3300 *consecutive brains examined* (1835 *male and* 1465 *female*).

Form of vascular lesion in cerebral hemispheres.	Totals.					Males.					Females.				
	T.	R.	L.	B.	C.	T.	R.	L.	B.	C.	T.	R.	L.	B.	C.
Meningeal hæmorrhage .	133	45	47	7	34	73	25	31	3	14	60	20	16	4	20
False membrane over brain .	45	9	8	12	16	24	6	7	5	6	21	3	1	7	10
Recent cerebral hæmorrhage	63	25	30	5	3	39	19	18	1	1	24	6	12	4	2
Localised softening (central)	207	68	86	53		89	28	42	19		118	40	44	34	
Localised softening (superficial)	30	11	10	9		20	7	9	4		10	4	1	5	
Excessive localised atrophy .	70	15	24	31		27	6	14	7		43	9	10	24	
Cystic spaces . . .	32	14	10	6	2	18	8	8	2		14	6	2	4	2
Total number of lesions .	580	187	215	123	55	290	99	129	41	21	290	88	86	82	34

A word or two of explanation may be necessary with regard to the above table.

The cases of meningeal hæmorrhage were, with but few exceptions, the immediate cause of death. Recent cerebral hæmorrhage includes cases in which bleeding has taken place into one or other of the cerebral hemispheres, and was at once fatal. The false membrane referred to is most usually the hæmatoma of the dura mater that has resulted from an old meningeal hæmorrhage, but possibly includes cases where the membrane is of inflammatory origin, a true pachymeningitis; these are not usually separately recognised from one another, and when both are of long standing they may be almost indistinguishable. Small foci of softening I have separated into two divisions: those that were found superficially situated in the cortical grey matter of the convolutions, and might have arisen either from a vascular lesion within the hemisphere or from one in the covering membranes; and those that occurred in the white substance of the centrum ovale, or in or near the grey matter of the basal ganglia. The central softenings, although by far most frequently situated in the usual neighbourhood of the corpus striatum, internal capsule, and optic

thalamus, was not, however, invariably so, for it occurred in all the lobes into which the hemisphere is divided. The morbid conditions classed under this heading varied from a distinct brown blood-clot that was evidently not the immediate cause of death, although it might have been comparatively recent in date, to old discoloured areas and small foci of softening that had lost all signs of blood extravasation. The latter were the most frequent, and some of these doubtless owed their existence to embolism, thrombosis, or to some inflammatory condition; but the last mentioned were, I believe, not great in number. The wasting or atrophy include only such excessive instances as those that have already been exemplified. Under cystic spaces are to be found cavities of some size that have resulted from the absorption of old blood extravasations.

In the figure columns are given first the total number of cases of each lesion, and then these are distributed according to the right or left hemisphere in which they occurred. Where similar lesions were found on both sides they are entered under the fourth column. There still remained a certain number of cases where it was either specially mentioned that the lesion was centrally situated, or no indication was given to which side it belonged. These I have therefore placed together in a separate column. In but a few cases only is the same case recorded twice, but this occurs occasionally, as when there has been a recent fatal cerebral or meningeal hæmorrhage associated with an old clot or localised softening within the brain.

Without doubt there are included in this table some cases under the headings of false membrane, localised softenings, localised wasting and cysts that are not the result of vascular lesions, but I have not thought it necessary to extract these from the general totals, a matter which from the data given would generally have been well-nigh impossible.

The main point shown in regard to the lesions in general is that though there is a slightly higher percentage in favour of the left side, being thirty-two on the right to thirty-seven on the left, and thirty-five to thirty-nine for recent hæmorrhage alone, this is scarcely as great a difference as my own personal experience at least would have led me to suppose. It shows the necessity when giving proportions of having a sufficiently large number of cases at hand from which to draw conclusions. This proportion

is not far removed from that given in Fagge[1] as the seat of cerebral hæmorrhage, viz. right thirty-six, left thirty-four—practically equal, although the advantage is reversed to the opposite side. Strange to say, Gowers[2] states that the two hemispheres are affected with equal frequency. The more or less general belief that the lenticulo-striate artery (the so-called special artery of cerebral hæmorrhage) on the left side is the one that most frequently ruptures, and the explanation of the bursting of this vessel as dependent upon the more direct anatomical relation of the left carotid with the heart, and consequently increased force of the blood-stream is reduced in significance.

In centrally situated softenings, with or without old blood-clots, and in excessive localised atrophy, the numbers are far heavier on the left side; for whereas on the former the right hemisphere of the brain contained little more than three quarters the number which the left did, in the latter nearly twice the number were on the left side. It is only of those lesions where the actual numbers are low that the predominance, if it exists at all, is on the right side. Foci of softening occurred simultaneously in both hemispheres nearly as often as it was confined to one side of the brain, whereas a large recent hæmorrhage was rarely found in both hemispheres.

Thus we have, as a result of the examination of 3300 brains from the insane, 580 instances of gross lesions within the cranium which may with more or less accuracy be put down to vascular origin; and out of these 215 were situated on the left side and 187 on the right, while in 123 cases similar lesions had occurred in or around both sides.

With regard to the sexes, it may be remarked that intra-cranial hæmorrhage is universally believed to be more frequent in men than in women; Gintrac, according to Gowers,[3] giving a percentage of 56·6 for males to 43·4 for females. The 580 cases given above are exactly equally divided between the two sexes. This is on account of the great predominance of localised softenings and atrophy in the table of female cases. If we take actually fatal cases of hæmorrhage (cerebral and meningeal), we find that 28 more men died from this cause than did women. But the brains

[1] 'Medicine,' vol. i, p. 562.

[2] Loc. cit., p. 392.

[3] Loc. cit., p. 386.

of male patients examined were 370 more in number. Thus, if we reduce these to the same proportions, we have but 231½ males to the 290 females, or just over 60 more in the latter sex, giving a percentage of 15·8 males and 19·79 females—a result different, I believe, from all writers on the subject. If we again take the cases only of recent hæmorrhage, we find meningeal hæmorrhage gives a proportion of 58¼ males to 60 females, with a percentage of 3·97 to 4·09, while cerebral hæmorrhage alone gives a proportion of 31⅛ males to 24 females, with a percentage of 2·12 to 1·63,—the former slightly in favour of the females, and the latter of the males. Very different is the result in the case of old hæmorrhages or softenings that have not proved fatal; here the proportions are 71 males to 118 females, with a percentage of 4·85 to 8·05.

An explanation of the astonishing result thus obtained is no doubt to be found in the fact that arterial degeneration and chronic renal disease does not differ to anything like so marked a degree in the two sexes of the insane as it does in the non-insane, a subject which I have elsewhere referred to.

January 15*th*, 1895.

II. DISEASES, ETC., OF THE ORGANS OF RESPIRATION.

1. *Sarcoma of the lung, secondary to subperiosteal sarcoma of the femur.*

By Harold B. Meakin, M.B.

This specimen was obtained *post mortem* from a patient under the care of Dr. Tooth, and subsequently of Mr. Paget, at the Metropolitan Hospital.

The patient, a delicate-looking girl aged 15, was operated upon by Mr. Paget a year ago for a subperiosteal sarcoma of the lower end of the right femur. Her right leg was amputated through the middle of the thigh. The tumour was a myxo-chondrosarcoma.

After recovering from the operation she remained apparently in perfect health until six weeks ago. She then noticed some shortness of breath, which increased at night-time, and was sometimes accompanied by a slight pain in the left side of the chest.

The shortness of breath and the pain were not persistent, and never in any sense alarming. No particular notice was taken of them till the middle of last February, when a medical man was consulted, and "pleurisy" was diagnosed.

On March 8th the patient came to the hospital, and was admitted for a supposed pleural effusion.

She was thoroughly examined on admission, and the following points were made out :

The left side of the chest was distinctly bulged, especially below and behind. Respiratory movements were limited almost entirely to the right chest and abdomen. Vocal fremitus was absent over the whole of the left lung. Percussion elicited an absolutely dull note over the whole of the left chest below the level of the second rib. The liver dulness behind was continuous with a dull area extending to the upper border of the sixth rib.

On auscultating the chest no breath-sounds could be heard on the left side below the level of the second rib, and there were no adventitious sounds.

On the right side vesicular breathing was easily heard as far down as the upper border of the sixth rib.

Vocal resonance was absent over an area corresponding with that in which breath-sounds were not heard.

The heart was acting forcibly. Its apex-beat, though very diffuse, could be felt in the fourth interspace just to the right of the sternum.

It will thus be seen that all the physical signs were those of a pleural effusion, and accordingly on March 12th an exploring syringe was introduced through the sixth interspace in the posterior axillary line. Nothing, however, but a small quantity of blood was withdrawn. The needle was again introduced in the fifth interspace, but with a like result.

On removing the exploring needle from the second puncture, its eye was seen to be plugged with some soft material. This was subjected to microscopical examination, and though not large enough to enable a certain diagnosis to be made, it suggested a small-celled growth.

On March 16th a note was recorded to the effect that the patient's breathing was becoming laboured, especially during sleep. The heart's apex-beat could be distinctly felt in the fourth interspace, one inch to the right of the sternum. Strong pulsation could be felt in the second and third interspaces on the right side.

The limits of percussion dulness showed no change since March 8th. A friction-sound was heard in the fourth interspace on the right side, synchronous with the cardiac systole.

On March 16th an anæsthetic (ether) was administered, and the thorax was again punctured on the left side in the fifth, sixth, and seventh interspaces in the anterior axillary line. As on March 12th, only a few drops of blood were withdrawn.

A small incision was then made along the fifth interspace, and the pleural cavity was opened.

A greyish-coloured irregular mass presented in the wound. A portion of this was removed with parrot-billed forceps, and on subsequent microscopical examination was shown to be myxochondrosarcoma. The patient did not take the anæsthetic at all well, and during the operation there was considerable dyspnœa.

From March 16th till March 26th, when the patient died, the dyspnœa increased steadily, but the patient was entirely free from

pain. The dyspnœa was relieved by the inhalation of oxygen. Death occurred with some suddenness. It was preceded by rapidly increasing dyspnœa and cyanosis, which the oxygen was quite powerless to relieve.

The *post-mortem* examination showed a large mass occupying the whole of the left side of the chest, with the exception of a small space above the level of the second rib. The growth was marked with depressions corresponding to the lines of the ribs. It was firm and somewhat nodular. It was not adherent either to the ribs or the vertebræ, but appeared to have replaced the whole of the left lung with the exception of the extreme apex. The mass contained many cartilaginous nodules, and in the upper part was a large blood-cyst, containing a quantity of blood-stained fluid. In the right lung, closely adherent to the bodies of the lower dorsal vertebræ, was another but much smaller mass of growth. This mass was adherent to the diaphragm, and occupied the floor of the right side of the thorax. The pleural cavity was obliterated on the left side, and partially so on the right.

The pericardium contained about five ounces of turbid fluid, and the surface of the heart was covered by a rough layer of plastic lymph. There was a nodule of growth about the size of a walnut in the wall of the left auricle. The upper end of the left kidney was flattened where it had been pressed upon by the lower surface of the growth.

The points of interest in connection with this case are the great disproportion between the size of the growth and the symptoms it produced, its extremely insidious onset, and the impossibility of forming an accurate diagnosis by any means short of opening the thoracic cavity.

The growth must have reached a very great size before it produced any symptoms whatever. That life was compatible with so great an interference with the respiratory organs is surprising, but that so little discomfort should have been caused even up to the time of death is still more so. *April 2nd*, 1895.

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2. *Mediastinal tumour invading the lung.*

By J. E. Squire, M.D.

A specimen was exhibited before the Society.

November 6th, 1895.

III. DISEASES, ETC., OF THE ORGANS OF CIRCULATION.

1. *Spontaneous rupture of the heart in the insane.*

By Cecil F. Beadles.

This is a heart from an insane female with spontaneous rupture of the left ventricle. It shows a typical organ in which such an event takes place—a large flabby heart with an enormous deposit of adipose tissue on its exterior, replacing to a great extent the true muscle-substance of the myocardium. The laceration has occurred about the centre of the left ventricle, all the valves are thickened, and the aorta is much diseased.

In addition to this I am able to give the notes of another case that occurred in Colney Hatch in 1878, and which I did not refer to in my previous communication. The patient was a man of about sixty-five years of age. For many years he had been in a completely demented state, although in fair bodily health. On getting out of bed at night to pass urine he suddenly fell forwards insensible, and died within a few minutes. There was found a rupture of the left ventricular wall at its middle half sufficiently large to admit the tip of the index finger, the cavity being filled with recently coagulated and liquid blood, and the pericardium distended with blood coagula. The muscular tissue was in a most unusually advanced state of fatty degeneration, easily breaking down at any point on moderate pressure being exercised between the finger and thumb. The transverse striæ were indistinct, and the muscular substance presented a greasy dirty yellow colour to the eye. The inner surface of the aorta, near its origin, was patched by atheroma, but the valves were competent. The heart was slightly increased in size, weighing 14 oz., owing to being coated externally with adipose tissue. The liver was nutmeg, and the kidneys advanced in the process of fatty degeneration. The

brain was in an extremely softened condition, apparently the result of defective arterial circulation, but the vessels at the base were free from atheromatous deposit; the convolutions much shrunken and wasted.

Since the above was written a case of rupture of the heart has been reported that occurred in the City of London Asylum.[1] This was an aged female who died suddenly while sitting in a chair. Rupture of the left ventricle existed, the heart being in an advanced state of fatty change, the arteries extensively diseased, and the kidneys granular and fibrotic.

I have now brought before this Society a considerable number of cases of spontaneous rupture of the heart in the insane. When we compare these with a recently published case of traumatic rupture,[2] we see that the chief point in which these differ is in the side of the organ that is injured, for whereas spontaneous rupture occurs invariably on the left side, external violence produces its effects upon the right.

Previously[3] I remarked upon the frequency of fatty heart in the insane, and the co-existing arterial and chronic renal disease which is so often found. In a paper[4] elsewhere I have more fully discussed this subject. *January 15th*, 1895.

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2. *Aneurysm of the ascending portion of the arch of the aorta.* (*Card specimen.*)

By James Galloway, M.D.

The specimen shows an aneurysmal dilatation of the ascending limb of the thoracic aorta. It consists of a semiglobular bulging of the aortic coats projecting from the right side, and

[1] 'Brit. Med. Journ.,' 1895, vol. i, p. 584.

[2] Ibid., 1894, vol. ii, p. 1427.

[3] 'Path. Trans.,' 1893, p. 18.

[4] "On the Degenerative Lesions of the Arterial System in the Insane, with remarks upon the Nature of Granular Ependyma," 'Journ. Ment. Sci.,' Jan., 1895.

commencing just above the aortic semilunar valves. The widest portion of the hemispherical bulging is that nearest to the aorta, and is about 4 centimetres in diameter. At the deepest part of the dilatation is a rupture through the aortic coats extending for about $4\frac{1}{2}$ centimetres. This rupture is irregular, and for about half a centimetre nearest the aortic valves the tunica intima is still untorn, while the other coats are ruptured.

Corresponding to this rupture is the sausage-shaped swelling attached to the right side of the aortic arch. This consists of recent blood-clot limited by the visceral layer of pericardium, which has been lifted up so as to make room for the blood escaping from the aorta. The pericardium was intact over the blood tumour, and no extravasation had occurred into the pericardial sac.

The aortic orifice was much dilated, its valves being stretched as a consequence, but there are only one or two spots of very early atheromatous change in the aorta or near the aortic valves, not more than may be seen almost normally at this age. No atheroma of vessels was detected.

The left ventricle was dilated and its walls considerably hypertrophied. The mitral valves seemed normal, the orifice somewhat enlarged. The left auricle was also somewhat dilated.

The right side of the heart showed signs of some dilatation and hypertrophy; its valves seemed normal. The commencement of the pulmonary artery was altered in shape, being somewhat flattened from behind forwards by the aneurysm in the aorta.

There was observed congestion of the liver, spleen, kidneys, bases of both lungs, but no further disease. No lesions of tertiary syphilis were observed.

The history of this case is somewhat remarkable.

The patient, a young man aged 21, was brought into the Great Northern Hospital, under the care of my colleague, Dr. Burnet, on November 17th, 1894. He was in quite an unconscious condition, with pupils dilated, heart-sounds very faint and the beat irregular, and cyanosis of face, ears, and extremities. It was stated that he had partaken freely of sardines for breakfast, and had also eaten two sausages. Whilst at work he was seized with sudden severe pain in neck. Soon after he said, "Oh, my stomach!" suffered from pains in the abdomen, became rapidly unconscious, and vomited. The police constable who accompanied him to the hospital said that the vomit contained fish.

Acting on the idea that this condition might be due to some toxic action produced by his food, the house physician on duty washed out his stomach. On being kept warm, and stimulated with brandy and ether, he recovered consciousness and rapidly improved.

In twenty-four hours he was able to state that he had always suffered from cold hands and feet, that he had been troubled with shortness of breath on exertion for long, and that his attack of unconsciousness came on after lifting a heavy basket of clothes—an unusual exertion on his part.

He continued to improve under judicious treatment, with the exception of a slight fainting attack on the afternoon of November 20th.

On the morning of the 22nd November, whilst sitting up, laughing and talking to the patient in the next bed, he suddenly fell back, lost consciousness, and passed into a condition similar to that on admission. He remained cyanosed for about thirty minutes, developed typical Cheyne-Stokes respiration, the colour improving during each period of respiration, becoming worse towards the close of each period of apnœa; then death ensued.

December 4th, 1894.

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3. *Thrombosis of the left renal vein.* (*Card specimen.*)

By Wm. Wallis Ord, M.D.

Specimen taken from a boy aged 1 year. History of scarlatiniform rash in November, 1894, followed by desquamation. Said to have been treated for "bronchitis and inflammation of the kidneys" in February last. Doubtful history of melæna.

Came to Victoria Hospital for Children on February 25th for œdema of face and feet. Feet were peeling. Urine obtained four days later showed nothing abnormal. Improved under treatment till April 13th, when he was suddenly seized with pain in the abdomen and vomiting. Bowels relaxed. Was brought up to hospital in a state of collapse, and died in four hours.

Post-mortem.—Left kidney purple in colour, twice the size of right. Thrombosis of vein extending into inferior vena cava, but not occluding that vessel. Artery unaffected. Right kidney normal. Left kidney under microscope shows great engorgement of vessels, with numerous small extravasations; no sign of interstitial nephritis. *May 7th*, 1895.

IV. DISEASES, ETC., OF THE ORGANS OF DIGESTION.

1. *On perforation of the soft palate in scarlet fever.*

By E. W. Goodall, M.D.

The specimen which I show to-night was taken from the body of a girl aged 6 years, who was admitted into the Eastern Hospital on May 7th, 1894, certified to be suffering from diphtheria. She was found, however, on being examined in the receiving room, to be desquamating profusely, and her mother stated that the illness was of three weeks' duration. The child was very ill and somewhat emaciated. There was a discharge from the nose. There was so much sticky mucus covering the fauces that it was impossible to see what was the exact condition; moreover the child most strenuously resisted examination. Temperature 102° F. No albuminuria.

On May 9th signs of bronchitis were observed, and she was troubled with a cough that was described as "croupy." It was not until the 10th that a good view of the fauces was obtained, on account of the quantity of mucus and exudation that covered the palate and adjoining structures. It was then found that there was ulceration of the edge of the soft palate and slightly of the uvula. There was a perforation in the left anterior pillar of nearly the size of a threepenny piece. The angles of the mouth and anterior nares were excoriated. The patient had become more emaciated.

On May 12th there was subcutaneous emphysema over the front of the trachea extending laterally to the sides of the neck, and downwards over the clavicles, over the pectoral muscles on the right side, and on the left as low as the first rib. There was slight stridor and decided dyspnœa. The patient was much weaker.

She died early the next morning. The temperature during the time she was under observation ranged from 100° to 102·8°.

A *post-mortem* examination was made on May 15th. There was superficial ulceration, irregularly distributed, all over the soft palate and uvula, in front and behind. Nearly all the right anterior pillar had been destroyed. The right tonsil was in a sloughing state. The edge of the left anterior pillar was fairly normal, but in the left anterior pillar was a large oval perforation, the edge of which was clean-cut. The left tonsil also had sloughed. There was slight ulceration of both posterior pillars. The ulcerative process had extended downwards, involving the base of the epiglottis, which was swollen. There was very superficial ulceration of the laryngeal mucous membrane, but no deep ulceration. The emphysema extended behind the pharynx and into the anterior mediastinum. There were patches of lobular pneumonia scattered through both lungs, and pleurisy over the base of the right lower lobe. The other organs were normal.

That this was a case of scarlet fever and not diphtheria I have no doubt; the history given by the mother, the extensive desquamation, and the nature of the lesions in the palate and its neighbourhood are proofs of the correctness of this view. Including this case, I have notes of sixteen cases in which I have observed perforation of the soft palate. Fourteen of them were cases of scarlet fever, and of these nine were first seen in the eruptive, the remaining five in the desquamative stage. Of the other two cases one was certainly diphtheria; membranous shreds and casts were obtained from the fauces, larynx, and trachea; moreover the *Bacillus diphtheriæ* was detected in the membrane. The other case was probably diphtheria, though there was a suspicion of its being scarlet fever; membranous shreds were discharged from the nose, and membrane was seen on the palate. There was no scarlet rash nor desquamation. Both these last cases were fatal. In the former the perforation was first observed on the 7th, in the latter on the 11th day. Of the fourteen scarlet fever cases four died; and all the rest were severe. The throat symptoms were prominent, and nearly all were complicated with otitis, adenitis, or cellulitis of the neck. In two facial paralysis occurred—the only two cases, by the way, in which I have seen facial paralysis arise during an attack of scarlet fever. All the patients were children, varying in age from one to six years. Nine were females, five males. In

two of the cases there were three perforations; in three, two; and in nine, one. The perforations were observed to have occurred at dates varying from the ninth to the twenty-eighth day of the disease. The perforation is always found in the anterior pillar, especially near its attachment to the side of the mouth. It is never found in the middle of the soft palate. In the cases in which there were three, two were on one side and one on the other. The edge of the perforation is clean-cut. The size varies from a quarter of an inch to three quarters of an inch in diameter. The one I exhibit to-night is the largest I have seen. Some are round, others oval. The clinical history is usually as follows:—When the patient is first seen there is much exudation on the palate, which is several days in clearing off. It is then noted that there is a patch of membrane or deposit in the anterior pillar, and in a few days more that the patch has been replaced by a hole, which seems to be formed quite suddenly. The perforations may completely heal up in a few weeks. On the other hand, I have seen them plainly visible at the end of eight to twelve weeks, though they have been usually smaller than when first noticed. Often there is sloughing or ulceration of the tonsils and soft palate, as in the specimen. I have seen the free edge of the anterior pillar give way after a perforation has been formed, and a large gap result. The perforation is the result of a local necrosis of the palate. Only a few days before I obtained the specimen I show, I made an autopsy on another case of scarlet fever in which I found the following condition:—The left tonsil was in a sloughy state; on the right anterior pillar was what appeared to be a greenish patch of exudation; but on cutting into the patch I found it was not exudation, but the surface of a localised patch of gangrene which extended right through the anterior pillar. The gangrenous had not begun to separate away from the healthy tissue, but it would, no doubt, have done so in a few days, and then a perforation such as I have described would have been the result. In the 'Lancet,' 1889, vol. ii, p. 1113, is a communication from Dr. Walter Fowler on "The Significance of Perforations through the Anterior Pillars of the Fauces." He expresses the opinion that they are probably a sign of antecedent scarlet fever. My former colleague, Dr. G. G. Morrice, in a short paper in the 'Lancet,' 1892, vol. ii, p. 142, combats this view, and gives notes of three cases in which such perforations occurred in

diphtheria. In two of the cases there was subsequent paralysis. He also mentions cases of perforation in scarlet fever. My own experience entirely corroborates Dr. Fowler's opinion. I have been on the look-out for these cases during the past two and a half years, and I am decidedly of the opinion that perforation of the anterior pillar is an almost characteristic lesion in certain severe cases of scarlatina anginosa. *November 6th*, 1894.

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2. *Myeloid sarcoma of the oro-pharynx.*

By Stephen Paget.

A man aged 64 was admitted to the West London Hospital, under the care of Mr. Eccles, on the last day of June, 1894. He had complained of sore throat for seven months. He was stout and florid, and had been a heavy smoker for many years. His breathing was at times noisy and difficult; he kept spitting mucus tinged with blood; the veins of his face and neck were swelled and prominent, and his lips were bluish; he was unable to take solid food; a large hard ulcerated mass round the arytænoid cartilages could be seen with the laryngoscope and felt with the finger.

Three days after admission he had an urgent attack of dyspnœa, and tracheotomy was done by Mr. Sutter, one of the house surgeons. He was much relieved for a time, but a few days after the operation fluids began to come through the tracheotomy wound, and he quickly became weak and emaciated.

I first saw him on July 30th. He was then failing fast, and he died on August 3rd.

Post-mortem.—The whole of the upper end of the œsophagus was filled with a large firm ulcerated growth, which was attached to the posterior aspect of the right arytænoid cartilage. The growth is a good deal shrunk by the spirit now; but at the *post-mortem* it was as large as a walnut, and occupied all the œsophagus behind the larynx. In comparison with the size of the mass its attachment to the arytænoid cartilage is very small; it might,

indeed, fairly be called a pedunculated growth. To my surprise, it seems to be a true myeloid sarcoma; it is mainly composed of connective tissue, in loose wavy bundles, swollen by immersion of the specimen in fluid; mixed with the connective tissue are masses of small cells, mostly of an embryonic type. Here and there are scattered very large irregular multinucleate cells. The general appearance of the sections seems to me to make it certain that the growth is a myeloid sarcoma. *November 20th*, 1894.

Report of the Morbid Growths Committee on Mr. Stephen Paget's specimen of malignant disease of the oro-pharynx and larynx.—We have examined the specimen and prepared microscopical sections of the same.

The growth is entirely extra-laryngeal, being attached to the right pyriform fossa and projecting into the lower part of the pharynx. It is conical in shape with the apex upwards, which is quite free and on a level with the tip of the epiglottis. Its extreme length is two inches and breadth one inch. Its base or area of attachment extends upwards nearly to the right arytæno-epiglottidean fold, outwards to the right ala of thyroid cartilage, downwards for half the breadth of the body of cricoid cartilage, and inwards nearly to the middle line. Its surface is ulcerated and friable. The inner border of the projecting tumour overlaps the superior aperture of the larynx, and must have produced considerable obstruction. But there is no part of it within the larynx proper, the interior of which is normal. The tumour shows no evidence of connection with the laryngeal cartilages, and there are no signs of extension of the growth round to the anterior surface of the thyroid cartilage. There are some enlarged lymphatic glands along the trachea which are free from secondary deposits.

Microscopical sections from the edge of the tumour show that it is a spindle-celled sarcoma composed of interlacing bundles; and scattered throughout the tissue are many large, irregular, multinucleated cells. The growth probably originated in the submucous tissue, and it may be compared with the submucous sarcoma of the œsophagus described in 'Trans. Path. Soc.,' vol. xl, p. 76, in which specimen very large tailed cells containing three or four nuclei were present among the interlacing bundles of a spindle-cell sarcoma. Three specimens of sarcoma of the œsophagus have been

described in the 'Transactions' of this Society, but in none has the pharynx or the upper part of the œsophagus been involved.

We would agree with Mr. Paget that the growth is a sarcoma, but are of opinion that it has originated in, and is limited to, the oropharynx.

J. H. Targett.
G. Newton Pitt.
S. G. Shattock.

January 30th, 1895.

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3. *Unusual form of malignant disease of œsophagus.* (*Card specimen.*)

By Stephen Paget.

The case was that of a man aged 50, feeble, emaciated, and depressed, who two months ago brought up blood, and again more lately; and during the fortnight before admission to hospital had suffered several times from dyspnœa; and on admission he was found to have paralysis of the left vocal cord. No signs of aneurysm were found, or of any disease of the heart or of the lungs. He had constant and painful dysphagia; a little milk, swallowed very slowly, most of it came back with a rush; at other times it would stop down for some minutes, and then be brought up again. But the dysphagia varied; a few days before death he ate some fish without difficulty, but, as a rule, he could hardly swallow fluids. No particular change in the ordinary sounds of swallowing were heard when one listened over the œsophagus, save that they were retarded; and a medium-sized bougie could be passed into the stomach easily.

As a bougie could be passed, and as the stricture seemed at first likely to improve under dilatation, gastrostomy was put off for a time; and though he bore the operation well, yet the night after it he was seized again with severe dyspnœa, and died of this in a few hours.

The specimen shows that he was the subject of that unusual form of malignant disease of the œsophagus, where the growth is

diffused in a thin layer through a considerable extent of the œsophagus without blocking it. The disease, in the fresh specimen, had the appearance of a long, flat, tough yellowish plaque, three or three and a half inches in length, fixed in the posterior wall of the middle of the œsophagus, looking like a thick strip of wet wash-leather stuck to the œsophagus. The œsophagus was not markedly hard or thick; that part of it which lay between the disease and the cardiac orifice of the stomach was pitted with small superficial erosions. There were a few small hard glands near the œsophagus. Above the disease there was a perforation, a quarter of an inch in diameter, through the fifth and sixth rings of the trachea, straight into the œsophagus. No secondary growths were found in the viscera. Dr. Kanthack kindly examined the specimen, and found that it was well-marked spheroidal-celled carcinoma. *May 21st*, 1895.

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4. *Traction diverticulum of the œsophagus.* (*Card specimen.*)

By H. D. Rolleston, M.D.

On the anterior wall of the œsophagus, opposite the bifurcation of the trachea, there is a pouch measuring $\frac{3}{4} \times \frac{1}{2}$ inch, which is adherent to the bifurcation of the trachea.

The bronchial glands are not enlarged, and do not contain any calcareous or caseous material.

There is no tubercle in the lungs or in any part of the body.

The production of this traction diverticulum may have been due to past inflammation of the bronchial glands, producing adhesions to the œsophagus, and subsequent cicatrisation exerting traction on the œsophagus, as explained in the exhaustive article on traction diverticula in Morell Mackenzie's 'Diseases of the Throat and Nose,' vol. ii, p. 126. But the proof is wanting.

The margin of the pouch is quite smooth, and in the recent condition was of the same colour as the rest of the œsophagus.

The mucous membrane lining the pouch is healthy, but much wrinkled.

From a man aged 52, who died of urethral stricture. No symptoms were connected with the presence of this pouch.

October 16*th*, 1894.

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5. *Fibrous polypus of the œsophagus invaded by epithelioma.*

By J. H. Targett, M.S.

Clinical History.—Henry P—, aged 61, was admitted into an infirmary for dysphagia. About three months previously he began to have some difficulty in swallowing, the food seeming to be delayed about the middle of his chest. Occasionally he was sick at the beginning of a meal, and then after vomiting would go on with his food and retain it. He had never brought up any blood. He had been gradually getting worse and losing flesh. When admitted he looked fairly healthy, considering his age, though somewhat thin. Abdomen a little retracted, no tenderness, nothing abnormal to be felt there. Superficial epigastric veins somewhat prominent; heart-sounds normal. On listening just below ensiform cartilage a loud noise, like liquid being forced with air through a narrow passage, could be heard on almost every occasion about fifteen seconds after swallowing. This gurgling sound was not heard over the œsophagus behind. He had never taken corrosive fluids, or anything likely to have injured his œsophagus.

For a few weeks after admission the patient was able to swallow liquid nourishment fairly well, but all attempts to pass soft rubber catheters down the œsophagus failed. Four days before death he complained that he could not swallow anything. A mouthful of water was returned immediately, and set up a severe attack of coughing. He had lost 56 lbs. in weight. Death occurred somewhat suddenly nine weeks after admission. He had seemed much as usual the night before.

Autopsy.—Body extremely emaciated. Dense pleuritic adhesions on right side, but no growth in the pulmonary tissue. Some congestion of the bases of the lungs. No food in the air-passages.

Heart, liver, and kidneys healthy. The œsophagus showed near its cardiac orifice an annular malignant stricture, which very nearly occluded the whole calibre of the gullet. About four inches above this was a large polypoid tumour, which projected into the œsophageal passage and appeared to block it, but in reality a fairly large tube could be passed by the side of it. The cervical glands were infiltrated with growth, and closely adherent to the œsophagus. Some of them at the level of the upper end of the sternum had broken down into a ragged cavity, which communicated by a small opening with the back of the trachea. At the same spot the wall of the gullet was so thin that it was torn in removal, and it was found impossible to determine whether a fistula had existed before death. The mediastinal glands also contained secondary deposits.

Description of the specimen.—The strictured portion of the œsophagus, which was just above the cardiac end of the stomach, presented a broad band of new growth in the wall of the gullet. This growth was deeply ulcerated in the centre, and involved the entire circumference of the passage. The edge of the ulcer was thickened, slightly raised above the level of the adjacent mucous surface, and sinuously excavated. A section through the growth showed that the muscular coat was extensively invaded, and that a rounded nodule had formed in the loose connective tissue outside the muscular coat. Histologically the growth was a typical squamous-celled epithelioma with numerous cell-nests.

The stomach was healthy, and the mucous membrane of the œsophagus between the stricture and the level of the polypoid tumour above it appeared free from disease. But immediately around the base of the polypus there was a zone of superficial ulceration.

As already stated, the polypus was situated four inches above the epitheliomatous stricture. It was sessile, with a distinctly constricted attachment to the wall of the œsophagus; and in shape it was elongated in the long axis of the œsophagus, so that it measured an inch and a half vertically, three quarters of an inch transversely, and projected rather more than an inch into the air-passage. Its surface was lobulated and covered with adherent flakes of lymph. No covering of mucous membrane was discernible in any part. A section through the tumour and subjacent wall of the œsophagus exhibited a small white core continuous with the tissue of the submucous coat, bearing a thick cap of new

growth. This growth appeared to be divided into rounded areas by thin strands of fibrous tissue proceeding from the central core.

Microscopical examination of the polypoid tumour.—Vertical sections of the polypoid tumour and the subjacent wall of the œsophagus were made. Owing to imperfect preservation of the specimen the histological examination was not altogether satisfactory, and many sections had to be prepared before the structure of the tumour could be determined. The deepest part of the section was formed by the muscular coat of the œsophagus, which appeared normal. Upon this was a broad layer of loose fibrous tissue, with scattered bundles of muscular fibres and large tracts of epitheliomatous growth. Above this was a rounded mass of very cellular tissue, forming the chief part of the substance of the tumour. Though easily distinguished from the subjacent layer it was not encapsuled, and it was already invaded by branching processes from the epithelioma beneath. As to the structure of this rounded mass, it may be said that it was composed of round and spindle-shaped nuclei embedded in a finely granular ground-substance. The bodies of the cells were scarcely recognisable, but the arrangement of the nuclei showed that the cells formed interlacing bundles—at least in the deeper parts of the tumour. The bundles, however, were not so coarse, nor the interlacement so distinct and regular as in myomata of the uterus or œsophagus; further, the nuclei were not those of muscle-cells. Towards the convex surface of the tumour the tissue appeared to be the same as that just described, but it had become degenerated and stained badly. No vestige of the mucous membrane was seen on section; hence it must have been removed by ulceration. Starting from the base and centre of the tumour the epithelial processes radiated outwards in the form of narrow alveoli, which insinuated themselves into the substance of the tumour. Around these growing alveoli the spindle-shaped cells of the tumour were particularly well marked, and in sharp contrast with the large squamous cells of the epithelioma. On the other hand, the older and larger alveoli of the epithelioma were embedded in tissue which was dense, sparsely nucleated, and presented the usual characters of mature fibrous tissue. A few large vessels were seen in the base of the polypus continuous with those in the submucous and muscular coats of the œsophagus.

It should be added that the epithelioma met with in the polypoid tumour was squamous-celled like that at the seat of stricture, and exhibited many small cell-nests.

Remarks.—In considering the nature of this polypoid tumour we have to deal firstly with the structure of the tumour itself; and secondly, with its relation to the malignant growth in the œsophagus. Is it a mass of organised lymph or blood-clot, a myoma, a sarcoma, or a fibroma? The first two of these suggestions are easily excluded, though a thick cap of adherent blood-clot may be met with covering a vascular new growth, and it is possible that such clot might become organised. Histologically the tumour bears some resemblance to the submucous sarcomata occurring in the bladders of children. But apart from the inherent improbability of a sarcoma secondarily invaded by epithelioma, I think that the cells themselves are wanting in that uniformity of size, shape, and distribution which characterises a sarcoma. Between a myoma and a fibroma the distinction is more difficult. Myomata of the œsophagus are usually embedded in the submucous and muscular coats, though they become extruded when large, and may project into the lumen of the passage. They are also well encapsuled. Hence in its coarse, no less than its minute features as above detailed, this polypus differs from a myoma. If, then, it be a fibroma originating in the submucous tissue, in what relation does it stand to the malignant growth at the lower end of the œsophagus? The marked way in which the epithelial processes radiate from the base into the substance of the polypus seems to show that their presence has not excited the development of the fibroma—in other words, that the fibroma existed first, and was subsequently invaded by epithelioma. The situation of a secondary deposit so far *above* the malignant stricture needs a word of explanation. Mr. Shattock has suggested to me that the base of the polypus was infected by the use of instruments in the treatment of the stricture. The clinical report states that "all attempts to pass catheters down the œsophagus failed," implying that instruments had been repeatedly used. Such a mode of infection is therefore by no means improbable.

Lastly, the invasion of an innocent tumour by malignant disease (which must not be confused with malignant transformation of a simple growth) has been met with in certain rare cases of uterine myomata associated with epithelioma of the cervix

uteri. This specimen is preserved in the Museum of the Royal College of Surgeons, No. 2322A. *October 16th*, 1894.

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6. *Bullet wound of liver, stomach, and kidney; extravasation of gastric contents; abdominal section; suture; death in eleven days from broncho-pneumonia.* (*Card specimen.*)

By T. H. Openshaw, M.S.

J. K—, aged 14, admitted into the London Hospital on April 4th, with symptoms of irritative peritonitis and collapse, two hours after a bullet wound of the thoracic wall. The bullet entered in the left nipple line through the fifth intercostal space. The liver dulness had disappeared. Abdominal section revealed a perforation in each wall of the stomach, which was sutured. The peritoneal cavity was washed out and closed. Patient was fed on the fourth day. The perforation in the liver and kidney were found *post mortem*. The patient died of broncho-pneumonia. Beyond two small collections of pus the peritoneum was healthy and the stomach soundly healed *post mortem*. *May 7th*, 1895.

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7. *Carcinoma developing in the wall of a chronic gastric ulcer.* (*Card specimen.*)

By G. Newton Pitt, M.D.

The specimen consists of a large chronic ulcer on the posterior wall of the stomach, near the pylorus. The central part of the ulcer, over an area of 2 by $1\frac{1}{2}$ inches, is formed by the liver, which has adhered to the edges of the aperture in the stomach. The adhesions have yielded above for half an inch, and led to a fatal peritonitis. The mucous membrane is destroyed by the ulcer over an area $2\frac{3}{4}$ by $2\frac{1}{4}$ inches, the floor round the periphery of

the ulcer being formed by the muscular coat. The portion on the side next to the pylorus is infiltrated by an encephaloid carcinomatous growth, which projects beneath the mucous membrane in this region, but does not fungate nor nodulate the mucous membrane.

There was a secondary nodule in a gland in the portal fissure.

The appearances indicate that the growth has developed in the wall of the ulcer, and not that the ulceration is a sequel to the growth.

The specimen was taken from a gentleman aged fifty-seven. History on p. 66. *May 7th*, 1895.

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8. *A specimen of gastro-enterostomy for pyloric cancer.*

By Leonard A. Bidwell.

The specimen shows the stomach, duodenum, and the first part of the jejunum, with an anastomotic opening between the stomach and the jejunum.

The following are brief notes of the case.

Mrs. C—, aged thirty-one years, was admitted into the West London Hospital, under the care of Dr. Ball, in December, 1894.

For six months previously she had suffered from pain after food, which was relieved by vomiting. She was very anæmic and much emaciated, but the lungs and heart were healthy.

The abdomen was slightly tumid, and an ill-defined tumour was felt in the right hypochondriac region, over which, however, resonance was very little impaired. The stomach was dilated, and its lower edge extended below the level of the umbilicus; at intervals it became distended with flatus, and became prominent through the abdominal walls, resembling a distended coil of intestine.

At Dr. Ball's request the abdomen was opened, under ether, in the right linea semilunaris. A large tumour was found to be involving the pyloric end of the stomach, and was intimately adherent to the liver, so that its removal was out of the question. A gastro-enterostomy was done by Halsted's method for lateral intestinal anastomosis. The jejunum was attached to the posterior

surface of the stomach by eighteen square stitches, and a piece of omentum was wrapped round the completed anastomosis, which was then returned into the abdominal cavity. The patient took the ether badly, and suffered from a good deal of bronchial irritation after the operation. Food was given by the mouth after twenty-four hours, and was taken in good quantities without causing any pain or vomiting. The patient, however, developed broncho-pneumonia, and died ten days after the operation.

At the *post-mortem* examination both lungs were found to be broncho-pneumonic.

The abdominal wound was quite healed, and there were no signs of any peritoneal irritation; even the omentum, which had been wrapped round the anastomosis, was scarcely adherent to the joint. The stomach, duodenum, and part of the jejunum were removed in one piece, together with the adherent portion of the liver. There were no deposits in any of the other viscera.

Description of the specimen.—There is a large mass of new growth surrounding the pylorus, and extending some distance into the stomach. It also invaded the under surface of the liver; the pyloric orifice only admitted the smallest sized catheter. Nearly at the centre of the stomach is the anastomotic opening between it and the jejunum. The opening in the stomach was on the posterior surface, and that in the jejunum was about an inch and a half from the duodenum. The anastomotic opening at the *post-mortem* admitted a finger freely, but it has contracted since it has been in spirit. The mucous coats of the stomach appear to be soundly joined to that of the jejunum, and their peritoneal surfaces are firmly adherent. The stitches are not seen.

Microscopic examination of the pyloric growth showed typical carcinoma.

The specimen is of interest on account of the youth of the patient—thirty-one years. The orifice between the stomach and jejunum was made rather too small in the first instance, but there was no contraction of the opening during life. The subsequent contraction has occurred since the specimen has been in spirit. The anastomoses effected by Senn's plates, on the other hand, show a great tendency to contract. *April 2nd*, 1895.

9. *Two stomachs showing the results of gastro-jejunostomy.* (*Card specimens.*)

By Cyril Ogle, M.B.

1. A stomach greatly dilated. The pylorus obstructed by new growth, which has spread to the umbilicus, producing there an excrescence of the size of a small chestnut.

A coil of jejunum is strongly attached to the stomach, and there is a communication half an inch in diameter between the two. Gastro-jejunostomy was performed eight months ago, with much temporary benefit, by Mr. W. H. Bennett. Senn's plates were used. Death was preceded for six weeks by copious vomiting and difficulty in bowel action. Much secondary growth of peritoneum was found at the autopsy, especially in the mesentery, hampering the small intestine. This, together with the contraction of the communication between the stomach and jejunum, would account for the later symptoms. The growth appears to be a tubular carcinoma.

2. A stomach much obstructed towards the pylorus by new growth, which probably grew into its walls from a mass lying close by it. The patient was a woman aged twenty-three years. The growth appears to be a sarcoma. Gastro-jejunostomy was performed by Mr. Herbert Allingham a month before the death of the patient. She derived great benefit from the operation, but died of acute peritonitis, due to a rupture of the growth infiltrating the stomach's wall, at a spot removed from the site of operation.

The communication between the stomach and jejunum has remained of good size, and easily admits the last joint of a large finger.

In this case Mayo Robson's bobbin was used.

In both the specimens are still to be seen silk sutures traversing the wall, and lying partly in the stomach and partly in the jejunum. These were used to attach the plates to each other, and thebobbin to the stomach. They have produced no ill result by remaining in the wall of stomach. *February 19th*, 1895.

10. *Fibrous stricture of pylorus.*

By Cyril Ogle, M B.

The first specimen shows a stomach contracted and thickened in its pyloric half, the internal diameter of which measures only two and a half inches, the walls half an inch in thickness on an average, with gradual increase to the pylorus. The duodenum is quite natural.

The second case shows extreme contraction of the pylorus, which admits a No. 8 catheter only. The cause is seen to be a localised thickening of the pylorus, of the size of a small chestnut.

Although there is an old ulcer on the small curvature, it is at some distance from the pylorus, and has evidently nothing to do with the constriction.

I have thought these cases to be worth bringing before the Society, the first on account of the nature of the obstruction. Beneath the microscope the thickening is seen to be due to hypertrophy of the muscular coat, and to increase of fibrous tissue in the submucous coat.

The mucous membrane is thrown into folds, but is intact, and there is nothing to suggest malignant disease. There have been several cases reported in the Society's 'Proceedings' (vol. xlii) of fibrous change near the pylorus, but almost always with either ulceration or cicatrisation of the mucous membrane, and, in most, with at any rate a suspicion of poison having previously been taken.

The second specimen is, I think, unusual in the degree of stenosis produced by pyloric disease; and although there is evidence of its cause being carcinoma, there were no adhesions to the neighbouring parts and no secondary growths.

The patient was not admitted into hospital on account of any gastric symptoms, but for rapid tuberculosis of the lungs, of which she died a few hours after admission.

Dr. Fagge seems to have regarded cases of pyloric stricture where fibrous tissue is mainly found, as carcinomatous, and explains the absence of secondary growths as due to the fact that it is the stomach which is affected, and this being a vital organ, death

occurs too rapidly for the formation of secondary growths. But the present specimen, at any rate, can hardly be one of rapid growth, and both Dr. Wilks and Dr. Bristowe describe the existence of fibrous stricture distinct from scirrhus of the pylorus.

In neither of the above cases could a tumour be felt during life; and both, had they been diagnosed, would have been very suitable for operation,—the first by gastro-jejunostomy, and the second by pylorectomy or pyloroplasty: and it would seem that the existence of fibrous thickening with obstruction of the pylorus —apart from malignant disease, or even as the result of malignant disease which is no longer active—must be of great importance in prognosis as regards the future condition of patients operated upon for pyloric obstruction. *January* 15*th*, 1895.

Addendum.—Since the above paper was read a number of sections of different parts of the stomach first described have been made, and in these also there appears, microscopically, no evidence of carcinoma.

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11. *Perforating duodenal ulcer in women.*

By Lee Dickinson, M.D.

The specimen shown is an acute, small, simple ulcer perforating the anterior wall of the duodenum three quarters of an inch from the pylorus. It was taken from the body of a housemaid aged 29, a patient of Dr. Parr of Kensington. The patient was not in the least anæmic, and had had excellent health, in spite of dyspeptic pains during the last few months, till she was suddenly seized by violent pain in the right hypochondrium, which, as she was slightly jaundiced at the time, was thought at first to be due to a gall-stone. She became collapsed, and died in fourteen hours with acute general peritonitis. There were no other ulcers or scars in the duodenum or stomach.

The ulcer is of a kind sufficiently familiar to this Society, whether in the stomach or the first part of the duodenum. Its

interest lies in the fact that, being duodenal, it occurred in a woman.

The great majority of perforating duodenal ulcers occur in men, a fact which is perhaps sufficiently recognised. The preponderance of men is well shown in a recent paper by Drs. Perry and Shaw,[1] who found that in fifty-six cases the ratio was 42 to 14, or if burns were excluded, 42 to 8 (? 7).

It happens that I have lately seen two fatal cases in women at St. George's Hospital. The first was a laundrymaid aged twenty-seven, with a history of dyspepsia for six years, but otherwise good health and no anæmia, who was under Dr. Dickinson in August, 1891. The perforated ulcer was of the same acute nature as that shown. There was the scar of another in the duodenum.

The second was a dressmaker aged twenty-seven, with a history of dyspepsia for five years, but no anæmia, who was under Dr. Whipham in December, 1894. Laparotomy was performed by Mr. Sheild, and the ulcer was sutured. It was of a more chronic nature, with a raised and much-thickened edge.

The *post-mortem* books of St. George's contain one other case in a woman (not including one which was due to a burn). She was under Dr. Whipham in July, 1882. Her age was twenty-two, and she was expressly stated to have had no preceding illness except slight occasional headache and dyspepsia. The fatal illness was sudden and short. There were three acute duodenal ulcers, one of which had perforated.

In contrast to the three in women the same *post-mortem* books contain fourteen cases in men. Of perforated gastric ulcers they contain 54 cases—42 women, 12 men.

Now as to simple gastric ulcers in general, it may be doubtful how much greater is the liability of women, and Dr. Pye-Smith has shown that men suffer oftener than has been supposed; but of this there can be no doubt—the great majority of the gastric ulcers which perforate into the peritoneal cavity, a class consisting largely of the acute latent ulcer of the anterior wall of the stomach, occur in women, especially young anæmic women.

The perforating duodenal ulcer, on the contrary, prefers men; and those women whom it affects are seldom not anæmic.

In the four women whose cases I have described there was neither anæmia at the time, nor any reason to suppose it had

[1] 'Guy's Hospital Reports,' vol. l, 1893, p. 203.

ever existed. Of the cases quoted by Drs. Perry and Shaw only two were anæmic (197 and 203 in the original report), and the average age was much higher than in mine.

It is quite exceptional for gastric and duodenal ulcers to co-exist in the same patient. I would suggest that though these ulcers are so similar in their morbid anatomy, apparently differing only in being on one or the other side of the pylorus, they depend for their initiation upon a different diathesis, and that anæmia has very little share in the causation of the duodenal ulcer.

Subphrenic abscess from duodenal ulcer.—Comparing perforating gastric and duodenal ulcers, one is struck by the fact that while the former not infrequently cause only a limited peritonitis in the form of a subphrenic abscess, the latter almost always cause a diffuse peritonitis, or if not, a local abscess beneath the right lobe of the liver. This is what might be expected from the position of the duodenum. But a subphrenic abscess results from duodenal perforation oftener than might be supposed.

Among the eighteen cases of duodenal perforation in the St. George's *post-mortem* books two resulted in this. One of these has been published. The other was remarkable because, in consequence either of previous adhesions or an unusual position of the pylorus at the time of perforation, the abscess was on the *left* side, like the ordinary subphrenic abscess from gastric perforation. This case was communicated to the Medical Society by Mr. Sheild on October 22nd, 1894.

For the convenience of those who may be interested in this subject references to the published cases of subphrenic abscess from duodenal perforation with which I have met are appended.

Maydl, 'Über subphrenische Abscesse,' Wien, 1894. (Eight cases.)

Mason, 'Transactions of the Association of American Physicians,' vol. viii, p. 223.

Dickinson, 'British Medical Journal,' 1894, vol. i, p. 234.

Cayley, 'Clinical Journal,' May, 30th, 1894.

April 2nd, 1895.

12. *Malformation of the alimentary canal; atresia at the middle of the duodenum.*

By A. T. Collum (introduced by G. Newton Pitt).

The canal *above* the seat of obstruction, consisting of the stomach and upper part of the duodenum, is dilated and rendered hour-glass shape by the constriction of the thicker and more resisting pylorus. This portion ends below in a blind *cul-de-sac*. *Below* the seat of obstruction the intestine is of normal size. The bile-duct, ligatured at the time of removal from the body, has been dissected out, and can be seen to enter the commencement of the gut on the distal side of the obstruction.

The upper and lower portions are connected together by a little connective tissue with some blood-vessels. Part of this has been removed during preparation.

The *cæcum* presents an example of the persistence of the fœtal type, being conical in shape, and gradually tapering to an apex, to which is attached the vermiform process.

The specimen was removed from the body of a "full-time" child, who appeared healthy at birth, and presented no other malformation. The mother had "hydramnios," and was delivered by a midwife. The child passed meconium stained with bile, and took the breast, but retained nothing. On the third day Dr. Bluck, of Plaistow, to whom I am indebted for the specimen, was consulted, the child having passed no urine. Dr. Bluck passed a catheter, but found the bladder empty. Only once afterwards was a little urine noticed on the diapers, and death ensued on the sixth day, meconium being passed at intervals, and vomiting continuing to the end.

A specimen very similar to this one was shown in October, 1893, by Mr. Edgar Willett, and is described in vol. xlv, p. 78, of the 'Transactions' of the Society. In Mr. Willett's case the obstruction seemed to be at the termination of the duodenum; the dilated portion of bowel above passed down towards the pelvis behind the cæcum, and was opened on the third day, as no meconium had been passed, and the child was vomiting; partly digested milk, stained with bile, escaped. In that case, therefore, the bile-duct

entered the bowel on the proximal side of the obstruction, while in the present one it can be seen to join on the distal side.

Pathology.—As to the causation of the malformation, one naturally suspects a developmental error, and seeing that an offshoot of the primitive gut proceeds from the duodenum during the development of the liver, it is probable that this diverticulum produces first a puckering, and subsequently a complete interruption in the canal. As tending to corroborate this theory, I have brought from the museum of Charing Cross Hospital a specimen of imperforate pharynx, in which the block is situated behind and a little below the cricoid cartilage, and would seem to have been caused by the budding off of the lungs. *May* 21*st*, 1895.

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13. *Emphysema of small intestine.* (*Card specimen.*)

By Hector W. G. Mackenzie, M.D.

The specimen is a portion of the jejunum dried, and shows numerous vesicles of air in the submucous tissue. The emphysema was much more marked in the recent state. The first six inches of the jejunum presented a very unusual appearance. The valvulæ conniventes appeared to be the seat of raised vascular-looking growths, the whole of the mucous membrane being intensely congested. The same condition recurred at intervals of one or two feet throughout the upper half of the jejunum. What appeared to be growths were soon found to be simply due to the presence of air in the submucous tissue. Pressure with the finger shifted the position of the swellings, while incision caused them to disappear.

The specimen is from a man aged thirty, who died from acute and chronic pulmonary tuberculosis. The patient complained of great abdominal pain on the day he died. The body was examined within twelve and a half hours after death. The small intestine, from the duodenum onwards, contained a large quantity of dark blood. No cause for the hæmorrhage was discoverable. The liver was fatty and slightly cirrhotic. The stomach was normal. There was no sign of intestinal ulceration or tubercle.

A minor degree of emphysema of the stomach and intestine due to decomposition is not very rare.

The remarkable features about this case were the extent of intestine affected, and, if the emphysema were due to decomposition, the great rapidity with which it must have developed.

May 21st, 1895.

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14. *Strangulated hernia on the left side of the abdominal wall.*

By Stephen Paget.

This specimen was taken from the body of a woman aged 50, who was admitted to the West London Hospital on August 6th. I am very sorry to say that the swelling was at first thought to be inside the abdominal cavity, both by myself and by some of my colleagues: thus there was some delay before operation, and it is just possible that an immediate operation might have saved the patient's life.

For four or five years she had been subject to attacks of abdominal pain, with vomiting and obstruction of the bowels. These attacks had at first occurred at intervals of about three months, but of late they had been more frequent, occurring every ten or fourteen days. About the time when they first occurred she began to be aware of a swelling in the left side of the abdomen, and this swelling had lately got larger. Her first attack of pain was soon after a protracted labour.

She was admitted to the hospital on the evening of August 6th, with signs of acute obstruction. In the left side of the abdomen, outside the left semilunar line, and between the ilium and the umbilicus, was a rounded swelling, about four inches in diameter, very slightly raised above the level of the surrounding skin, moveable but not freely moveable, not clearly defined, not tender, not clearly resonant on percussion. Her general condition was fairly good, her tongue clean and moist, her temperature normal. On August 7th she seemed better; she had passed flatus, and had gone for many hours without vomiting. The general opinion was that the

swelling was inside the abdominal cavity, probably an ovarian or parovarian cyst, pressing or dragging on the bowel, and that the pain and sickness might subside as on former occasions, and that an operation might then be done under more favorable conditions. On August 8th she had lost ground, and the vomiting had returned, and now had a marked fæcal odour. I opened the abdomen in the middle line, and found that the swelling was a hernial sac lying between the abdominal muscles and the subcutaneous fat, and filled with a loop of small intestine. There was a collection of thin offensive pus among the coils of intestine which lay near the mouth of the sac, and these were glued together by soft bands of lymph. The strangulated bowel was drawn back without difficulty out of the sac, and was found to be already gangrenous; it gave way just after it was set free. It was quickly secured in the wound, but the patient died soon after the operation.

The specimen has shrunk in spirit, but it shows well the position of the sac between the muscles and the subcutaneous fat. The opening into the sac was about three quarters of an inch in diameter; the diameter of the sac was about two and a half inches. *October 16th*, 1894.

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15. *Ulceration of the large intestine in typhoid fever.* (*Card specimen.*)

By C. Arkle, M.D.

The transverse and parts of the ascending and descending colon from a man aged 26, who died of typhoid fever on the forty-third day of the disease in Charing Cross Hospital under the care of Dr. Abercrombie. The intestine is most extensively (practically universally) ulcerated, the ulcers being deep and irregular in outline—everywhere exposing the muscular coat, and in several places causing perforation. The appearances suggest dysenteric rather than typhoid ulceration. The chief focus of the disease was in the large intestine, but a few healing ulcers were sparsely found as high as four feet above the ileo-cæcal valve. All the large intes-

tine was ulcerated to within six inches of the anus, but for one foot below the ileo-cæcal valve the ulcers were small and rounded, a good deal undermined, and evidently situated in the solitary glands. There was very little glandular enlargement. The patient died of peritonitis.

The case was a typical example of severe typhoid fever, and during the first fortnight of the patient's stay in hospital he was constipated, but latterly there had been much diarrhœa.

February 19th, 1895.

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16. *Ulcerative colitis (human).* (*Card specimen.*)

By J. H. Targett, M.S.

A portion of a descending colon affected with ulcerative colitis. The mucous surface presents a large number of deep ulcers, whose chief diameter is transverse to the long axis of the bowel. The margins of the ulcers are undermined, and their bases are composed of the serous and muscular coats. In several instances, however, the floor consists only of translucent peritoneum. The persistent strips of mucous membrane project so far beyond the general level of the wall of the intestine that they appear like elongated ridges between the excavations. The surface of the mucous membrane forming these ridges is covered with shreds of tissue, or dotted with small oval ulcers. By the enlargement and confluence of such ulcers the extensive destruction of the mucous coat has been produced.

Microscopical examination of the wall of the colon showed abundant inflammatory changes in the submucous tissue and between the bases of Lieberkühn's tubules. At the edges of the ulcers the mucous membrane showed much catarrh of the lining epithelium of the tubules, their mouths blocked, and their acini distended with secretion. The lymphoid nodules were much swollen.

Clinical history.—From a woman aged twenty-three, a parlour-maid, admitted to a hospital for diarrhœa and melæna. Her illness began six weeks previously, with passing blood from the

rectum, the bowels being constipated at the time. Diarrhœa supervened, and persisted till death. The motions were very offensive, and contained bright red blood in abundance. The general symptoms were anorexia, thirst, tenderness in the right iliac region and over the lower part of the abdomen. She gradually sank ten days after admission.

Autopsy.—On opening the abdomen some general peritonitis was seen, indicated by stickiness and adhesion of coils, and a few masses of lymph. No perforation was found, but on attempting to remove the intestines the colon was so rotten that it ruptured in more than one spot. The adhesions were most numerous about the cæcum, sigmoid, and splenic flexure of colon. The transverse colon was much dilated, forming a broad bag across the upper half of the abdomen. Appendix cæci normal.

A few small round ulcers were found in the lowest part of the ileum, apparently follicular in origin. But the chief change here was the blackening of the mucous coat by bismuth administered medicinally. From the caput coli to the inner margin of the anus was one continuous stretch of severe and acute ulceration, most marked in the transverse colon. The mucous membrane that remained was swollen and injected, and marked with punched-out ulcers, as in the accompanying specimen. Under water the edges of the ulcers were shaggy from sloughing and undermined. The bases of the excavations were of a florid colour. The rectum was not worse than the sigmoid, so that there was no indication of extension of the disease from below upwards.

Kidneys, liver, and spleen normal. Mesenteric glands much enlarged and hyperæmic; genital organs normal.

This specimen is preserved in the Royal College of Surgeons' Museum, No. 2472B. *May 21st*, 1895.

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17. *Ulcerative colitis.* (*Card specimen.*)

By Cyril Ogle, M.B.

Throughout the colon large tracts denuded of mucous membrane, separated by ridges and shreds of membrane of intense red colour. The small intestine and the last few inches of rectum were healthy. No perforation; no tubercle.

Slight lardaceous reaction of kidneys. None elsewhere.

Some old scars about the knees.

Patient a married woman, of about 35 years. Never abroad.

Blood and slime passed for twelve months, with diarrhœa, abdominal pain, and occasional vomiting.

On admission, diarrhœa, slime, and shreds of mucus passed. She suffered from fæcal vomiting.

Symptoms somewhat relieved by injections, with no return of vomiting. Irregular raised temperature and gradual weakness.

Urine s. g. 1015, with much albumen. *May* 21*st*, 1895.

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18. *Local dilatation of the colon at the sigmoid flexure.* (*Card specimen.*)

By G. Newton Pitt, M.D.

The specimen was taken from a man aged 57, who died from perforation of a gastric ulcer which had become malignant (vide p. 53). For some months he had vomiting and pain after food, and was fed *per rectum* for several weeks. Latterly he had extreme constipation, with more or less evidence of intestinal obstruction. There was the greatest divergence of opinion as to the diagnosis during life, and shortly before his death it was supposed that he was suffering from intestinal obstruction due to growth in the colon.

The sigmoid flexure of the colon was longer than usual, and the two ends were more fixed to the brim of the pelvis and to the ileum than is generally the case. The convexity of the curve was dilated into a pouch about four inches long, the circumference of which measured eight inches, while above and below this the measurement was only three inches. The wall was greatly thinned in this region. The yielding of the wall was very noticeable when the bowel was first laid open.

This dilatation of the sigmoid flexure leading to a paralysis of the bowel, and suggesting during life intestinal obstruction, was doubtless due to the long-continued feeding *per rectum*, and to the frequent use of large enemata.

Specimens of a general dilatation of the lower part of the colon or of the cæcum may be met with, not infrequently; but I am not familiar with a local pouching limited to the convexity of the sigmoid. Its formation in the present case greatly added to the difficulties of diagnosis. *May 7th*, 1895.

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19. *A case of post-rectal dermoid forming a rectal polypus.*

By C. H. Golding-Bird.

In July, 1894, Mary G—, aged 36, was admitted under my care into Guy's, as a case of piles. Twice before she had been operated upon for this condition, and now it had reappeared. In taking her history the account she gave of rectal tenesmus was very noticeable; and she further stated that latterly a lump would come down and partly extrude itself at the anus, and that she had to return it by manipulation.

When examined I found, in addition to the piles, that on passing the finger well up the rectum, a globular polypoid tumour could be just felt, but its attachment could not be reached.

Placed under an anæsthetic with a view to operation, a further examination revealed a pear-shaped polypus protruding from the posterior rectal wall, and of the size of a small hen's egg. With some difficulty, after stretching the sphincter, the bulk of it was extruded from the anus, and I was at once struck by the fact that it was of doughy consistency, retaining exactly the impression of the examining fingers, and it was covered with normal mucous membrane. Its point of attachment was quite beyond reach. It could be, however, certainly determined that it projected into the posterior rectal wall, and that its point of attachment was external to the gut.

I decided to enucleate it, and this was easily done by a vertical incision through the covering rectal mucous membrane. Toward the end of the operation, however, a small rent was made in the tumour, and its stiff, clayey contents began to extrude. The actual point of origin of the tumour could not be reached, so peeling back the mucous membrane as high as possible, a ligature was

applied round the stump, and the tumour removed. The rectal mucous membrane now fell into its place, and was entire, save for the vertical incision through which the enucleation had been conducted. The patient recovered perfectly.

The tumour was entire except the extreme tip at its narrow attached end where the ligature had been placed. The contents were clayey material, without hair or bone or teeth, and presented under the microscope no organised structure. The cyst was smooth internally; externally rough where the overlying mucous membrane had been peeled off it.

A section of the wall shows from within outwards the following structures:

(*a*) Mucous membrane of lymphoid tissue having embedded in it tubular glands like those of Lieberkühn.

(*b*) A well-marked layer of muscularis mucosa.

(*c*) Submucosa of connective tissue.

(*d*) Layers of transverse unstriped muscle.

(*e*) Layers of longitudinal unstriped muscle.

(*f*) The rough exterior—strands of connective tissue.

The rarity of post-rectal dermoids growing in connection with the mesenteric canal, and the still greater rarity of one appearing and playing the part of a rectal polypus, require that this case should be placed on record.

It entirely agrees with the description of one given by Middeldorpf and quoted by Bland Sutton,[1] and removed by the former surgeon from near the anus of a child. The tumour, says Sutton, "contained connective tissue, mucous membrane with characteristic follicles, submucous tissue, longitudinal and circular layers of muscle-fibres."

I am indebted to Mr. Bellingham Smith, the Surgical Registrar, for the microscopical preparations of the cyst-wall.

December 18*th*, 1894.

[1] 'Tumours, Innocent and Malignant,' p. 319.

20. *A case of malformation of the liver.* (*Card specimen.*)

By Hector W. G. Mackenzie, M.D.

The specimen shown is the liver of a man aged 50, who died from the effects of extravasation of urine. The size and weight of the organ are average, but the shape differs widely from the normal, and it is difficult to recognise the various parts. The left half of the organ is considerably the larger, and its lower border descends about two inches below the right. The normal configuration is thus, roughly speaking, reversed.

The cause of the alteration of form depends on two factors: (1) the left lobe exists only in an atrophied or rudimentary form; (2) an extra lobe—a large somewhat pear-shaped mass, equal in size to about a fourth of the whole organ—is wedged in just to the right of the gall-bladder. This additional lobe has pushed the gall-bladder, the quadrate and Spigelian lobes, and the left lobe upwards and to the left. The left lobe occupies the left upper corner. The gall-bladder instead of being vertical is nearly horizontal, while the quadrate lobe lies immediately above it.

A deep notch separates the extra lobe from the main part of the right lobe, and from this notch a furrow runs obliquely upwards and to the left on the upper surface, terminating in a notch on the upper border between the right and the rudimentary left lobe.

The gall-bladder lies in a fissure between the extra and the quadrate lobes, and this fissure nearly meets the furrow just referred to. The quadrate lobe shows a tendency to subdivision, and in consequence of the existence of the fissure for the gall-bladder, is much better defined than usual.

There are a number of gummata in different parts of the organ. Thus there are two in the right lobe to the right of the deep notch. There is one in the supernumerary lobe close to the gall-bladder. There is also one in the rudimentary left lobe. None of these, however, are large, and they seem quite unconnected with the formation of the fissure, notches, and furrows which mark out the extra lobe. It is, however, possible that the syphilitic disease has had to do with the atrophy of the left lobe.

It does not seem likely that a syphilitic process should while

causing atrophy in one direction have induced hypertrophy in another. I believe the association of syphilis with this malformation to be an accidental one. In support of this we see a tendency to secondary lobulation shown in the upper surface of the quadrate lobe.

Mr. F. G. Parsons has called my attention to a specimen in the comparative anatomy series of the Museum of St. Thomas's Hospital, showing the division of the liver into four main lobes, two

FIG. 1.

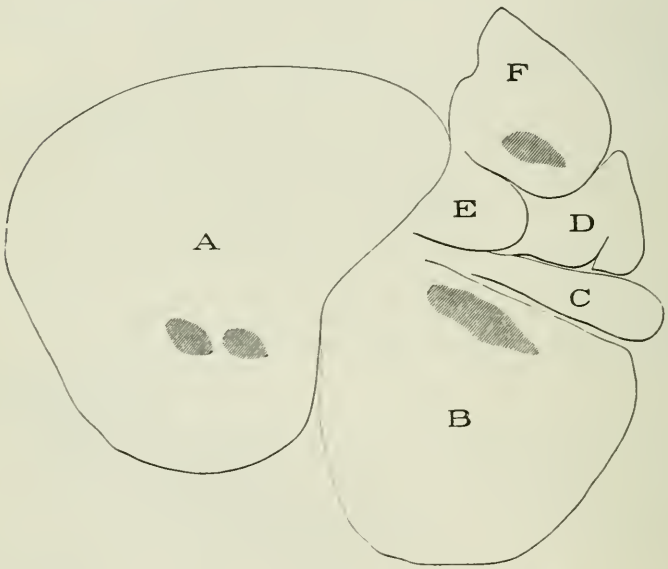

Diagram of the upper surface of the liver. A, B, D, E, make up the right lobe, C being the gall-bladder. F is the rudimentary left lobe. B is the supernumerary lobe. The shaded areas represent the situation of the gummata.

right, a central and a lateral, and two left, similarly central and lateral, of nearly equal size, in addition to the Spigelian and caudate lobes. This type, he says, is found in many of the lower animals. The quadrate lobe is peculiar to man, and is caused by the sinking in of the gall-bladder, and is really part of the right central lobe.

I show the four-lobe type of liver for comparison, and it will be

seen that as far as the right lobes are concerned there is a certain amount of resemblance.

Mr. Parsons suggests that in the human specimen we have the two main right lobes of the more generalised type represented. The lobulation here met with would therefore be a reversion to a type not infrequently met with among the lower animals.

I should like to refer, in conclusion, to the difficulty of diagnosis a liver of such a form as this might give rise to. The patient was admitted to the hospital for quite another malady, which required immediate operation, and he died within twenty-four hours. Careful examination of the liver region was out of the question. It is probable that most physicians would have been quite led astray by the tumour which the supernumerary lobe formed. It might have been taken for a tumour of the liver, a tumour of the kidney, or possibly for a hydatid. It is worth while, therefore, to bear in mind the possibility of such a tumour in such a situation being an abnormal lobe.

May 21*st*, 1895.

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21. *Cirrhosis of the liver in a child.*

By F. Parkes Weber, M.D.

The liver and spleen shown to-night are those of a girl, J. S—, aged 14, who died at the German Hospital in February, 1895. She had been, as the father thinks, more or less jaundiced all her life, and had always been weakly and thin, though she had never had any serious acute illness (never scarlet fever).

For her age she was extremely ill-developed, looking much younger than she really was. Her skin was very dark all over from pigmentation, probably a result of the chronic jaundice; one or two venous stigmata were seen; the superficial veins over the front of the body were much enlarged. The liver could be felt considerably below the costal margin, and the spleen extended to below the anterior superior iliac spine. Ascites was first detected about eight and a half weeks before death, and for a rather longer period than this there was fever (sometimes high fever)

of an irregular type, probably not entirely due to the bronchitis, which was also noticed during part of this period.

At the *necropsy* the fluid in the peritoneum was clear. The *liver* was green, hard, "hobnailed," and weighed 26½ oz. Microscopic examination showed a large amount of fibrous tissue, situated much as in ordinary cirrhosis, dividing the glandular substance into unequal compartments, and sometimes invading the lobules, entering between the individual hepatic cells. Green inspissated bile could, however, be seen (at least in the sections stained only with orange-rubin) situated between or in the hepatic cells. The gall-bladder contained a moderate amount of clear almost colourless fluid. There was no perihepatitis.

The *spleen*, uniformly enlarged, weighed 20½ oz.; on section its substance seemed rather firm, but otherwise normal; the microscope showed increase in fibrous tissue, and considerable deposit of pigment in some of the trabeculæ. The *lymph-glands*, especially those of the hilum of the liver, were somewhat enlarged and much pigmented; under the microscope the pigment-cells were seen, as usual, to be situated chiefly in the lymph-sinuses of the glands. The *common bile-duct* was unfortunately not examined.

Four of the brothers and sisters are healthy, three others died in infancy; the eldest of the family, a girl, became jaundiced at about the age of thirteen, and died at nineteen with symptoms somewhat resembling those of her sister J. S—. The father is living, and looks healthy. Although the mother had several miscarriages, there is no definite history of syphilis. The four healthy children were born in the interval between the births of the two sisters who suffered from chronic jaundice. The history of alcohol is likewise not quite clear, for the father never saw the mother give the child alcohol, though the mother, who died at forty-eight of phthisis, was a great drinker at the later period of her life when J. S— was born, and may have given the child alcohol without the father's knowledge; she used to be out "on the drink" for a week at a time. It may be mentioned that the child was nevertheless brought up on the breast in the ordinary way.

The fever which existed during about the last ten weeks of the child's life was, I think, in part at least due to an auto-intoxication, the material absorbed from the liver probably affecting the thermotaxic centres; it may be regarded as taking the place of

the nervous symptoms noted at the end of some cases of hepatic cirrhosis in both children and adults. The late development of the ascites is noteworthy, but perhaps more interesting from both a pathological and a clinical point of view is the great size of the spleen, which by palpation during life appeared even larger than it actually turned out to be. A possible explanation of this striking feature of the case is to suppose that a cirrhosis of the liver in the case of the growing tissues of a child may cause a much greater relative enlargement of the spleen than in an adult, when the spleen and other tissues of the body have reached their full development.

April 2nd, 1895.

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22. *Infarcts in the liver.*

By Cyril Ogle, M.B.

The specimen shows infarcts in the liver similar to those found in the spleen and kidneys: buff-coloured areæ, of sizes varying from a pea to a hazel-nut, surrounded by zones of redness. The hepatic artery is also shown, and is seen to be blocked at its bifurcation by adherent brick-coloured clot.

It is usually stated that infarctions do not take place in the liver, when either the portal vein or hepatic artery is blocked, on account of the free anastomosis of the capillaries of the artery, and of the vein, between the lobules of the liver. In the present case the portal vein and its divisions were not blocked, and there was no fibrosis of the liver to obstruct the portal circulation. Perhaps the explanation of the infarcts is that so extensive a blocking of the hepatic artery is not common, and that this took place in an old man with feeble venous circulation, suffering from the effects of a severe injury.

Dr. Wooldridge in vol. xxxix of the 'Path. Soc. Trans.' described some experiments on dogs, in which he obtained hæmorrhagic infarctions in the liver by injecting a certain poison into the blood, which caused thrombosis of the portal vein; and he explains the hæmorrhagic character of the infarctions as being due to the chemical changes in the blood, which prevented its clotting,

and favoured its extravasation from the vessels. Perhaps a similar explanation might be applied to the present case; the blood appeared to be in a septic condition, as shown by petechiæ in the mucous membranes, and this was perhaps due to a collection of evil-smelling pus around a fracture of the spinal column, and a bedsore. So that, without this condition of blood, the red character of the infarcts would not have been perhaps manifest, and the infarcts themselves, if present, being of a buff colour, would be overlooked. Possibly this may not infrequently be the case, such a patch in the liver being looked upon as a patch of fatty infiltration.

In the present case, at any rate, there appears to have been an extensive blocking of the hepatic artery in a feeble old man with, possibly, a septic condition of blood.

The origin of the embola seemed to be a soft patch of fibrin attached to a calcareous aortic cusp. There were also infarcts in the spleen and kidneys. *December* 18*th*, 1894.

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23. *Cases of portal thrombosis with and without infarction of the liver.* (*Card specimen.*)

By G. Newton Pitt, M.D.

Case 1.—A man, aged 36, was admitted with an injury to his abdominal wall, having fallen over a rail and bruised his side. He vomited and became collapsed. He was found to have a strangulated right scrotal hernia. Herniotomy was at once performed by Mr. Lane; the bowel was found to be severely bruised. He died five days later with severe membranous enteritis and paralysis of the bowel.

At the Inspection, a branch of the portal vein to the right lobe of the liver was found to contain a recent thrombus; corresponding to this, an area in the upper part of the liver, two inches across, with a sharply-defined margin, was found to be deeply engorged with blood. The liver was fatty. No ecchymosis nor laceration of the tissue was noticed, but it appeared probable that a branch of the portal vein had been injured and an infarction had resulted.

Microscopically it was found that the capillaries in the affected area were engorged with blood, and a number of hepatic cells contained numerous granules of brown pigment.

Case 2.—W. M. S—, aged 44, was admitted under Dr. Washbourn in a state of unconsciousness with left hemiplegia. Six hours later, he was conscious and free from any paralysis. He remained fairly well, and six days later was about to leave the hospital, when he developed hemiplegia and coma, which proved fatal in six hours.

At the Inspection, a very wide-spread thrombosis was found to have taken place. Thrombi were found in the descending thoracic and in the abdominal aorta, with complete obliteration of the lumen by thrombi of the splenic, of the lower branch of the left renal, and of the right middle cerebral arteries, and of the right hepatic vein. Softening thrombi were found in the branches of the portal vein.

Death had occurred from cerebral hæmorrhage.

On section the liver presented numerous sharply-defined pale areas with other deeply-engorged dark areas. Microscopically there was an increase in cells in the portal canals, and in linear tracks radiating from them, producing a condition of early cirrhosis. Some of the veins were thrombosed, and many of the capillaries were engorged with blood to an unusual extent, but limited to certain areas.

Generally the formation of a thrombus in a portal vein produces no very obvious change in the liver-tissue. Dr. Wooldridge showed before this Society, in 1888, that under certain conditions, as by the injection of tissue-fibrinogens, thrombosis in the portal veins can be experimentally produced, and that infarctions in the liver also result. If the animals survived a fortnight, early cirrhotic changes take place, while the clot is reabsorbed. On the other hand, Cohnheim, Litten, and others have shown that the production of portal thrombosis by the introduction of foreign bodies does not induce infarction. He came to the conclusion that not only must a vessel be blocked, but that there must also be changes in the blood to produce an infarction.

The condition Dr. Wooldridge induced, produced not only a wide-spread thrombosis, but also a liability to hæmorrhage; both of which conditions were present to an extreme degree in the second case.

The early condition of cirrhosis is very suggestive, and according to Dr. Wooldridge's experiments may be the direct result of the thrombosis.

A feature of interest is the large hæmorrhage which took place from the distal part of the middle cerebral artery beyond the spot at which it was thrombosed, a condition extremely difficult to explain, but which has been noted in other cases in our *post-mortem* records.

I would also direct attention to the fact that there were only small areas of softening in the brain and of infarction in the spleen, although main trunks supplying much larger areas were thrombosed. *February* 19*th*, 1895.

To these may be added a third case:—

Catherine P—, aged 36. Admitted under Mr. Symonds with an ovarian tumour, which he removed. Intestinal obstruction ensued, and death took place six days later.

An ante-mortem clot was found in a branch of the portal vein, to which corresponded a sharply-defined anæmic area.

Microscopical sections were made, and the only noticeable changes were the empty state of the capillaries and the large amount of granular pigment in the hepatic cells: so that when the section was held up to the light, the pigmentary deposit mapped out the affected area. *May* 10*th*, 1895.

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24. *Congenital obliteration of the ductus communis choledochus.*

By Francis H. Hawkins, M.B.

The specimen now exhibited shows the ductus communis choledochus to be obliterated and appear as a mere thread about one inch before joining the duodenum; no opening into the duodenum can be found. The hepatic and cystic ducts are pervious, as is also the ductus communis choledochus for more than one inch prior to its becoming obliterated. The gall-bladder is not enlarged, and at the autopsy was empty. The vessels appear

normal. The liver was slightly enlarged, very firm, and of a dark olive-green colour with fibrous-like bands running over the surface, which was slightly irregular, and had the appearance of Morocco leather. On section the cut surface was also of a dark olive-green colour, with numerous yellowish trabeculæ crossing it.

The pancreatic duct is pervious, and opens into the duodenum. Microscopical sections of the liver show it to be traversed by a network of fibrous tissue, which not only surrounds the lobules but also the cells.

Other conditions found.—The spleen was enlarged, but otherwise normal; kidneys normal. An inguinal hernia containing the cæcum and appendix was present on the right side. There was no fluid in the peritoneal cavity. There was a slight excess of pericardial fluid, but the heart was normal. Adhesions were found to exist between the layers of the left pleura, and at its lower limit in the mid-axillary line there was a small localised collection of pus.

History.—This specimen was removed from a male child, aged at death 4 months and 2 weeks, who was admitted into the children's ward of the Royal Berkshire Hospital under my care two months previous to death, said to be suffering from jaundice and rupture. The mother stated that the child had never been of the proper colour, but she first noticed it to be jaundiced eight days after birth; this she attributed to the fact of herself having been jaundiced some time before and at its birth. While under my observation the jaundice varied in intensity—first the child was of a deep olive colour, and the stools were white; then some time afterwards the jaundice became less marked, and on two occasions the fæces were of a pale green colour; subsequently the deep olive colour with white fæces returned, and remained persistent till death. On two occasions blood exuded through the mouth—there was no direct evidence as to its origin,—and on one occasion there was epistaxis. The temperature was high towards the end of life, and this was attributed to the condition of the lung.

Family history.—The father was said to be in good health, as also the mother; no history of syphilis could be obtained. The mother had two miscarriages, and of six children born living two died in infancy. No other children had ever been jaundiced.

Remarks.—The 'Transactions' of this Society contain but two

instances illustrative of the condition now shown; they, however, differ as regards the duration of life, neither having lived longer than eleven weeks, and while one case nearly resembles this one as regards the extent of the obliteration, the other differs in having the ductus communis choledochus dilated into a circular opening with the openings of the cystic and hepatic ducts separated by a considerable interval. In making a diagrammatic representation of twenty-nine cases of congenital obliteration of the bile-ducts, Dr. John Thomson, of Edinburgh, found only six instances, including the two above mentioned, where the ductus communis choledochus alone was obliterated. The cause of the jaundice is of some interest, for although the common bile-duct is obliterated, neither the gall-bladder or the cystic or hepatic ducts were dilated or contained bile. Hence it would appear that the jaundice was due to changes within the liver itself similar to that in cirrhosis, when towards the late stage of the disease jaundice occurs owing to the bile-ducts becoming constricted and obliterated.

I am indebted to Mr. Garrad, house-physician, for having dissected this specimen out.

The specimen is now in the museum of the Royal College of Surgeons. *April 2nd*, 1895.

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25. *Biliary fistulæ opening into pylorus, duodenum, and transverse colon.* (*Card specimen.*)

By Arthur Voelcker, M.D.

The gall-bladder is adherent at its fundus to the transverse colon, into which it has ulcerated.

It has also ulcerated into the duodenum. At the pyloric ring is an ulcer with a pigmented base, and into the floor there opens a small fistula connected with the gall-bladder.

The cystic and common ducts are natural. The gall-bladder contains a calculus.

From an elderly female. *December 18th*, 1894.

26. *Ulceration of the gall-bladder in typhoid fever.* (*Card specimen.*)

By Arthur Voelcker, M.D.

The gall-bladder shows numerous ulcers, one of which on the superior surface has extended into the liver.

From a man aged 48, who was admitted into Middlesex Hospital under the care of Dr. Coupland on the twenty-first day of his illness, and who died on the thirty-ninth day of the disease from perforation of an intestinal ulcer twelve inches above the ileo-cæcal valve.

There were no calculi in the gall-bladder. *April 2nd*, 1895.

V. DISEASES, ETC., OF THE GENITO-URINARY ORGANS.

1. *Solitary kidney.*

By W. Lee Dickinson, M.D.

This specimen was obtained from the body of a woman aged 47, who died of influenza and pleurisy in St. George's Hospital on December 9th, 1893.

On the right side there was no kidney, but the left kidney occupied its usual position. This organ resembles two kidneys joined longitudinally, but the fusion is quite complete. Its length is $7\frac{1}{2}$ inches. There are two separate hila on the anterior surface, and two separate ureters. The pelvic organs were matted together by old disease about the uterus and ovaries, and there was much difficulty in tracing the ureters to the bladder; but Mr. Pooley, who made a careful dissection, found that their terminations were natural, and that the upper one entered the right side of the bladder.

Solitary kidney is well known, but is yet sufficiently rare. Its varieties are well described by Dr. Sidney Coupland and Dr. Greenfield in vol. xxviii of these 'Transactions.' The specimen which I show illustrates a high degree of that fusion of the two organs of which the common "horseshoe" kidney is a lower example.

A still rarer condition is that in which one kidney is entirely absent and unrepresented. Such a case was recorded by Mr. Prescott Hewett in the St. George's post-mortem book for 1841 (No. 149). The subject was a young woman who died with chorea while pregnant, and the absent kidney was the right. Two cases of this kind are fully recorded in vol. xxxvi of these 'Transactions.'

2. *Kidneys increased fourfold in weight from acute nephritis (Card specimen.)*

By G. Newton Pitt, M.D.

Enormously enlarged kidneys from acute tubal nephritis in a boy aged 3. The kidneys weigh 13 ounces, the average weight at this age being $3\frac{1}{4}$ ounces—a fourfold increase, which in an adult would be equivalent to kidneys weighing 40 ounces.

The capsules peeled readily, the cortex was increased in size, and was uniformly pale. The outer part of the pyramids was engorged with some hæmorrhages scattered about.

Microscopically the change was practically limited to the epithelium of the convoluted tubes. These were dilated, and were lined by flattened regenerating epithelium.

History.—Two months' œdema. The heart dilated under observation, the impulse moving out to three quarters of an inch outside the nipple. Ten days before his death there was noticed to be albuminuric retinitis. The boy died with cellulitis of the scrotum and uræmia. *May 15th*, 1895.

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3. *Cystic kidneys of large size in an adult.*

By P. H. Pye-Smith, M.D., F.R.S.

The following is the history of the case:

F. S—, aged 27, was in good health and engaged in his daily work until a fortnight before his death. When admitted into Guy's Hospital (Philip Ward, No. 35) he said that he had frequently vomited during the last ten days, and had suffered from diarrhœa. He was not an intemperate man, and was well nourished and muscular. His breath was ammoniacal, and his urine contained a small amount of albumen with casts. The quantity passed was not excessive. He complained of feeling heavy and stupid during the ten days before his admission,

and this gradually deepened into coma during the four days he was in hospital. There were no convulsions and no paralysis.

On examination with the ophthalmoscope a patch of retinitis was seen in the left eye. There was no dropsy and no cardiac murmur. The impulse of the heart was displaced to the left, and the pulse was of high tension.

At the autopsy on the 9th of March, 1894, the brain, which weighed 48 oz., was perfectly normal, as were the lungs. The heart weighed 15 oz., the left ventricle being most hypertrophied. There was only slight atheroma in the aorta. The stomach, liver, and other abdominal viscera were normal, except the kidneys. Of these, the right measured ten and a half by five inches, and was two and a half inches thick; the left measured nine by four and a half inches, and was four inches thick; the right weighed 41, and the left 51 oz. On section, as well as on external inspection, they appeared to be made up of cysts of various sizes, from that of a marble, or rather more, downwards.

Microscopic examination disclosed numerous smaller cysts, and also showed the presence of unaltered renal tissue in considerable amount. Most of the cysts contained clear yellow serum, but many a thicker and darker liquid, which appeared to be the result of hæmorrhage.

Clinically the case had all the appearance of one of chronic Bright's disease, and the hypertrophied kidneys were felt during life.

I have brought the specimen before the Society because others are already recorded in its 'Proceedings,' and because their pathology is in many particulars still undetermined.

One of the first cases was recorded by Dr. Bright; and here, during life, the abdominal tumours were felt. Sir William Roberts recognised another during life, in which after death one kidney weighed 28 and the other 26 oz. We had one case in Guy's Hospital in 1867, in which the right kidney weighed 84 and the left 53 oz.

In the third volume of the 'Transactions' of this Society, Dr. Hare recorded a cystic kidney which far exceeded the above, for it weighed 16 lbs., and had formed during life a tumour that filled half the abdomen.

In the present case, as in others which have come under my notice, the symptoms have been those of chronic Bright's disease,

from which there is nothing to distinguish them unless the renal tumours are detected by abdominal palpation. As in the present case, we find all the characteristic symptoms present—the discharge of serum and tubular casts into the urine, the characteristic condition of arterial tension and cardiac hypertrophy, albuminuric retinitis and uræmia,—in fact, all the characters of the chronic interstitial form of Bright's disease, with its insidious origin, slow progress, and absence of dropsy until the last stages.

These megalocystic kidneys, however, in addition to their size, are peculiar in the fact that they date from an early age. Some have already degenerated before birth, as in the cases long ago recorded by Virchow of fœtal renal tumours which may be so large as to interfere with parturition.

In his classical papers on the subject written in 1846 and 1854 ('Gesammelte Abhundlungen,' pp. 837 and 864) he quotes cases recorded by Meckel, Nichat of Lyons, Cormack of Edinburgh, and others, and minutely describes two recent specimens and two museum-preparations. These cases all occurred in new-born children. He refers the formation of cysts ("hydatids," as they used to be called) to the same cause as that of other cysts in secreting glands—obstruction of the ducts and dilatation of the passages above the obstruction by mechanical pressure of the secretion. His cases are called hydrops renalis congenitalis, with atresia of the straight tubes at the papilla of the pyramids or elsewhere in their course.

There seems every reason to accept this explanation, which is that now generally received for the microcystic contracted kidneys of chronic Bright's disease in adults. And there seems no reason for drawing a sharp distinction between the congenital cystic kidneys and those of adult life.

In the present case there is no record which enables us to determine the origin of the disease. Death from interstitial nephritis under thirty is rare, and it is quite possible that the disease may have existed from birth. In the oldest patient in whom I have found this condition after death, a man of fifty-three, the illness, as in the present case, was short, and the disease was certainly present for many years, possibly during the whole of his life.

The circumstances which as a rule we find accompany cirrhosis of the kidneys, such as intemperance, gout, plumbism, and atheroma, are, I believe, absent in these cases.

We meet occasionally with cases of chronic albuminuria free from dropsy, and with symptoms of high tension of the vascular system, in persons who have not attained adult life.

In one case now under my care the patient, a girl of thirteen, has had scarlatina, but the renal symptoms were present more than a year previous, as I then ascertained. In another instance a girl of sixteen, with marked cardiac and retinal symptoms, had a brother a year younger who she told me was affected in the same manner. In a third case, recently seen, a girl of seventeen has had dry skin and abundant pale urine since two years old, and has now albuminuria and other symptoms of chronic interstitial nephritis. In none of these cases have I been able to feel an abdominal tumour.

The morbid histology of these large cystic kidneys is, in all probability, the same as that of the microcystic kidneys. The cysts are retention-cysts, caused by obstruction of the convoluted tubules from contracting fibrous tissue,—analogous, therefore, to dilatations of the œsophagus, the stomach, the bladder, or the left ventricle, due to stricture of the œsophagus, the pylorus, the urethra, or the sigmoid valves respectively.

What is at present unexplained is why the same pathological process causes at one time shrinking and diminution of bulk into a hard, solid, contracted kidney, at another produces numberless minute cysts in the still shrunken organ, and in a third and rarer series of cases produces so large and numerous cysts that the total bulk and weight of the organ is multiplied ten, twenty, or even fifty fold.

There does not appear to be any true overgrowth of tissue, for the walls between the cysts are in extreme cases very thin, and after puncturing and draining the cystic structure the loss of bulk is considerable.

It appears, then, to be clearly established that these large cystic kidneys in adults are pathologically identical with the congenital cystic renal tumours described by Virchow and other pathologists, and that both are essentially the same as the small cystic kidneys of chronic Bright's disease; in all cases the cysts being not new formations nor dilated Malpighian corpuscles, but dilated tubules. Whether all large cystic kidneys are congenital is hard to say. It seems difficult to believe that patients can live to twenty-seven or to fifty-three years with such advanced renal

disease. On the other hand, microscopic examination shows how much more healthy tissue remains than we should suppose from mere inspection; and it may be that the absence of shrinking of the organs may delay the vascular constriction and high tension which are perhaps the most formidable effect of renal cirrhosis. The large cirrhotic kidneys might be compared to the large cirrhotic liver, which is less often accompanied by early ascites than the small contracted one.

Lastly, what is the relation of these megalocystic kidneys to cysts in other organs which are sometimes observed in the same cases?

Examples of the co-existence of hypertrophic cystic kidneys and cysts in the liver have been recorded in the seventh and tenth volumes of our 'Transactions' by Dr. Bristowe, and in the seventh by Dr. Wilks, by myself in our thirty-second volume, and by the late Dr. Mahomed in the thirty-fourth, as well as by Rindfleisch, Frerichs, and other foreign writers. Still more strange is the association of cysts, not only in the kidneys and liver, but in the pancreas and the brain. Of this I have myself seen one case, and another was fully described by Drs. Savage and Hale White in 1883.[1]

In the case of the liver I convinced myself from the histological appearances shown to the Society (see Plate xvii, 'Path. Trans.,' 1881) that the cysts arise by vacuolation of the hepatic cells; and in this view I found that I was anticipated by so excellent an histologist as Dr. Lionel Beale. The cysts in the pancreas may very probably be retention-cysts like those of the testis, the mamma, or the parovarium. The cysts in the brain must have a totally different origin.

Since writing the above my friend Dr. Pitt has drawn my attention to an abstract of a graduation thesis, "Du gros rein polykystique de l'adulte," by F. Lejars (Paris, 1888) in Virchow and Hirsch's 'Jahresbericht' for the same year (vol. ii, p. 307). He collects sixty-two cases, of which only thirteen were recognised as abdominal tumours during life. In seventeen of the sixty-two cases there was cystic degeneration of the liver as well as of the kidneys. *December 4th*, 1894.

[1] 'Path. Trans.,' vol. xxxiv, p. 1. Compare Dr. Paterson's paper on the subject in the 'British Medical Journal,' 1890, vol. ii, page 735.

4. *Cases of congenital cystic adenoma and of carcinoma of the kidney.*

By Edgar Willett.

(With Plate I.)

The first of these occurred in an infant aged 10 months, a patient of Dr. Ilott's, and the operation was performed by Mr. Walsham early in 1892. The case was reported in the 'British Medical Journal' of April 1st, 1893, p. 694, but the specimen has not been shown before. Permission from Mr. Walsham and Dr. Ilott has kindly been given for its exhibition. The kidney and the tumour were hardened in spirit, and then divided longitudinally.[1] One half was shown, the other being in the collection of the Royal

Fig. 2.

Congenital cystic adenoma. From a photograph, $\frac{2}{3}$ natural size.

College of Surgeons. The cut surface shows a tumour of considerable size projecting from the outer border, and pushing the cortex, nearly the whole of which is involved, to one side. A well-

[1] Specimen No. 2392c in St. Bartholomew's Hospital Museum.

marked capsule separates the kidney substance from the tumour; this is glandular in appearance, consisting of minute cysts, which are just visible to the naked eye. On the outer surface the capsule of the kidney is thinly spread out over the new growth. Microscopically (cf. Pl. I, fig. 1) the structure consists of numerous minute cysts of various sizes, each of which is lined by a single layer of short cubical epithelium. The cavity of the larger cysts seems to have contained a fine granular material; in many places there is an appearance as though the thin cyst wall had ruptured, but nowhere are any intra-cystic growths or tufts to be seen. As it was suggested that these cysts were in reality tubes in cross-section, other sections were made on a plane at right angles to the first, but these gave an exactly similar appearance. The structure most resembling the tumour is the thyroid gland, though there are of course many differences. The essentially glandular look of the tumour seemed at the time of the operation to warrant its being considered an adenoma, especially as there was a definite limiting membrane to the growth. The subsequent history, however, shows its more serious nature: recovery followed the operation itself, but eleven months later a recurrence took place, and the child died.

The second case,[1] that of the carcinoma, occurred in private, and was removed by Mr. Thomas Smith, who also has given leave for its publication. The patient was a young gentleman aged 19, who gave the following history:—He first noticed a swelling in his right loin in November, 1892; it gave him no pain, but increased rather rapidly; there was then no alteration in the quantity or quality of the urine. The operation took place early in May, 1893, and the whole kidney was removed through the right linea semilunaris; a good recovery followed, and the patient was able to hunt regularly throughout the following winter, and remains in good health at the present time.

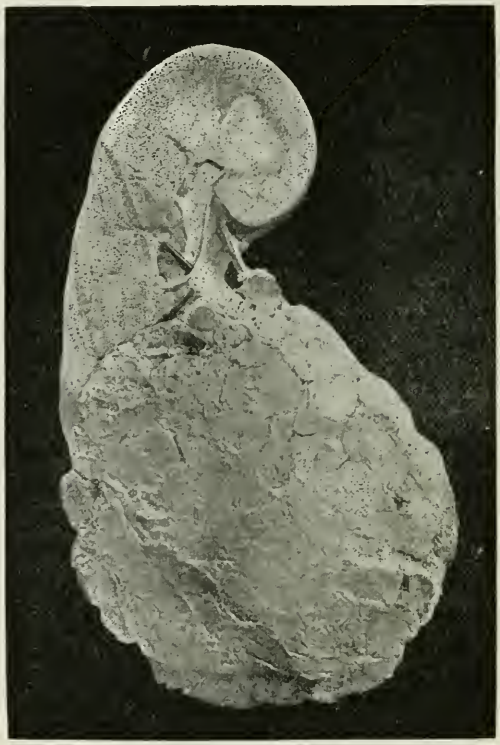
The specimen shows a large mass, nodulated on the outer surface, and involving the greater part of the kidney, especially its upper part; the cut surface is rugged and uneven, and shows to the naked eye a number of spaces or cysts filled by a soft homogeneous growth; under the microscope (cf. Pl. I, fig. 2) there are seen numerous branching processes covered by stout columnar cells, which project into and fill the spaces or cysts, and which seemed to indicate a carcinomatous origin. The whole tumour when

[1] No. 2392D in St. Bartholomew's Hospital Museum.

removed weighed two pounds. Microscopical sections, with careful drawings of the same by Mr. Gwilliam, were shown.

The microscopical and naked-eye appearances of these two tumours led me to class the first as an adenoma: it had a definite capsule, and showed no intra-cystic growths; while the second one,

Fig. 3.



Adeno-carcinoma of the kidney. From a photograph, ½ natural size.

for the reasons that it had no capsule, involved the kidney tissue directly, and showed numerous intra-cystic growths, led me to consider it a carcinoma. The clinical history in each case entirely upset the diagnosis. In the first case the child died within the year, with recurrence and numerous secondary deposits, while in the second case the patient is still alive.

DESCRIPTION OF PLATE I,

Illustrating Mr. Edgar Willett's paper on Two Congenital Renal Tumours. (Page 86.)

FIG. 1 shows the structure, drawn under a half-inch objective, of the congenital cystic adenoma of the kidney (Case 1).

FIG. 2 shows, under the same power, the structure of the intra-cystic growths (Case 2).

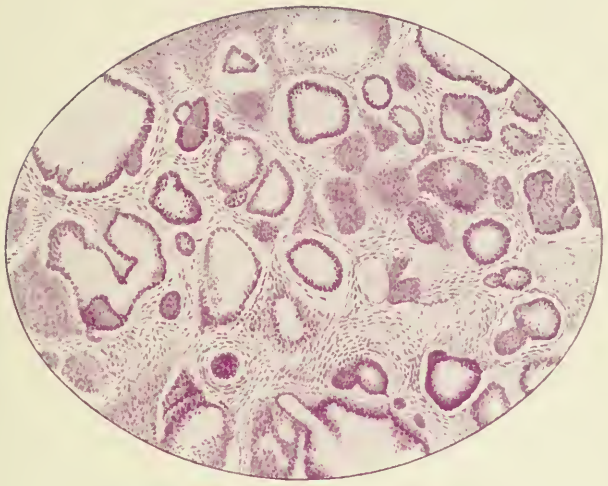


Fig. 1.

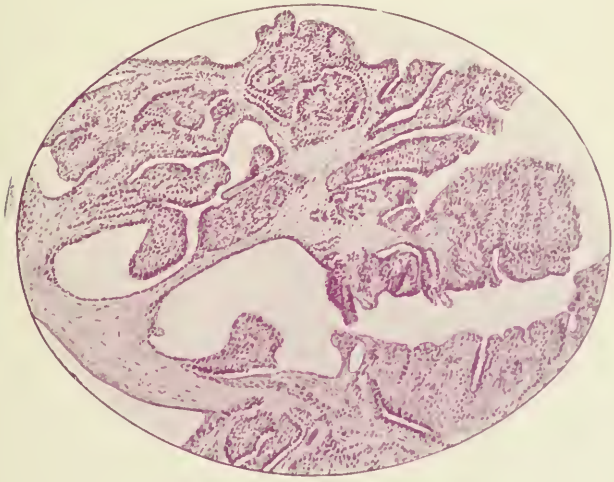


Fig. 2.

In vol. xliii (for 1892) of the Society's 'Transactions' Dr. Walter Edmunds describes a case of cystic adenoma of the kidney from a girl of eighteen, removed by operation with a good recovery. A drawing is there given of the naked-eye appearances, from which it is evident that the disease was not quite the same as either of the cases which form the subject of this communication.

November 6th, 1894.

Report upon Mr. Willett's case of congenital cystic adenoma of the kidney.—The microscopical section submitted to us, which was apparently taken from the centre of the growth, consists of numerous small cavities, averaging 120 μ across, but a few reaching 300 μ, lying in a stroma containing numerous elongated nuclei and some large thin-walled vessels.

The cavities, which are lined by cylindrical epithelial cells 20 μ across, and generally in a single layer, vary in shape, many being indented on one side. They are often oval, indicating that in some instances they are sections of tortuous tubes, and not always of spherical cysts. In none of the cavities, however, is the length more than three times the breadth. The total area of the cavities is about equivalent to that of the stroma. In some parts of the stroma groups of densely packed masses of immature glandular epithelium occur, and form imperfect tubes with barely any lumen.

We prepared another section near the renal margin of the tumour. This shows a layer of dense fibrous stroma in which the remains of secreting tissue can still be traced, forming the internal margin of the tumour.

The adjacent edge of the tumour shows large alveoli filled with spheroidal epithelium, without any cystic and with very slight tubular formation. The stroma in this part of the tumour is much less abundant than in the first section. The cystic spaces appear to be formed in two ways,—the majority by the liquefaction of the central cells of the alveoli, while others are due to dilatation of tubules. In some places irregular spaces have evidently formed by the merging of two adjacent tubes. The appearances are those of a glandular carcinoma, and the structure bears no resemblance to that of supra-renal tissue.

G. Newton Pitt.
J. H. Targett.
S. G. Shattock.

Some members of the committee, however, are of opinion that the tubular structure is of the same nature as congenital cystic disease, and that the cell masses are possibly of connective-tissue origin and sarcomatous in nature.

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5. *Calculi removed from the bladder of an infant aged eighteen months.* (*Card specimen.*)

By L. A. Dunn, M.S.

The three stones weigh 103 grs., 42 grs., and 11 grs., making a total of 156 grs. They are facetted and composed of uric acid. They were removed by supra-pubic lithotomy at the East London Children's Hospital in May, 1893. The child's recovery was rapid. *February* 19*th*, 1895.

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6. *Renal calculi in infants.* (*Card specimen.*)

By G. Newton Pitt, M.D.

1. A minute uric-acid-containing calculus about one tenth of an inch across, which weighed just over four grains when recent, and was found in the pelvis of an infant, fifteen months old. The child was admitted with laryngeal diphtheria, from which it died on the fourth day. On inquiry, it was elicited that the mother had noticed that the infant passed water much more frequently than had been the case with her other children. No blood had been noticed on the napkins.

2. Uric-acid calculus of flattened pyramidal shape, with edges about 5 mm. long, corners slightly rounded, not facetted; weight when dry 2 grains. There was found pus at the exit of the ureter from the left kidney. Pelvis normal.

The infant was eleven months old, and died with laryngeal diphtheria.

3. A similar calculus was found in the pelvis of the kidney in an infant aged twenty-one months, which died with broncho-pneumonia. In this case hæmaturia had been noticed during life.

The early age at which these calculi were found seemed to merit that they should be put on record.

February 19*th*, 1895.

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7. *On the microscopic structure of urinary calculi of oxalate of lime.*

By William Miller Ord and Samuel G. Shattock.

(With Plates II—VI.)

Synopsis.—The chief macroscopic forms of urinary calculi composed of oxalate of lime.—The variations which oxalate of lime may present in the urine and under conditions outside the body.—The detailed microscopic description of the calculi, with remarks where indicated.—The general structure of the nucleus, and its comparicon with natural and artificially produced elements.—The general structure of the body of the calculus, and its comparison with natural and artificially produced elements.—The structure of the calculi as a whole, and the relationship of the microscopic to the macroscopic forms.—The coloration of calculi of oxalate of lime.—Note of previous observations by others, and bibliography.

In this paper we devote our attention to calculi composed exclusively of oxalate of lime, or of oxalate of lime with as little admixture of other constituents as occurs in the purer calculi of the kind.

In the human subject calculi of oxalate of lime appear under four chief macroscopic forms.

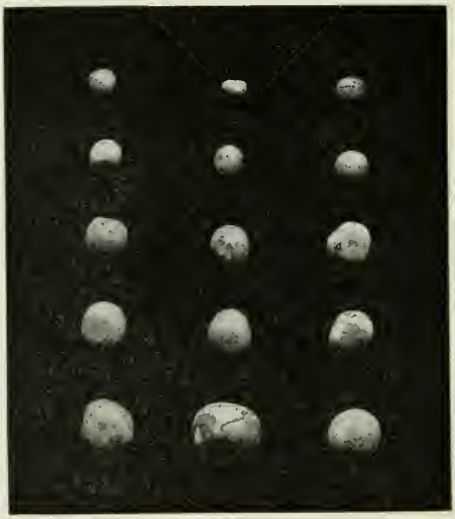
In one (Fig. 4) they are remarkably smooth, and when dried present a highly glazed or polished surface.

Such calculi, indeed, are the smoothest of all urinary calculi met with in the human subject, whatever be their composition.

The best examples of this kind occur in the pelvis of the kidney and in cysts in the renal substance, and they vary from the size of hemp-seed or less up to that of haricot beans. They are commonly of flattened oval form or remarkably spherical, but at times present facets, arising from their having grown whilst in more or

less immoveable apposition; in colour they are usually of a pale ashy grey, light yellow, or reddish brown.

Fig. 4.



Some of a small collection of smooth facetted calculi of nearly pure oxalate of lime, which were taken from the kidney after death. Their surfaces are highly polished.

It is seldom that calculi taken from the bladder exhibit the same smoothness and regularity of form, although, of course, small calculi of such a kind formed in the renal pelvis would, immediately after their descent into the bladder, present similar appearances.

Vesical calculi of this character are not of any magnitude (*e. g.* c. 84, c. 86, c. 124, Museum of the Royal College of Surgeons, London).

The second variety of oxalate calculus has, in its most pronounced form, a notably irregular tuberculated figure; and is, as contrasted with the foregoing, the roughest and the most irregular of all known kinds of urinary calculi. This is the most common met with in the urinary bladder.

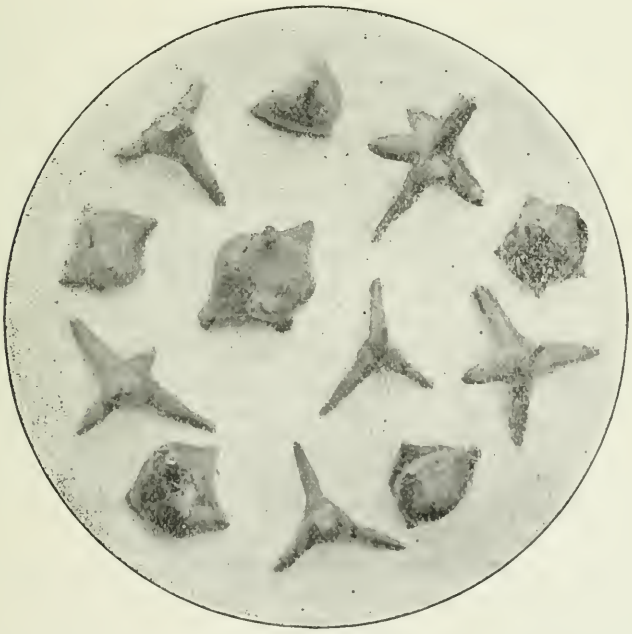
But that small calculi of similar shape are formed in the pelvis and calyces of the kidney is shown by their being voided after

renal colic. We have examined by microscopic section typical examples of this nature. When not encrusted with phosphates the calculus is commonly of a reddish brown or sepia colour. The tuberculated surface and the deep colour of these have conferred on them the title of "mulberry calculus." But the colour varies, whether at the surface or in section, within wide limits, between deep blackish brown and the palest grey, or even white. The degree of tuberculation varies; in the least pronounced degree the general contour is merely granulated.

The other two forms are of rarity but of interest.

In one (Fig. 5), from different parts of the surface of a calculus otherwise smooth, there project sharp thorny processes or spines in

FIG. 5.



A collection of twelve markedly spinous calculi (natural size) taken from the pelvis of the kidney of a woman who died of cancer of the uterus. (Jeremiah McCarthy, Esq., Mus. Coll. Surgeons.)

varying numbers of one and upwards. Calculi presenting this form are sometimes quite minute. Examples of such have been

found in the renal pelvis, in cysts of the kidney, and in the bladder. In the fourth and last form the surface is brilliantly crystalline, formed by large uncoloured octahedral crystals of oxalate of lime. Small calculi, of which we have examples passed after attacks of renal colic, are sometimes constructed solely of such an aggregation of brilliant flattened crystals, forming a peculiarly sharply-pointed concretion.

Calculi presenting such a crystalline surface are not, however, always crystalline throughout. It is not rare to see typical mulberry calculi sparkling with small octahedra of oxalate of lime; and calculi of other composition (as urate of ammonia), when encrusted with oxalate of lime, may present a similar appearance. The deposit under such circumstances "sometimes presents the appearance of an assemblage of fine crystalline needles arranged perpendicularly to the surface of the calculus" (Catalogue of Calculi, Royal College of Surgeons, London); or the deposit takes the form of crystalline plates radiating from the nucleus, the outer ends of the plates projecting sharply from the surface. Calculi, however, composed exclusively of crystals do not, so far as our observation goes, attain any considerable magnitude. The largest we have seen was extracted from the pelvis of the kidney during life, and was of a flattened, somewhat triangular form, three quarters of an inch along its sides; save for a small amount of amorphous white deposit (phosphate of lime) lying in the interstices, this calculus is wholly constructed of uncoloured crystals of oxalate of lime, which have an ill-pronounced radial arrangement. No ammonia-magnesia phosphate was present in it.

We propose in the next place to notice briefly the variations in form which oxalate of lime may present in the urine, and under various conditions outside the body. In the urine these may be dealt with under three headings: first, the octahedron; secondly, the sphere; thirdly, the tablet.

Firstly.—It is unnecessary to describe the perfect octahedron, but it is important in regard to future remarks to note some of its modifications.

The more important of these consist, first, in its flattening, either by a depression of the two pyramids composing it, the two apices being approximated; or, secondly, in a change in the proportion of the facets, some of which become relatively so large that the crystal as a whole is flattened, and suggests at first sight

the rhombohedral form: the enlargement affects opposite faces in diagonally corresponding portions of the pyramids. Thirdly, the "macle" is a form in which the apposed bases are rotated so that the angles of one pyramid project across the sides of the base of the other, giving rise to an eight-pointed star; the apices of the pyramids are usually depressed.

Secondly.—The spherular form. The perfect sphere of oxalate of lime is certainly rare in urine. So far as we know, it is not found in urine unless the latter contain an abundance of colloid. The sphere under such circumstamces is usually small, and presents slight indications of radial fibrillation. The more common variety of the spheroidal form is the well-known dumb-bell. This consists of two hemispheres, sometimes in complete appositiou, at others joined by an isthmus, and not invariably equal. The minute structure of the dumb-bell offers slight variations. It may be homogeneous and highly refractive, or may present markings radiating from the centre of the flat face of the hemisphere, and others concentric in relation to the imaginary centre of the hemisphere.

It is important to note that whereas some dumb-bells truly comprise two hemispheres, others are only hemispherical when viewed in one position, and present when rotated an elongated oval form—they are hemispheres which may be described as though parallel portions had been shorn away symmetrically from opposite sides.

Again, whilst some dumb-bells have a perfectly smooth edge in optical section, others present a finely toothed border, as though composed of the short pyramidal ends of a series of fine tablets which by their collocation construct the dumb-bell.

Thirdly.—The tabular form. From the dumb-bell to the tablet we may trace many transitional forms. What we speak of as the tablet is a flattened, elongated, crystalline body, usually about four times as long as broad; its ends sometimes present each three sharp edges, a median and two lateral, the outline of the entire element being then octagonal. Sometimes the flattened ends are rounded along the border, and a sort of oval results. In good specimens three or four markings may be observed in each half of the tablet, conformed to the angular or rounded outline, and diminishing in size as the middle is approached, *i. e.* they are concentric in their disposition. Very often a distinct line runs

across the middle of the tablet, and is bisected by lines diverging towards its narrow extremities. Such tablets, when viewed edgewise, refract light markedly, and are sometimes oval, though more frequently quadrangular, the angles projecting beyond the intermediate substance. When so viewed lines are again observed diverging from the centre towards the angles.

In a few instances a tablet of this kind, when viewed on edge, offers indications of the "wheatsheaf" form, one which may be best described by comparing it to what would be presented by a number of long pieces of card tied tightly together at the middle.

The key to the interpretation of these appearances is supplied by the well-known experiments of Mr. George Rainey. Mr. Rainey showed more than thirty years ago that carbonate of lime and other crystalline substances departed from the crystalline form when deposited in what he called viscous substances—in other words, in colloids. His first experiments were made with strong gum water in which chloride of calcium and carbonate of potassium were allowed to mix slowly, with the result that dumb-bells and spheres of calcium carbonate were formed when crystals might have been expected.

Subsequently Dr. Ord applied Mr. Rainey's observations to the elucidation of the changes presented by oxalate of lime in urine. Dr. Ord employed, in addition to solution of gum, gelatine and albumen. The experiments consisted in plugging open tubes at one end with a diaphragm of gelatine or albumen; the tube was filled above the diaphragm with solution of oxalic acid or of neutral oxalate of ammonium, the lower end of the tube being kept immersed in a solution of chloride of calcium. As diffusion took place into the diaphragm the two salts underwent double decomposition, and formed a dense stratum in the plug; sections of the gelatine plug were subsequently made and variously prepared; most were allowed to dry and subsequently mounted in Canada balsam.

On microscopic examination such sections present a remarkable series of modified forms of oxalate of lime, ranging from octahedra to perfect spheres; the latter are obtained readily in albumen, rarely in gelatine.

The intermediate forms include tablets, dumb-bells, and wheatsheaves.

Of the spheres, some, usually of relatively small size, present

an unbroken outline, and an internal fibrous crystalline structure radiating from the centre. This radiating structure is traversed by concentric lines, which are often very numerous, and darker than the rest of the sphere.

Certain of the larger spheres have a nodular surface. The nodules are rounded transparent projections, and correspond to wedges of crystalline material running towards the centre of the sphere. In such spheres the nodules and the wedges often vary considerably in size; sometimes a sphere will present one or two large hemispherical projections, and the corresponding wedges frequently fail to reach the centre of the sphere. It would seem here as if a process of coalescence of two spheres was in progress but not completed. In fact, the whole appearance of these nodular spheres suggests the possibility that they may be the result of the coalescence of a number of smaller ones. There is another spherical form of great interest in relation to urinary calculi composed of oxalate of lime. The kind of sphere referred to presents strongly marked radial lines separating fine crystalline wedges; these, however, instead of terminating in rounded ends project as jagged crystals. Mixed forms are also to be found in which radiating crystals of some size are seen in the interior of the sphere, while the outer portion presents the radiating and concentric markings described in the sphere first referred to, the margin being sharp and uninterrupted. Finally we append a drawing of much interest in relation to the construction of calculi. It represents a dumb-

Fig. 6.

bell of oxalate of lime deposited in gelatine, having attached to its outer surface several elements, set radially or at right angles to its surface; these are somewhat elongated in the radial direction, vary in size, and, although of no regular crystalline figure, are nevertheless crystalline in appearance; they are evidently crystals modified by the circumstances under which they have been produced. The dumb-bell itself presents shallow indentations cor-

responding with the points of attachment of these subcrystalline bodies.

Numerous experiments were made with other salts. In the case of carbonate of lime and oxalate of copper perfect spheres were obtained; in the case of sulphate of calcium larger agglomerations of spheres were produced, curiously resembling certain forms of the urinary calculi.

As the structure of such artificially produced spheres has an important bearing on that of the calculi to be described, we may recount what this is in typical cases, selecting for examples oxalate of copper and carbonate of lime.

Oxalate of copper deposited in gelatine.—This salt assumes the spherical form much more readily than oxalate of lime.

A very large proportion of the forms deposited in the gelatine are perfect spheres, having a sharp unbroken outline. They exhibit a fine radial striation extending from the centre to the surface, the dark lines marking the striæ being so numerous as to render the central part of the sphere actually opaque, except in certain cases when a brilliant centre of transparent green colour is found in the midst of the striated substance.

Besides these are found numerous lobulated spheroids, which would appear to be composed of lesser spheres in process of aggregation, like those depicted in Mr. Rainey's work (loc. cit., fig. 4, p. 12) as met with in carbonate of lime. In the larger spheroids may be clearly seen a compound nucleus, composed of considerably smaller spheres. There occur also numerous small but singularly perfect dumb-bells. It is impossible, on examining a series as they increase in size, to fail to perceive that the dumb-bells pass by transitions to spheres; indeed, in some of the perfect spheres there may be seen an incomplete partition of dark striæ bisecting the sphere, and corresponding to the original interval between the hemispheres of the dumb-bells. These spheroidal elements entirely replace all angular crystalline forms.

Carbonate of lime deposited in gelatine.—These preparations confirm Mr. Rainey's observations on the same salt. The spheres show at comparatively wide intervals delicate concentric striæ, in addition to the radial markings noticeable in these and the foregoing. In some of the spheres the centre consists of a perfectly homogeneous spherule, defined from the surrounding substance by a sharper line than exists elsewhere. In others the centre is

markedly striated, presents a subdivided border, and is evidently composed of a closely coherent mass of elements.

In addition to the spheroids there occur spherules, aggregates of minute crystals, comparable to the crystalline centre of certain of the spheres just described. There are, moreover, several flattened oval elements resembling the spheres in general structure.

Although there are no perfect dumb-bells, there is an approach to these forms, *i. e.* there occur bilobed spheres, or large spheres constricted across the middle, or marked by a strong diaphragmatic line, and having two distinct centres. There occur also dumb-bells without other structure than that of minute granules, which have in consequence a granulated surface, as have some dumb-bells of oxalate of lime met with in gelatine.

Spherular forms have been obtained in addition from barium sulphate, calcium sulphate, barium chromate, nitrate of urea. It is possible to obtain them from the last-named on so large a scale as to be visible to the naked eye, by adding strong nitric acid in excess to albuminous urine of a specific gravity of 1028 and upwards; in proportion as the quantity of albumen is increased the size of the spheres is diminished, and when examined under the microscope they are found to be composed of crystalline spicules arranged radially from a centre, and forming a dense spherical tuft, somewhat resembling but coarser than the tufts in which urate of soda is deposited from an aqueous solution.

From these observations we may conclude that the modifications of the octahedron of oxalate of lime observed in the urine depend upon the admixture of colloids. Of these colloids the one which exercises most influence is undoubtedly albumen. After albumen, mucus; if in considerable amount, as Dr. Beale has noticed, casts of urinary tubules sometimes contain the dumb-bell form of oxalate of lime. Of other abnormal constituents of urine, sugar, so far as can be made out, has no modifying influence on the form of crystalline oxalate of lime.

Of the possible modifications occurring in peptonuria we have no observations, although from the ease with which peptone passes through the dialyser its influence as a colloid is probably small.

Mr. Rainey's opinion was that the formation of spheres arose from some kind of combination between the crystalline material and the viscous substance. He also believed it could be demonstrated that if two spheres were brought into apposition, they

gradually coalesced to produce a single one. The other remarkable phenomenon observed by Mr. Rainey, and termed by him molecular disintegration, has also to be kept well before us in endeavouring to interpret the constitution of larger calculi. He found that the spheres formed in one solution of gum became rapidly altered when placed in another, even of approximately the same strength; the spheres lost their perfect outline, became more and more striated, and gradually fell to pieces.

After this preliminary consideration we may proceed to the immediate subject of the paper, viz. the microscopic structure of calculi composed in the main of oxalate of lime.[1]

Description of the microscopic appearances presented by illustrative sections of calculi of oxalate of lime.

The arrangement of the following specimens is in order of simplicity. The letters are those originally used in the preparation of the sections; references to the calculi are made not by these, but according to the number of the section.

Section 1. *Calculus Nc* 29, Royal College of Surgeons.—From a very large collection of hemp-seed calculi taken from a hydronephrotic kidney. The nucleus is not differentiated in structure from the rest of the calculus. The whole is constructed of transparent radially and concentrically striated cones. It is double—*i. e.* the cones diverge from two centres, and as they abut laterally remain for some distance uncoalesced: it may be compared to a gigantic dumb-bell. Towards the surface, however, the radial striation of the doubly striated substance becomes abruptly more pronounced, so as to differentiate a kind of crust. In this crust the elements arise in diverging tufts in three or more tiers at different distances from the centre of the calculus: in some situations the tufts arise on narrow zones of molecular substance. Minute reddish-brown granules are distributed through all the parts of the calculus in concentric but ill-defined lines.

[1] The preparations were made in the following way:—The calculus was first rubbed down on a file or glass-paper and then on a hone with water until the centre was reached; the ground surface was then well washed beneath a gentle stream of water, and allowed to dry under a shade: it was then cemented to a glass slide with solid Canada balsam liquefied by heat. The calculus was subsequently ground from the opposite aspect by the same process, and when sufficiently thin, washed and allowed to dry. A drop of ordinary mounting fluid was then placed on the section and a cover-glass applied.

DESCRIPTION OF PLATE II,

Illustrating Dr. W. M. Ord's and Mr. S. G. Shattock's paper on the Microscopic Structure of Calculi of Oxalate of Lime. (Page 91.)

FIG. 1.—*Section 7. Calculus C.* × 40. Showing the nucleus of coarse crystals suggesting octahedra; and the body of the calculus consisting of zones of radially striated crystalline substance and non-crystalline zones marked into concentric layers by lines of brown granules.

FIG. 2.—*Section 7. Calculus C.* × 140. Showing the more peripheral portion of the body of the calculus. The growing surface is constituted by non-crystalline substance marked into concentric layers by lines of brown granules. The body is made up of radially striated crystalline substances and non-crystalline zones marked into concentric layers by lines of brown granules (urate).

FIG. 3.—*Section 7. Calculus C.* × 140. Showing the nucleus of coarse crystals in places suggesting octahedra, and which exhibit a secondary cleavage. Towards its periphery are irregular collections of small crystals. To this succeeds the body of the calculus, which is made up, as seen in figs. 1 and 2, of radially striated crystalline substance and non-crystalline zones marked into concentric layers by lines of brown granules. In many places the points of departure of the crystalline material can be seen in the form of cones or diverging brushes of long crystals. The two kinds of structures first mentioned are variously intermingled, or cross one another.

Fig. 2.

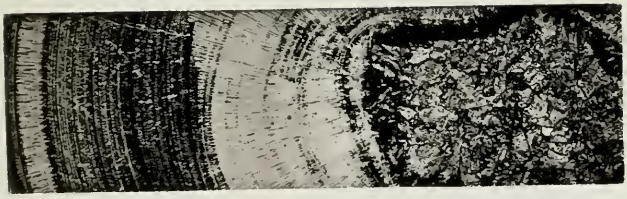


Fig. 1

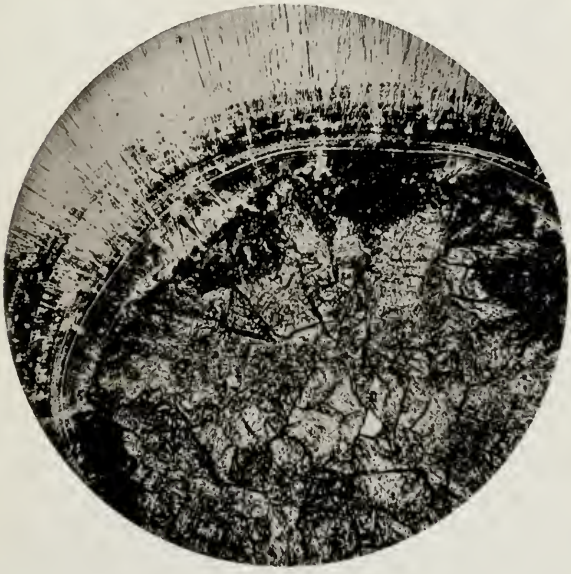


Fig. 3.

Chemical composition.—No carbonate, no phosphate, a trace of iron, no murexide reaction. Notwithstanding the last-mentioned fact the granules distributed through the calculus may be regarded as urate, the quantity of which is too minute to give signs of murexide reaction: this may be assumed, since when murexide reaction is obtained such granules occur in considerable bulk.

Section 2. *Calculus O.*—From the same collection of hemp-seed calculi. Shows the same structure as the preceding. Nucleus of massive cones; these are made up of comparatively coarse crystals individually more evident than usual, so that where divided obliquely or transversely the section appears much as a huge crystal in which coarse parallel cleavage has occurred.

Section 3. *Oa* (Plate V, fig. 1).—From the same collection. Nucleus of crystalline cones, starting from two centres as a gigantic dumb-bell.

Section 4. *Ob.*—From the same collection. Shows nothing new.

Section 5. *Oc.*—From the same collection. Shows in the nucleus asymmetrical rosettes, fan-shaped elements passing into cones, as well as ill-formed flat elongated crystals which also merge into cones. These elements are described in detail in certain of the calculi noticed further on. The "body" beyond the nucleus is constructed as in the rest of the same group.

Section 6. *Od.*—From the same collection. Shows nothing new.

Section 7. *Calculus C* (Plate II, figs. 1, 2, 3).—A small hemp-seed calculus, smooth, facetted; one of several taken from a cyst in the substance of the kidney (St. Thomas's Hospital Museum). Oxalate of lime and a small amount of urate or uric acid, as told by the murexide test. Dr. Bernays, on testing three of the group for iron, reports, "The coloured areas visible on the calculi remained visible in the ash as separate from the carbonate of lime resulting from the combustion: they appeared as reddish spots, therefore consisted of a ferric compound; very dilute HCl dissolved the carbonate before the reddish-brown material, which is shown to be a ferric salt. A considerable precipitate was obtained with ferrocyanide of potassium, *i. e.* Prussian blue."

Nucleus.—No foreign body. Coarsely crystalline, and composed of large variously misshapen crystals, in some places suggesting octahedra, in others tablets. These massive crystals show a secondary cleavage leading to a highly complex condition. In

most instances it is clear that the cleavage runs in parallel planes, but whether across the long axis or parallel with one of the faces it is impossible to say. Towards the periphery there are irregular collections of small crystals closely and irregularly packed without intervening substance, and of short prismatic or tabellar forms. To this succeeds the proper "body" of the calculus.

The body is constructed, firstly, of a broad belt of transparent colourless crystalline material, marked by radiating interrupted lines. In several spots the points of departure of this crystalline substance appear as conoidal collections of long slender crystals, the apices of the cones being directed towards the centre of the calculus, *i. e.* they are set on the surface of the crystalline nucleus; the substance is crossed by extremely fine and very close-set concentric striæ. Moreover there are sparsely embedded in it minute dark reddish-brown granules of the kind so usual in calculi of oxalate of lime.

These granules are in places arranged in concentric lines, and are continued into the other striæ in which no such granules are discernible and which appear to be due to differences in refraction only. The coarser lines of granules occur in the deeper parts of the zone.

There occur concentrically, intersecting the crystalline material, yellow zones of a finely molecular, faintly brown substance, with or without dark embedded granules, through which zones the radial striæ of the crystalline substance pass without break.

To this succeeds a zone of nearly the same breadth, of molecular, faintly brown, not apparently crystalline substance, marked by fine concentric and remarkably regular lines of reddish-brown granules.

Again comes a crystalline zone like that next the nucleus, but considerably narrower, and in this zone there occur long rows of granules between the crystals, *i. e.* having a radial direction, and like those that are arranged concentrically in the non-crystalline material on the inner side of the zone: the granules present in this crystalline zone are most numerous in its inner fifth.

In a few situations the concentrically marked non-crystalline zone on the inner aspect of the outermost crystalline belt is radially intersected by long wedges of crystalline substance in which few or no granules are present, and in which the lines of the crystalline material converge to the apex of the wedge. These

wedges or cones are continued from the midst of the non-crystalline into the crystalline zone on the outer side, the concentric lines of the granules being interrupted in these situations. The calculus is completed by a zone of non-crystalline material like those before described.

Chemical examination.—No carbonate; no phosphate; a trace of iron; a small amount of urate as told by the murexide test. From one of the sections of the same group of calculi which had been mounted in Canada balsam and showed microscopically the same kind of nucleus, the latter was isolated by removing the cover-glass, and scraping away the body of the calculus till no microscopic remains of anything except the nucleus were left. The balsam was then dissolved with xylol, absolute alcohol, and finally ether. On submitting the solid particles to the murexide test no trace of uric acid was obtained.

Section 6. *Calculus H.*—From a cyst of the renal tissue; the same group of calculi as C.

Nucleus.—This shows even more clearly than in C the massive irregular subcubical crystals composing it; they all present fine parallel striation, indicating the occurrence of secondary cleavage. At the peripheral part of the nucleus the crystalline material is set in coarse parallel columns, the lateral limits of which are very distinct and somewhat irregular; many of these present a horizontal parallel cleavage. This columnar arrangement obtains, however, only in places. The nucleus terminates quite abruptly, and the rest of the calculus is as described under C. This nucleus was subsequently used for the chemical test described at the close of Calculus C.

Section 8. *Calculus K* (Plate III, fig. 1).—A small dark brown typical mulberry calculus.

Nucleus.—This consists of gigantic uncoloured transparent crystals, some of which present delicate traces of parallel lines of secondary cleavage; some are square or rhombohedral in the section, and are apparently octahedra. Here and there are still larger polyhedral masses very like some of those described later under oxalate of lime gravel, but having somewhat sharper outlines. The nucleus is much like that in Section 7, except that in this the crystals are so cleft as to lead to opacity. This crystalline centre is traceable outwards as irregular radii into certain of the long crystalline nuclei of the prominent processes of the calculus.

In these extensions of the main nucleus the crystals are smaller, and mingled with forms such as occur in Section 12 and will be presently enumerated.

In some places the "body" arises directly upon the large crystals of the nucleus; in others on a zone of smaller elongated octahedra and other forms. It has the usual character of laterally sutured columns or cones, the entire structure being both radially and concentrically striated.

In the secondary or subordinate nuclei the crystals are not so massive, and they are confusedly mingled with other elements of the kind fully described under Section 10, viz. fan-shaped elements radially striated, and with coarse dentate edges indicating their composite structure; fan-shaped elements both radially and concentrically striated; and circular aggregates radially striated. There occur also crystalline rosettes, of which portions are finely striated both in the radial and circumferential directions.

There is, in fact, no sharp line of division between the fan-shaped crystalline aggregations and the doubly striated cones, the jagged edges of the latter being due to their having a compound crystalline structure.

The "body" around the secondary nuclei is structurally like that about the primary.

The growing surface of the calculus is formed for the most part by broad stunted cones closely packed, in places without much order, and striated radially and concentrically. In some spots it is plain that the original element was a rosette or crystalline sphere, the elements of which have grown inordinately on the outer or peripheral aspect. In other parts of the surface the columns terminate in a regular series of crystalline points, into some of which the fine radial striation of the subjacent substance is prolonged. In yet other places the growing surface is of diverging tufts of long crystals finely striated in the radial direction only; the lateral borders of the tufts abutting obliquely upon each other, so that the extent of the different aggregates is quite readily distinguishable. Where most regular the surface is not curvilinear, but crenate in correspondence with the coarser radial striæ of the columns forming it; these coarser striæ indicate the compound structure of the columnar substance, which is composed of diverging tufts of comparatively coarse crystals in which a finer secondary striation has occurred as well as a transverse.

DESCRIPTION OF PLATE III,

Illustrating Dr. W. M. Ord's and Mr. S. G. Shattock's paper on the Microscopic Structure of Calculi of Oxalate of Lime. (Page 91.)

Fig 1.—*Section* 8. *Calculus K.* × 80. Showing large clear crystals constructing the nucleus. At the periphery of the nucleus the crystals are smaller, and on the left are set vertically as a palisade. On the crystalline nucleus the substance of the body of the calculus arises in the form of crystalline cones. The lower portion of the calculus is arranged round another nucleus, the zigzag fissure marking the apposition of the two different series of aggregated cones.

Fig. 2.—*Section* 12. *Calculus F.* × 260. Showing the outer part of the nucleus. There are shown clusters of fan-shaped elements and rosettes, to which succeeds a zone of minute crystals, and to this the doubly striated substance of the body.

Fig. 3.—*Section* 10. *Calculus E.* × 120. Nucleus, showing the large crystals that mostly compose it; portion of the body of the calculus is shown arising upon the nucleus in cones of diverging crystals which form a radially striated general mass crossed at right angles by a second series of lines concentric with the nucleus.

Fig. 4.—*Section* 10. *Calculus E.* × 120. Showing the general structure of the body of the calculus, which is composed of a fusion of long crystals arranged in diverging tufts or cones, and crossed by fine striæ at right angles to their long axes. The preparation shows one of the clefts which correspond with the situation of recesses in the contour of the nucleus, the growing ends of the divergent cones coming to abut, without being strictly continuous, in planes which correspond with the recesses mentioned.

Fig. 1.

Fig. 2.

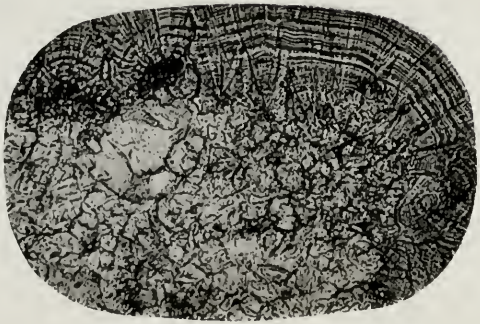


Fig. 3.

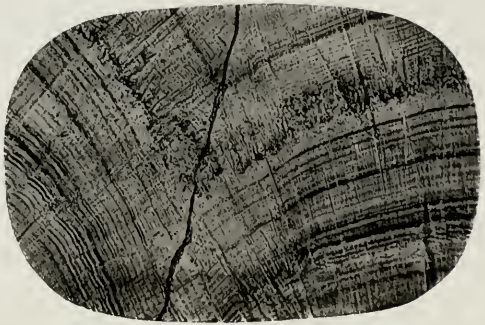


Fig. 4.

Section 9. *Calculus G.*—A small calculus of deep brown colour, with a stout spine projecting at one spot; passed after renal colic accompanied with hæmaturia.

Nucleus of the spine.—Of beautiful massive crystalline structure. Its component crystals are angular, some showing the octahedral form; all are of large size.

Most of them exhibit a delicate parallel striation; in some there lie embedded in the crystals lines of dark brownish granules parallel with the finer striæ. In one place there occurs a fan-shaped group of long clear crystals with pointed free ends. On this nucleus is implanted the body of the calculus, which has the usual crystalline character, and is radially and concentrically striated—an aggregate of diverging cones.

The body has a general light brown coloration.

Section 10. *Calculus E* (Plate III, figs. 3 and 4).—A smooth-surfaced flattened oval calculus from the renal pelvis. Oxalate of lime with a trace of uric acid, as shown by the murexide reaction.

Nucleus.—No foreign body. It is entirely crystalline and tuberculated in outline. Its component crystals are mostly of large size, and with irregular wavy or jagged outlines in the form of tablets; some are octahedral, more or less perfect, homogeneous, colourless, transparent. Here and there the crystalline material is arranged as rosettes, which exhibit certain differences in their more intimate structure.

In the simplest of these a few of the crystals lie with one end set centralwise.

From such a simple arrangement may be traced the formation of finely radially striated spherular masses lying in the conglomerate of crystals.

Certain of the rosettes appear, for instance, as composed of slender crystalline plates pointed centralwise, *i. e.* to a centre, about which they converge, and abruptly truncated or bluntly pointed peripherally: the outer ends of the several crystals, or of the different elements resulting from the cleavage of such, do not so accurately correspond as to give to the whole the form of a perfect sphere. *These correspond closely with the aggregates of oxalate of lime crystals deposited in gelatine, as figured in pl. v, fig. 3h, and pl. vi, fig.* 2, of Dr. Ord's monograph, 'The Influence of Colloids upon Crystalline Form.'

There may be seen also in the crystalline conglomerate, be-

sides the rosettes noticed, smaller fan-shaped arrangements of the crystals, that is segments of spheres, or incomplete rosettes.

The importance of such forms lies in the fact that the body of the calculus starts in similar but more perfectly formed elements. Such forms are to be seen at the outermost parts of the crystalline nucleus, and some are finely striated in a radial direction, and have the pale brown colour presented by the body of the calculus which follows immediately upon the nucleus.

The most remarkable structures in the nucleus, however, are what appear as still more perfectly developed spheres, but which are really cross-sections of processes arising from the nucleus. They are of considerable size, lie amid the true crystals of the nucleus, and offer to view not only a fine radial striation, but a very distinct slightly undulatory concentric marking in addition, precisely like that presented by the body of the calculus as is described later on. The crystalline character of these is very evident in the sharp dentate edges which in places they present, the divisions between the teeth of which correspond with the main radial striæ of the sphere.

Of some of the larger of such spheres the centre is truly crystalline like the main substance of the nucleus; the true crystalline elements, however, are smaller than the crystals of the conglomerate which form the proper nucleus of the calculus as a whole. These crystalline spheres, like the body of the calculus, have a pale brown colour, and they present a double radial striation,—a coarser corresponding with the divisions between the component crystals, and a finer within the latter.

To this nucleus succeeds the "body" of the calculus, and this is crystalline.

The crystalline substance takes its point of departure in the form of tufts of diverging crystals, the outer ends of the component elements being in places remarkably plain.

In most situations the fusion is more complete, the result being a radially striated structure in which a coarser striation exists indicative of the main lines of the crystalline fusions, and a finer radial striation, perhaps of secondary production.

The fusions are beautifully cross-striated with fine close-set wavy lines, in some of which granules of reddish-brown substance (urate) occur.

The crystalline cones are set with their long axes at right angles

to the subjacent surface of the nucleus. Hence, as the latter is irregular, the growing or outer parts of the cones come to meet in places corresponding with the recesses between the projecting processes of the crystalline nucleus. This meeting is marked by zigzag or wavy lines continued far into the body of the calculus, the striæ proper to the cones abutting obliquely along this line, which is in reality a fissure; *i. e.* the crystalline material is here discontinuous.

The entire body of the calculus may be regarded as composed of a series of independent wedge-shaped or conoidal masses set upon the outer surface of the crystalline nucleus. As the distance from the centre increases, the width between the coarser radial striæ becomes correspondingly greater. So the structure continues to the surface. The exterior is not absolutely smooth, though the general contour is ovoidal without visible tubercles; the section offers to view the rounded ends of crystalline columns, the clefts between which are continued for some distance inwards as radial lines.

The radiating masses have much the appearance of striated muscle-fibres with their points of insertion directed towards the centre. In oblique or transverse section their outline is festooned, indicating that they are composed of aggregations of elongated closely-applied crystals. In such sections of the cones also there occur in certain places irregular collections of minute brownish granules, the explanation of this disposition being that such extended collections represent what in a section along the axis of the cones appears as one of the concentric coarser granular lines or striæ.

In one spot may be well observed the introduction of a new centre, some distance from the proper nucleus. This occurs as a spheroidal collection of moderately sized crystals, and from this secondary nucleus start a new series of crystalline fusions or cones, which at their commencement form in the section a considerable segment of a circle; the cones show a radial and transverse striation like the rest of the body of the calculus. For some distance the interposition of this new centre leads to disturbance in the concentric striation; moreover the radial striæ of this pertaining part of the body, owing to their more abrupt divergence, abut obliquely upon the radial striæ of the substance on either side.

The presence of the granules disposed concentrically in the

substance of the crystalline fusion is to be explained thus:—the growth of the calculus proceeds by the deposition on to the free ends of the crystals of fresh oxalate of lime; during this process of growth the granules of urate come to be embedded in the crystalline material. This accounts for the undulatory character of the granular lines, the growing surface during the deposition being slightly undulatory from the projections of the crystalline columns.

Chemical composition.—Contains a trace of uric acid, as shown by the murexide reaction.

Section 11. *Calculus P.*—A miniature mulberry calculus.

Nucleus as described in Section 10; crystals and crystalline rosettes minutely striated radially, and jagged at the edge. Also fan-shaped, finely radially striated elements, and similar elements showing also cross-striation. There are, moreover, asymmetrical rosettes of which the larger part is cross-striated, and the rest only radially: here and there at the periphery occur collections of small crystals. On the nucleus start the typical crystalline fusions, striated in both directions. Secondary nuclei occasion the production of the typical mulberry form, though the whole calculus is not so big as a pea. Such secondary nuclei are of small crystals, as in Section 10. There occur frequent and irregular interpositions of new elements in the body in the form of striated cones. Most externally is a zone very finely striated in the radial direction, crystalline, but for the most part opaque in consequence of the mingling with it of blackish-brown granules; where in least abundance these are disposed in coarse concentric lines, and in finer radial lines corresponding with the finer radial crystalline markings.

Section 12. *Calculus F* (Plate III, fig. 2, and Plate VI, fig. 1).—A calculus of mahogany-brown colour, three quarters of an inch in diameter.

Nucleus.—Composed of colourless transparent closely aggregated crystalline material. Portion consists of the transverse and oblique sections of crystalline cones, other portions of what appear at first to be crystals of medium size. The former portion presents itself as closely arranged, large, highly irregular jagged areas, which towards the outer part of the nucleus, at one or two spots, where divided vertically, pass into fragmentary blocks of radially striated substance like that to be hereafter described in the

"body" of the calculus, and like it crossed by lines concentric with the centre of such crystalline fusions. With such exceptions the crystalline cones are arranged with the utmost irregularity; and although individually they present both a longitudinal radiating and a transverse striation, they are so disorderly apposed that no continuously striated substance results.

The other portion of the nucleus, which appears at first to be a compact mass of crystals, consists of elements without any regular shape, more or less angular, and accurately adapted to one another by their edges. A higher power, however, shows that these elements are closely allied in their nature to those already described. Many are circular in section, and may be best described as rosettes; they are constructed of long crystals radiating from an imaginary centre; their inner ends tapering and pointed, the outer truncated and not terminating regularly, so that the outline of the aggregate is correspondingly notched or jagged: these present no concentric striation. Were they cross-sections of cones they would not offer the regular and perfect radial striation which they do. Such elements, however, do not appear always as completely circular; they may be fan-shaped, and except that they want a transverse striation, such resemble the broad doubly striated cones confusedly arranged in other parts of the nucleus,—indeed, they occur mingled with them.

In yet other cases a doubly striated rosette is prolonged on one aspect into a broad cone, in the distal part of which the concentric striation is incomplete, in correspondence with the fact that here the structure represents a section only of the circle.

To the nucleus succeeds a well-defined compact zone of fine elongated crystals inextricably intermixed (compare the first crystalline zone beyond the nucleus in Calculus A). Next, a zone striated both radially and concentrically; in this there occur minute dark brownish granules (urates), both concentrically and, in less numbers, radially disposed. The points of departure of this striated zone are obvious in places as cones of various sizes, the pointed inner ends of which abut on the finely crystalline zone immediately surrounding the nucleus; in other places, however, fine long crystals, such as compose the cones, arise without any such aggregation.

Next comes a belt of discrete or non-confluent crystals of moderate size, of no regular form though tabellar, and without

order: at its periphery, however, the crystals are more minute, elongated, and like those which immediately succeed the nucleus as before described. The most internally placed, unlike the rest, are arranged with considerable regularity, and like a palisade lie directly upon the ends of the radially and horizontally striated columns beneath them, in series with which they are and which they, as it were, cap.

To this succeeds a zone of doubly striated crystalline substance, and this, with little variation, continues for a considerable distance, the general contour of the calculus so far being oval, the only variation in the structure consisting in the interposition of zones of intermixed fine acicular crystals which interrupt the continuity of the doubly striated substance, which latter again arises on these zones as described around the nucleus.

But now the typical mulberry form arises. As seen under an ordinary lens, there project about ten processes like the tentacles of a polyp, bluntly conical, some presenting constrictions in their course: in some there is visible a less transparent centre, like that composing the nucleus of the main calculus. The irregularities thus produced in the contour are in this particular calculus subsequently filled in with opaque crystalline deposit and the oval contour restored, the concretion in its final condition wanting a typical mulberry form.

To describe the microscopic structure of one such process in which the section has traversed its middle:—The projection shows a distinct nucleus of precisely the same structure as that of the main calculus, already fully described, and consists of radially striated rosettes, and broad, stunted, doubly striated crystalline cones, the whole being quite devoid of any orderly arrangement. On this secondary nucleus there are set doubly striated cones of crystalline substance, which coalesce, or, more correctly, are sutured by their sides, to form a continuous structure like that of the rest of the body of the calculus.

In the outer parts of the protuberances there occur two or more incomplete zones at different levels, which break the general monotony of structure: these zones extend in places for considerable distances, following the contour of the calculus as at this level existing, or they occur only in short disconnected fragments. They are constructed of large perfectly colourless and transparent crystals, which in the main affect the character of prisms; some

such have a fan-like or even stellar disposition: in some of the collections, however, these crystals present the form of very irregular plates or tablets of considerable area. That these plates are not phosphates is shown in a negative way by there being a complete absence of the chemical reactions of phosphates in the calculus, which should have been obtainable, since the substance in question occurs in considerable amount; but in a positive way their nature is shown by the fact that in some places the prismatic forms are continuous with the radiating columns of the doubly striated substance immediately to their inner side, the elements in such circumstances having a corresponding radial arrangement: certain of the irregular tablets, moreover, have a fan-like form, allying them with the stunted cones which lie in certain situations on the outer aspect of the fragmentary zones in question, and with some of which they are directly continuous. They correspond closely with certain of the forms of oxalate of lime in gelatine figured by Dr. Ord (loc. cit.) in pl. vi, figs. 1, 5, 7.

At a certain level the recesses between the protuberances are all filled up with another substance, with the result that the irregular contour is replaced by one that is regularly oval.

The substance occupying the recesses is, to the naked eye, quite obvious by its whiteness and want of complete transparency even in the section as it is mounted in Canada balsam. It consists mainly of radially disposed prismatic crystals, though the regularity of such an arrangement is not very well pronounced. Here and there the elongated crystals take their point of departure as diverging tufts; and here and there a well-marked rosette is to be encountered.

Where the elongated crystals are most parallel they produce a columnar structure, but one in which no regular cross-striation is present as in the transparent parts of the calculus, though the elements are irregularly and somewhat minutely fissured from secondary cleavage: it is this cleavage, combined with the presence between the prisms of closely packed minute crystals of similar nature (for all gradations of size are traceable), that produces the relative opacity of these areas even in the microscopic section after its treatment with Canada balsam solution.

In these parts there occur, moreover, very ill-defined zones of shorter irregular crystals, but of similar nature, and exhibiting the same kind of secondary cleavage. As a whole this deposit has a

pale yellow colour, and since the calculus contains urate of soda, and the crystalline prisms resemble such as this salt may present (compare Dr. Ord, loc. cit., pl. iv, figs. 1, 8), and because the general structure is to be observed in microscopic sections of calculi of the uric acid series, it must be concluded that the substance in question consists of urate, and not—as the first impression would be—of phosphate.

From the outer surface of the urate deposits the clearer substance of the oxalate of lime beyond takes its point of departure in crystalline cones radially and concentrically striated, and with such the rest of the calculus is made up.

Chemical examination.—No carbonate; the murexide test shows the presence of uric acid, combined as urate of soda; a minute trace of iron; no phosphate. The opaque zone is urate of soda.

Section 13. *Calculus V* (Bb. 6, St. Thomas's Hospital Museum), —Nucleus of opaque, drab-coloured urate of ammonia, succeeded by oxalate of lime, and thin laminæ of similar urate interposed between the wavy layers of more transparent, pale brown oxalate. Surface granulated; patches of similar urate, in places, fill the bottom of the hollows between the hemispherical eminences at the surface. The laminæ of oxalate are individually continuous, *i.e.* the granulations are not due to the formation of discrete calculous spheres.

The structure of the uratic zones we reserve for a subsequent communication. We may mention, however, that in large part they consist of coarsely laminated spheres, presenting also a remarkably fine radial striation; they are characterised, moreover, by a certain degree of opacity and a distinct yellow coloration.

As to the general structure of the oxalate portions, there is nothing special; the section was made in order to study the *origin of the eminences*, which are not confined to the exterior, but are equally marked in the deeper laminæ, showing the granular character to have persisted during the growth of the calculus.

The eminences result from the formation of secondary nuclei constructed of different elements, such as coarsely crystalline rosettes; fan-shaped aggregates of similar coarse and elongated crystals without transverse striation; discrete crystals, of which some are elongated like those composing the rosettes, and others are larger transparent blocks suggestive of ill-shaped octahedra. The whole of these forms are such as are described in detail under

DESCRIPTION OF PLATE IV,

Illustrating Dr. W. M. Ord's and Mr. S. G. Shattock's paper on the Microscopic Structure of Calculi of Oxalate of Lime. (Page 91.)

FIG. 1.—*Section* 14. *Calculus A.* × 70. Showing the nucleus. In the darker centre may be distinguished certain of the spherules described in the text; then succeed a zone of non-crystalline substance, one of finely packed crystals, and on this another of non-crystalline material: there follows a zone of interlaced crystals, and next one in which large diamond-shaped collections of small crystals occur,—octahedra of oxalate of lime in which secondary cleavage has taken place. Beyond this is the body, which is firstly constituted by a broad non-crystalline belt marked into three or more concentric laminæ by brown granules of urate; to this succeeds the radially striated crystalline substance.

FIG. 2.—*Section* 14. *Calculus A.* × 40. Showing the body of the calculus beyond the diamond-spaced area. There comes firstly a broad non-crystalline nebulous zone divided into three or more concentric strata by coarse lines of brown granules; then a crystalline one marked by interrupted radial lines, in the deeper part of which are scattered considerable numbers of brown granules of urate; next, another nebulous zone, then a broad radially striated crystalline one incompletely intersected in the concentric direction by others that are non-crystalline and nebulous. For its outward half the structure of the calculus is finely laminated or striated in the concentric direction.

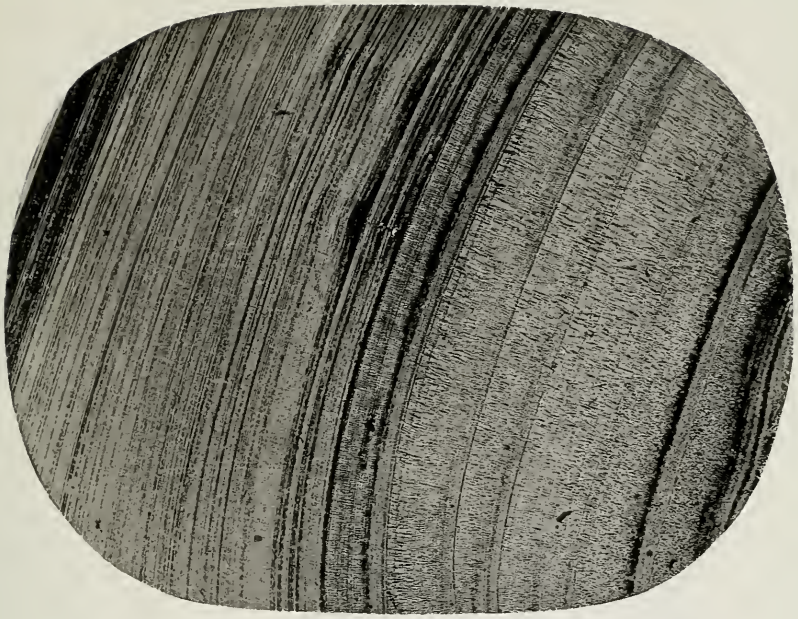


Fig. 2.

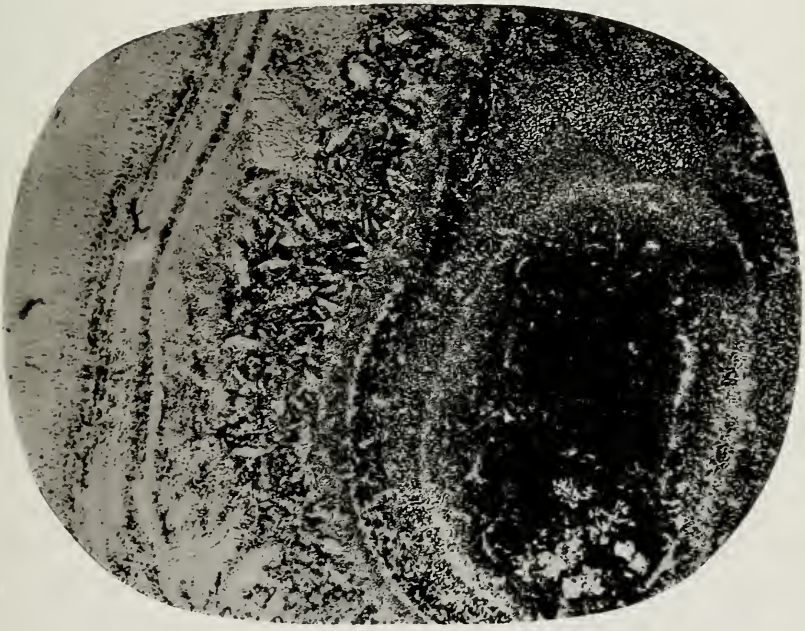


Fig. 1.

Sections 10 and 11. These secondary nuclei, however, are connected by a more or less continuous zone of similar elements, *i. e.* they arise as irregularities in the deposit of coarsely crystalline layers of oxalate interposed between the usual doubly striated substance.

It is also of interest to note that the section shows a more or less complete zone of small, colourless, glassy-looking spherules in process of fusion, the whole corresponding precisely with the nucleus of Section 18, Calculus D, and that of Section 19, Calculus L. In certain situations this zone takes the form of an undulatory glassy line, as described in the body of Calculus D. The line bounds what in its deeper part is a finely granular or nebulous uncoloured material, composed apparently of very minute crystals, seeing that this material merges further outwards into irregular blocks of crystalline substance which still more outwardly pass into the regular doubly striated general material of the calculus. On the outer aspect of the wavy line the substance of the calculus takes the form of cones of small size irregularly disposed, or fusing into an orderly layer.

Section 14. *Calculus A* (Plate IV, figs. 1 and 2).—A smooth calculus, one of many ; oxalate of lime with small quantities of urate and phosphate and much organic matter (Dr. Bernays). The calculus was from the renal pelvis in a case of malignant disease of the kidney.

Nucleus.—No foreign body, or space indicative of such. In outline it is irregularly oval. Structurally it consists of an aggregation of minute perfectly colourless closely packed crystals, with exceptions to be immediately noticed.

The other structures in the nucleus appear as discrete circular areas transmitting light more readily than the rest of the nucleus, and constituted by similar slender, uncoloured crystals, but arranged radially from a centre with great regularity.

These are of precisely the same nature as the crystalline spheres of nitrate of urea producible in albuminous urine by the addition of nitric acid, or as the crystalline spheres of oxalate of lime which may artificially be formed in gelatine. The close relation of such to the perfect sphere is proved by the transitions between the two in a single experiment; the radial striation presented by the sphere is the indication of its crystalline nature. In the case of carbonate of lime deposited in gelatine, *e. g.*, there may be observed

both perfect spheres and rosettes of fine acicular crystals with intermediate forms. The crystalline spheres in the nucleus are distinguishable from spherules of urate by their absence of coloration, their transparency, and absence of coarse concentric striation. Such spherules of urate are alluded to under the description of Section 13, Calculus V.

Beyond this, the very centre of the nucleus, is an incomplete narrow zone devoid of crystalline elements, in which lie embedded minute brownish granules. To this succeeds a zone of closely packed slender colourless prismatic crystals of small size, though considerably larger than those described as comprising the nucleus. They are inextricably interlaced, and packed either without intervening material, or in a substance thickly beset with small dark granules. Some of the crystals are shorter and broader than others, with ends cut sharply at right angles.

These elements may be compared with certain of the slender tablet forms of oxalate of lime met with under rare circumstances in urine, but producible in abundance when this salt is deposited in gelatine.

At one part the crystals are set radially, or at right angles to the subjacent surface, and here can be beautifully traced the fusion of the apposed crystals to form a radially striated, clear, crystalline substance such as will be presently noticed as constructing the chief part of the body of the calculus. Here, too, the reddish-brown granules lie in irregular groups, and have a radial direction in correspondence with the spaces between the crystals.

More outwardly the structure again becomes non-crystalline, a homogeneous basis-substance reappearing, interspersed with brown granules; but nearly everywhere fine acicular crystals are embedded in it exactly as in the nucleus itself, and this zone, like the nucleus, is limited on the outer aspect by a non-crystalline layer of varying thickness—a basis or ground-substance with embedded granules.

To this succeeds a zone of closely interlaced prismatic crystals short and somewhat broad; this merges into a remarkable zone of similar crystals, but of which the crystalline aggregate is parted out by the brown granules into large diamond-shaped areas, which apparently represent octahedra in which secondary cleavage has taken place. The crystals occupying the octahedral spaces are tabular, and not arranged in any definite order. Here and there

are irregular masses of crystals with radial arrangement and in process of fusion; they are not strictly radial in every spot, but set sometimes in such a manner that they converge bipinnately, *i. e.* meet on a median line directed towards the centre of the calculus.

These structures are succeeded by the main body of the calculus.

Firstly comes a broad, not obviously crystalline belt of a nebulous transparent pale brown substance, with minute brown granules sparsely distributed in it. This is marked out into concentric laminæ by closer collections of the same granules; the laminæ are three or so in number, and not sharply defined.

Close examination reveals delicate indications of crystalline structure in the ground-substance; it appears as if composed of interwoven fine crystals of the same kind as those described in the nucleus.

This zone probably consists of the organic matrix of the calculus with oxalate of lime in a fine state of division, the embedded granules being probably urate, of which this calculus contains a marked quantity.

The next zone is one of very uniform thickness, colourless, transparent, and although no crystals can be discerned individually, clearly crystalline and due to fusion.

The transparent substance is marked by interrupted lines, which have in general a radial direction with respect to the centre of the calculus, but themselves deviate so far from a precise radial course that if prolonged they would intersect at acute angles.

In the deeper part of this zone are scattered considerable numbers of the brown granules before so frequently referred to, and such occur also in the rest of its extent in fair numbers though widely apart, and without interfering with the general transparency.

This accumulation of what are doubtless urate granules is to be noticed generally under similar circumstances, and is comparable to the disproportionate amount of pigment met with at and about the centre of biliary calculi. Theoretically this result may be viewed as due to the attraction of the granules, whilst still embedded in the viscid matrix, towards the centre of the calculus. The same force acting upon the crystalline material determines its radial arrangement.

To this succeeds a zone like that preceding the last, viz. a nebulous or faintly granular substance with admixed reddish-brown granules arranged on its inner and outer borders, as well as in incom-

plete and not sharply defined concentric lines in its mid-substance.

With alternations of such structure and the radially striated crystalline fusions the rest of the calculus is made up.

As previously noticed, brown granules occur in the radially striated crystalline zones; and in certain of those zones the granules are arranged in linear series, not singly, but in collections which form narrow concentric lines crossing the radial striæ of the zone: other groups of the granules occur between the coarser radial striæ themselves.

Most outwardly of all and for a wide extent the calculus consists solely of a faint brown nebulous basis-substance, in which lie the coloured granules in concentric lines of variable thickness: the most peripheral layer of all consists of the ground-substance only.

Chemical composition.—Oxalate of lime with small quantities of urate and phosphate, and much organic matter.

Section 15. *Calculus M.*—From a collection of smooth oval calculi, a few of them spiked: Museum of St. Thomas's Hospital. They were taken after death from the pelvis of the kidney, and consist of oxalate of lime with urate.

The general microscopic structure is much as that of Section 7, Calculus C. There is, however, in all the zones of radially striated crystalline material a remarkable want of perfect transparency, such as in the case of Calculus C is confined to the large crystals composing the nucleus. This is due to irregular secondary cleavage of the crystals. The nucleus is throughout crystalline, composed of much elongated octahedra, confusedly intercrossing at the centre, where there exists an intervening ground-substance of minute crystals in which they lie, but radially arranged at the periphery, where the outer ends of the crystals can be seen embedded in the next, pale brown, concentrically laminated zone. All the larger crystals are wanting in perfect transparency by reason of irregular secondary cleavage.

The nucleus is succeeded by a fairly broad zone of homogeneous or molecular basis-substance, marked into concentric zones by somewhat coarse lines of reddish-brown granules (urate). To this succeeds a broad coarsely crystalline zone, constructed like the peripheral portion of the nucleus.

The rest of the calculus is composed of alternating narrow zones of these two kinds: in some of the outer crystalline zones

DESCRIPTION OF PLATE V,

Illustrating Dr. W. M. Ord's and Mr. S. G. Shattock's paper on the Microscopic Structure of Calculi of Oxalate of Lime. (Page 91.)

Fig. 1.—*Section* 3. *Calculus O* (*a*). × 36. A small spherical oxalate of lime calculus (one of many hundreds) from the pelvis of a hydronephrotic kidney. There is no differentiated nucleus, but the more central part consists of divergent cones of doubly striated substance starting from two centres somewhat as a gigantic dumb-bell. At the centre some of the cones are divided transversely, and are so discontinuous with the rest in the section.

Fig. 2.—*Section* 17. *Calculus M.f.* × 40. Showing a double nucleolus of doubly striated substance. The rest of the nucleus is made up of crystals in which secondary fission has occurred. Peripherally the crystals are of considerable size, and set more or less radially.

The body of the calculus, of which part is shown to the north, is non-crystalline and concentrically striated.

Fig. 1.

Fig. 2.

the crystals are not elongated and radial, but minute and devoid of arrangement.

Of this section the nucleus was subsequently isolated, and washed in a watch-glass first with xylol, then with absolute alcohol, and finally with ether: its elements became dissociated, but were not otherwise altered. The murexide test subsequently showed no uric acid.

Next, the rest of the section was tested in the same way: it included concentrically striated reddish-brown zones and zones of crystals similar to those comprising the nucleus.

Here the murexide test gave a very obvious and marked evidence of uric acid. From this it is evident that the urate is contained in the brown zones, and, so far as can be judged, is limited to the granules, for were the whole zone of urate the reaction would have been more pronounced.

Section 16. *Calculus Mc* (Plate VI, fig. 4).—From the same collection.

In the centre of the crystalline nucleus are remarkably long octahedra, the spaces between which are filled with a groundwork of small uncoloured crystals.

At the periphery the long crystals are arranged radially; but all are wanting in perfect homogeneity and transparency, owing to secondary cleavage.

The body of the calculus precisely resembles that in the preceding specimens from the same case (q. v.).

Section 17. *Calculus Mf* (Plate V, fig. 2).—From the same collection.

This calculus shows a double nucleolus of two perfect spheres joined by an isthmus of coarsely crystalline uncoloured substance, wanting in transparency from secondary cleavage of its component crystals. The connecting isthmus is of the same construction as the crystalline aggregate of the nucleus in which the nucleoli are embedded; it is, however, separated from it by means of a narrow line of pale brown non-crystalline material, in which lie reddish-brown granules, and which is continuous with similar material forming the most external parts of the nucleoli.

Each of the nucleoli is constructed of beautifully transparent cones radially and concentrically striated.

There are scattered, moreover, in the coarsely crystalline nucleus small rosettes finely striated in the radial direction.

Beyond the nucleus the calculus in all ways resembles the others of the same group.

Section 18. *Calculus D* (Plate VI, fig. 2).—One of a small group of smoothly polished facetted calculi, averaging about 8 mm. in diameter.

Nucleus.—This consists of small homogeneous closely-packed spherules, which at the periphery fuse into a glassy homogeneous substance (a similar construction is shown also in Section 19, Calculus L, and in Section 13, Calculus V). This is a rare form for oxalate of lime to assume. Such spheres may be produced, however, in gelatine, and are figured in pl. v, fig. 3, of Dr. Ord's work before cited.

To the nucleus,[1] which is abruptly defined, there succeeds a pale brown zone of nebulous substance, in which lie concentric lines of fine reddish-brown granules.

In part of its circumference this zone presents in addition the fine radial striation indicative of crystalline fusion. Then follows a broader belt of radially striated crystalline substance finely cross-striated.

In the deeper part of the zone there are present dark brownish granules in considerable collections between the radially set crystals, these collections having thus a radial direction.

In parts of its circumference the crystalline substance is interrupted by non-crystalline areas of pale brown substance traversed by coarse concentric lines of dark brownish granules; but both crystalline and non-crystalline parts merge into one another by all gradations. In this zone, towards the outer part, is an incomplete line of minute crystals, packed closely without fusion or order, and where this is present the radial striation is interrupted.

This striated part is followed by a complete zone of minute crystals traversed by a thin wavy or zigzag interrupted line, of singular homogeneity and transparency, and due evidently to crystalline fusion (compare the similar substance produced by the fusion of spherules in the nucleus of the same calculus).

Next, not sharply demarcated from the foregoing, a pale brown zone in which are discernible minute interlaced crystals.

Then follows a zone like that preceding the latter, minutely

[1] The structures hereafter described do not always uniformly encircle the calculus, so that the description in certain cases is drawn up from a particular section only.

DESCRIPTION OF PLATE VI,

Illustrating Dr. W. M. Ord's and Mr. S. G. Shattock's paper on the Microscopic Structure of Calculi of Oxalate of Lime. (Page 91.)

FIG. 1.—*Section* 12. *Calculus F.* × 127. Showing a collection of large crystals of oxalate of lime, some in stellar aggregations, in the body of the calculus, which on either side consists of the usual doubly striated substance. The transition between the crystals and the wedge-shaped aggregate forming the body of the calculus to the north of the figure is readily traceable.

FIG. 2.—*Section* 18. *Calculus D.* × 40. The nucleus consists of small homogeneous spheres in process of coalescence. The most external part of the body is formed of concentrically striated non-crystalline substance, and zones of the same occur in the more internal portions of the body, in different degrees intersected by radiating tufts of crystals. The other parts consist of minutely crystalline material traversed by fine wavy lines (clearly discernible on careful inspection of the photograph). The most peripheral zone of such material consists of somewhat larger crystals.

FIG. 3.—*Section* 19. *Calculus L.* × 220. Showing a zone of oxalate of lime in the form of doubly striated cones in the midst of spherules of the same substance; the spherules are in process of coalescence, and form the nucleus and much of the body of the calculus. No effervescence ensued in the spherules on the action of acetic acid, and with hydric chloride they cleared up without effervescence, leaving an organic matrix.

FIG. 4.—*Section* 16. *Calculus Mc.* × 40. Showing portion of the nucleus in which are long octahedra of oxalate of lime in which secondary fission has taken place. At the periphery the crystals are set radially, but the secondary fissuring destroys their proper transparency. The body of the calculus consists of non-crystalline substance in concentric layers darkened by deposit of urate, especially around the crystalline structure of the nucleus.

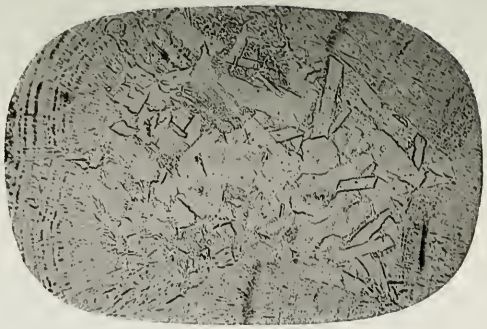


Fig. 1.

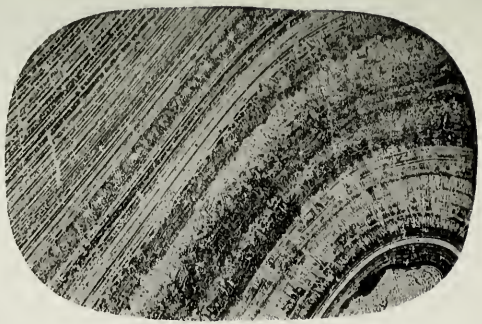


Fig. 2.

Fig. 3.

Fig. 4.

crystalline, and containing fragments of a narrow homogeneous wavy line. This is followed by a nebulous zone of the palest brown colour, finely striated in the concentric direction, and broken through in places by tufts or brushes of long crystals. The component elements of these tufts present a fine transverse striation, and this deviates in course from the concentric striation of the non-crystalline substance between, in correspondence with the direction of the long axis of the crystals, which long axes are crossed at right angles by the striæ. The striæ of this nebulous zone itself are in certain spots distinctly granular and of finely crystalline texture.

To this succeeds another zone of small intermixed crystals, in places traversed near its middle by a narrow slightly wavy line of bright structureless uncoloured material; then a broad zone of the non-crystalline pale brown material, concentrically marked by granules and finer nebulous striæ. There comes next a final belt of discrete crystals, of short prisms or flattened forms, some ill-shapen octahedra, and of larger size than those in the preceding zone; and finally a crust thicker than the rest of the calculus together, of the usual concentrically striated non-crystalline material.

On the deep aspect of that one of the confusedly crystalline belts which is nearest the nucleus it is instructive to notice the mode of termination of the subjacent crystalline columns of the radially striated zone which lies on its inner aspect; in some situations the outer ends of these columns are very distinct and produce a crenate edge, the divisions of which correspond with the radial markings in the zone: the edge represents what at one stage was the free surface of the calculus, the mode of formation having after this period ceased and been changed for another.

Chemical composition.—No phosphate; the murexide test shows no urate.

Section 19. *Calculus L* (Plate VI, fig. 3).—A minute spherical calculus, chiefly white in section, composed of oxalate of lime; passed after severe renal colic of several days' duration.

Nucleus.—Composed of beautiful bright spherules, homogeneous, without visible structure; towards the periphery these have fused into a glassy homogeneous substance, in which there occur short winding fissures where the coalescence has failed to take place. (A similar structure is previously described in Section 18, Calculus D, and it occurs in the body of Section 13, Calculus V.)

To this succeeds a doubly striated narrow zone composed of stunted cones of the usual character; or in places of fan-like tufts of comparatively coarse crystals, in which a finer secondary divergent and a transverse striation are present. This zone is incomplete, and here and there are isolated cones which lie in the midst of the spherular aggregate, the incomplete zone being succeeded by material similar to that composing the nucleus.

The outer parts of the calculus are wanting.

The sections were subsequently examined chemically. Acetic acid produced no result on the spherules: pure hydric chloride led to solution of the inorganic substance without effervescence, an animal matrix being left.

Uric acid had been noticed in the urine before the passage of the small calculus.

Section 20. *Calculus I.*—A crystalline calculus with sharp crystalline surface, and about the size of a small pea.

Pickings from the surface mounted in a cell of Canada balsam show in places perfect octahedra though flattened; some are of comparatively small size, others very large; the smallest are considerably larger than the forms common in urine. In most of the crystals lie multitudes of minute deep reddish-brown granules: these granules are for the most part arranged in planes parallel with those of the crystal, in which they seem to mark out coarse but accurately parallel laminæ. Some of the crystals are distinctly tabular with six sides. They cohere into irregular groups without intervening material.

Chemical composition.—No carbonate; a trace of iron; the murexide test shows no uric acid.

Section 21. *Calculus Q.*—A small dumb-bell shaped calculus not more than 3 mm. in greatest diameter.

Nucleus.—Crystalline.

Body.—Of the usual character, viz. doubly striated crystalline substance.

The specimen, though showing nothing new in other respects, is valuable in this, that in addition to the faint general brown coloration of the general substance of the body there occur groups of distinct crystals of brilliant orange pigment, derived doubtless from blood. This pigment lies in the nucleus as well as in the crystalline fusion of the adjoining portion of the body. The pigment takes chiefly the form of long fine needles in groups

of different numbers. In places these are parallel with and contained in the radiating crystalline fusion, probably between its component elements, and due to crystallisation having occurred from effused blood. In other places in the crystalline nucleus, in addition to such bunches of slender orange crystals, there occur associated with them comparatively large similarly coloured crystals of rhombohedral form, singly and in clusters. The crystalline substance of the body generally is of a pale reddish-brown colour. Oxalate of lime "gravel" passed from the bladder.

FIG. 7.

A crystal of oxalate of lime passed with others in the urine, and of sufficient size to be visible to the naked eye, "oxalate gravel." The figure is magnified 40 times.

Except that the crystals are not sharply angular, they are much like those artificially detached in Section 20, Calculus I.

Many of the masses are compound; a polyhedral pattern is discernible, the exterior presenting angular elevations, or being highly undulatory.

The forms presented by the nuclei of calculi composed of oxalate of lime.

The nucleus may be classed under the following chief forms, upon each of which we may make general observations.

1. Large transparent crystals of oxalate of lime (Section 8, Calculus K).

2. Similar crystals rendered more or less opaque by secondary cleavage (Section 7, Calculus C).

3. Minute crystals not of octahedral form (Section 14, Calculus A).

4. Rosettes or striated conoidal or fan-shaped elements like those which more outwardly construct by their regular juxtaposition the body of the calculus (Section 12, Calculus F).

5. Spherules in process of coalescence (Sections 18, 19, Calculi D, L).

These forms may occur in various combinations. Most commonly rosettes[1] are mingled with the crystals. The former are of different degrees of fineness in regard to their component elements, and vary considerably in size; the larger of them may be concentrically striated. Or fan-shaped elements presenting fine radial striation, and, it may be, concentric as well, may occur in conjunction with crystals of medium or larger size, and with or without rosettes, to make up the nucleus.

1. The nucleus of large transparent crystals of oxalate of lime.

It is of interest in regard to this form to note that similar large octahedral crystals are met with in the urine in rare cases, constituting one of the forms of "gravel." In such gravel either single crystals or groups of such may be found, as in the parallel case of uric acid. Such a nucleus appears to be a chance aggregation of crystals cohering without colloid. We know of no specimen showing that this simple construction ever obtains for any long period. We have never seen any calculus thus constituted larger than a bean. Such a nucleus is succeeded by the modified forms of oxalate noticed in the general remarks on the structure of the body as distinguished from the nucleus of the calculus.

This is due doubtless to the fact that the presence of such a calculus leads to the admixture of colloid with the urine by reason of the inflammation in the urinary passages which it excites; there occurs an increased secretion of mucus, and an inflammatory exudation from the vessels of the inflamed mucous membrane of that portion of the urinary passage in which the calculus lodges.

2. A nucleus of large crystals rendered more or less opaque by secondary cleavage.

This secondary cleavage indicates probably the action of colloid in an early stage and slight degree.

3, 4. The nucleus of minute crystals.

The crystals in such nuclei are to be regarded as tablets. This, although not traceable in the particular nucleus described (A), is plain in certain similarly constructed zones in the body of oxalate calculi, where minute tabellar forms are visible amongst others which are probably minute tablets viewed edgewise so as to appear more or less needle-shaped. Such forms are producible in large numbers experimentally when oxalate of lime is deposited in

[1] By a rosette we imply a compound form resulting from a radial disposition of elements, but flattened or discoid, and not spheroidal in figure.

gelatine. And in such experiments, together with these minute tablets, there may occur spherular aggregates of similar crystals of various degrees of coarseness, some small and comparable to the crystalline spherules present in the nucleus of calculi constructed of a conglomerate of similar minute crystals.

The crystalline spheres, in short, which occur in conjunction with the minute tablets, are comparatively small, and of similarly fine crystals. The coarser rosettes, or spheres of oxalate of lime produced artificially in colloids, are precisely like those often met with in conjunction with the crystalline forms of larger size, such as constitute the elements of nuclei 1 and 2.

The various elements of such a mixed nucleus as that last mentioned may be found in a single experiment made with a colloid; associated with octahedra (normal, elongated, and gigantic), with tablets, unfissured and in process of fission, there may be found coarsely crystalline spheres and rosettes of various degrees of complexity.

In the simplest phase the rosette, artificially produced, consists of four elements, somewhat like a Maltese cross. From such simple forms gradations are traceable to the more highly complex, which result from further fission directed from the margin to the centre.

The rosettes or flattened forms are related to fissure of tablets; the crystalline sphere, or the spherical aggregate of crystals, to the regular octahedral crystal.

The rosette may be imperfect, *i. e.* wanting in part of its circumference, so as to produce a fan-like aggregate.

The transition between rosettes and the fan-shaped aggregates appears in the asymmetrical forms of the first, of which the elements on one side may be prolonged far in excess of those around the rest of the circumference.

5. The presence of proper spherules of calcium oxalate in the nucleus is exceptional; we have observed it only twice out of a large number of preparations.

The spheres alluded to are, as observed in our preparations, homogeneous, glassy, and without the radial (or concentric) striæ which occur in the two forms already alluded to as "rosettes" and "crystalline spheres."

The structure of the body of calculi of oxalate of lime.

In considering this it will be most natural to proceed from within

outwards. In all cases the body arises in cones of crystalline substance sharply pointed at their inner ends, and diverging from the outer surface of the nucleus. These cones as traced outwards present no interspaces, and they can nowhere be followed individually for any great distance. This is evidently due to the fact that their sides, which are deeply fluted, lie in perfect apposition, or are sutured together. The general contour of the cones may be deduced from the appearances presented by oblique or transverse sections. When seen in these ways they are of extremely irregular outline, deeply sinuous or jagged. In all cases they present in longitudinal section a double striation—radial, and transverse or circumferential, although one marking only may be present at and about the apex, viz. the divergent or radial.

The radial striation appears as delicate interrupted or incomplete lines which diverge in correspondence with the increasing width of the cone; they cannot be traced continuously from apex to base, but are comparatively short, and terminate at various distances; neither do they diverge with mathematical exactness, but are so directed that if prolonged they would intersect at acute angles in various directions. These lines indicate that the cone is constructed of a series of somewhat narrow closely apposed rod-like elements, and the irregularity of the sides of the cones as studied in oblique or transverse section results from the same construction.

In some calculi such a doubly striated crystalline substance resulting from the lateral apposition and suturing of such structures is traceable to the very surface which may present a series of blunt or rounded points coinciding with its different elements.

The fact that the cones can never be traced individually for a long distance suggests that their axis is not straight; they appear rather to take a twisted or spiral path. Such an idea is suggested by the construction of large dumb-bells of oxalate of lime both natural and artificial: in these the leaflets or tabellæ are constantly found twisted, somewhat as the petals in the contorted æstivation of a flower, the direction of the rotation being, of course, reversed on each side of the centre; the crystalline fibres partake in the contortion like the strands of a partially twisted rope. It is obvious that if such a dumb-bell were cut longitudinally none of its fibres would be traceable continuously from its centre to the surface.

The radially striated cones present a second striation, viz. a

transverse, or one concentric with the centre of the calculus. In its typical form this is exceedingly delicate, and the appearance may aptly be compared with that of striped muscle-fibre. The lines are close, devoid of visible granules, sharply defined, and remarkably parallel. They are of the same nature as the concentric striæ seen in certain of the artificially produced spheres; but in neither case can we offer any satisfactory explanation of their production. It need scarcely be stated that in cross-sections of the cones this concentric striation is not to be seen. Sometimes the whole of the body of the calculus is composed of such cones so closely applied by their sides as to form in sections a continuous zone of clear crystalline substance, striated both radially and concentrically with respect to the nucleus of the calculus. In many cases, however, there occur in addition zones of another substance alternating with those just described.

Sometimes, and very commonly in the smooth variety of calculus, the second substance constitutes the chief portion of the outer part of the concretion. In its typical form this substance is non-crystalline, and consists of a molecular basis in which lie concentrically arranged lines of distinct granules, dark reddish brown in colour. These lines vary in thickness and density; and individually are not always of uniform thickness.

We regard the nebulous basis-substance as oxalate of lime combined with the colloid which forms the organic matrix of the calculus, the power of the colloid having obliterated all crystalline structure. The brownish granules we regard as urates embedded in the matrix during the growth of the calculus.[1]

That this view of the essential nature of the basis-substance is correct is supported by the fact that such zones present no sharp line of demarcation from the radially striated crystalline substance first described; every degree of radial striation is to be observed in such zones, sometimes faintly indicated, sometimes distinctly pronounced.

Such zones are probably, moreover, closely related to another or second variety, in which a very minute crystalline structure is discernible.

The minute size of the crystals, when visible in such substance, indicates the action of colloid added to the urine, but colloid acting

[1] When the calculus is at all largely composed of such substance the murexide test shows the presence of urate. That the test does not in all cases do the same when the calculus contains such material microscopically, depends probably on the minute quantity present.

with less power than in the case where such a structure is merely molecular, although even in the latter case the molecular appearance may be, theoretically, due not to the presence of minute spherical elements, but of crystals.[1]

In zones which show a transition between the crystalline and non-crystalline forms it may commonly be observed that the coloured granules (urate) are present in chief amount at the deeper, *i. e.* the inner parts, or those on the aspect of the zone proximal to the centre of the calculus.

This is possibly indicative of the attraction of the urate granules towards the centre whilst in the colloidal basis. A corresponding arrangement exists in those zones of biliary calculi which inter-

[1] It is interesting to observe that a substance of similar characters may be artificially produced, in which it is clear that crystallisation is concerned. If a saturated solution of sodium phosphate is added to a saturated solution of urate of ammonium, potassium, or sodium, both being previously heated to a temperature of over 100° F., the fluid becomes on cooling quite gelatinous, like freshly precipitated silica, so that the test-tube may be completely inverted without any escape of its contents. If the substance in this stage is examined under the microscope it presents no visible crystalline elements, but consists of a very delicately molecular ground-substance with embedded masses of spherical form, in some cases not very perfect in outline, in others perfect, where the forms are relatively small. In the same preparation, after a short space of time, the same ground-substance is found to be gradually replaced by crystalline elements which take the shape of fine curved needles, irregularly and sparsely scattered. At the same time the spheres undergo change; in their outer portion fine spicules make their appearance, and increase in number until the whole sphere bristles with needle points, rarely straight, but rather matted together, though always with their free ends directed more or less radially. It is apparent that in this case the urate of soda is at first precipitated in a colloidal form, and that this colloid acts upon its own crystalline material so as to determine its deposit in spherular form, the whole being ultimately broken up into crystals when the period of colloidal existence comes to an end.

It has long appeared to me probable that every chemical substance in passing from solution to the solid form, or in being born afresh, passes through a stage comparable to the colloid. I venture to propose the hypothesis that what is called the "nascent stage" of various substances when set free from combinations is really a colloidal one, in which they offer a readiness to combine with other substances which they do not present when they have passed into a further *quasi*-crystalline stage. This may be seen in precipitated oxide of iron and in silica, to name two very different substances. I venture to think it would apply to ozone and to many gaseous and liquid substances which at the moment of chemical dissociation from other substances are known to have remarkable readiness for fresh combination. (W. M. Ord.)

vene between the homogeneous peripheral laminæ and the strongly crystalline centre: two substances of different crystalline tendency, viz. the cholesterine and biliary pigment, separate after a time, though precipitated together, and during this process of separation the pigment is attracted towards the centre, whilst the crystalline material coheres at the periphery.

The structure of the calculi as a whole, and the relationship of the microscopic to the macroscopic forms.

One of the most interesting of the results offered by the structure of the calculi above discussed is its likeness to the microscopic spheres and crystalline aggregations which may be artificially produced, or occur as natural formations. Among natural products the urinary granules of the snail offer perhaps the most parallel examples.

Each form of calculus, however, is represented amongst the microscopic forms; besides the perfect sphere, with smooth surface, there are met with forms constructed of crystalline elements disposed radially about a centre, and of which the outer free ends give a sharply spinous character to the whole. The essentially crystalline nature of the most perfect sphere is shown in its radial striation; and no sharp line of division can be drawn between the spherical crystalline aggregates and perfect spheres.

The smooth hemp-seed calculus, then, is in its simplest form (in which it is devoid of a differentiated nucleus) comparable to the simple typical smooth-surfaced microscopic sphere. We do not meet, however, with calculi which present in microscopic section no concentric striation in conjunction with the radial, whereas in the microscopic sphere the concentric striæ may be wanting, or if present may be numerically few.

The smooth variety of calculus in which there are present zones of crystalline and non-crystalline substance is closely represented in certain of the microscopical spheres.

In the urinary granules of the snail several varieties of internal structure are to be observed. Some are striated only radially, though of as large a size as others; some are striated both radially and concentrically, the concentric striæ being less close than the radial which they cross, and terminating short of the centre: the concentric lines often cease abruptly, so as to define a nucleus of less transparency and striated only in the radial manner; but others, resembling the form of calculus under notice, present a

more transparent and structureless peripheral zone or crust, sharply separated from the radially striated more central part. We have observed almost similar forms to the last in urate deposited in the mucus of the renal pelvis of a child.

In the case of biliary calculi this double form of a single substance is particularly well marked; towards the centre of the calculus the substance will present a distinct radial striation, and peripherally a uniformly granular character where the cholesterine is intimately mixed with biliary pigment.

Again, the less tuberculated form of mulberry calculus, or that which may arise without the interposition of secondary crystalline nuclei, is accurately represented in certain of the microscopic forms of spherular oxalate of lime. Such spheres may, in short, be compound or composite in structure, and present a nodular surface, with a corresponding series of coarser radial striæ which mark out the sphere into closely applied conical processes. The dumb-bell itself is a closely allied form, two elements being here concerned in the production of the composite structure; in the next simplest, four; and so on with increasing complexity.

Further, the microscopic calculus composed of distinct crystals is represented in artificially produced forms by collections of crystals commonly arranged with perfect regularity about a centre, and so of more regular construction than the pathological concretion: in calculi of other composition encrusted with crystalline oxalate of lime, however, the crystals of the latter substance may be arranged with complete radial precision on the more central part of the calculus.

Finally, in the microscopic forms artificially produced may be seen the first stages in the formation of a distinct "body," such as occurs in the calculi.

Upon the exterior of dumb-bells or more complex compound forms there may be regularly arranged smaller elements of spheroidal figure with rounded angles, but separated by distinct intervals from one another. Such represent the crystalline cones so frequently referred to as composing the body of the most perfect forms of calculi of oxalate of lime (see Fig. 6, p. 97).

The coloration of calculi of oxalate of lime.

By Wollaston and Marcet the brown colour which such calculi present was supposed to be due to blood. That blood occurs ad-

mixed is undoubted. In one of the sections (Q) described in this communication brilliant crystals of hæmatoidin (an iron-free product of hæmatin) are present in the nucleus and the body of the calculus.

The presence of iron, demonstrable in many of the specimens, can in fact be explained by common hæmorrhage; but as normal urine contains small quantities of iron, in as yet an unknown state of combination, this does not exhaust the question.

As observed in urine, crystals of oxalate of lime are invariably devoid of colour. The same is true of the calculi, *i. e.* the proper crystals, whether in the primary or secondary nuclei, are uncoloured, and so are the large crystals of oxalate of lime that are sometimes easily recognisable on the surface of calculi of other chemical composition.

It is important to observe that the coloration is not limited to such non-crystalline zones as contain embedded granules of urate, and is certainly not due to the presence of the latter. It may be diffused through the doubly striated substance of the body even where this is most typical; and the molecular basis of the "non-crystalline" zones, in which the concentric lines of brown granules lie, is also itself of a pale brown colour. It varies in degree in different cases, and in different zones of the same calculus: sometimes it is, in thin sections, hardly recognisable.

The typical coloration is present in the intestinal calculi of oxalate of lime met with in herbivora. The usual macroscopic structure of these (of which there are excellent examples in the Royal College of Surgeons, London) is like that of the smooth variety of urinary calculus: they are composed of a compact substance both radially and concentrically striated; and they exhibit the characteristic dull brown colour, varying in depth in different zones, that is observed in the smoother varieties of the urinary forms. One of these specimens (W 4, 'Catalogue of Calculi,' Coll. Surg.), in composition nearly pure oxalate of lime, has a periphery of crystals which project at the surface, as in certain examples of urinary calculus described.

These considerations lead to the conclusion that the coloration of the urinary forms is due not to urinary pigment, but probably to hæmoglobin; and this coloration obtains not in connection with the perfect crystals but the crystalline fusions constructing

the body of the calculus and the molecular zones, in some of which a minute crystalline structure is discernible,—indeed, there is no sharp line of division between the two.

As to the organic matrix present in all calculi of oxalate of lime, its existence has been long known; and its nature has, most recently, been treated by W. Ebstein in his work on urinary calculi.

Notice of observations by other authors. — Beale ('Urinary Deposits,' 3rd edit., 1869) has observed cohering dumb-bells in the urine, and similar collections in the kidneys in the urinary tubules.

In pl. xi, figs. 12, 13, op. cit., he represents minute concretions of oxalate of lime from the case of a man who was passing dumb-bells of oxalate of lime and crystals of uric acid. One of them is a minute compound calculus formed by an aggregation of spheroidal elements which are doubly striated.

In fig. 12 he represents a microscopic calculus, doubly striated, without differentiated nucleus: to the exterior there adhere a few dumb-bells.

Dr. Vandyke Carter ('Urinary Calculi,' 1873) studied urinary calculi by examining fragments of the nucleus and surrounding layers with the aid of chemical reagents. He describes in oxalate of lime calculi (1) granules (so appearing under comparatively low magnification); (2) crystals; (3) rounded, ovoid, and dumb-bell forms (the simplest form, a minute, clear, rounded or oval crystal;[1] (4) spheroids (doubly striated).

When of large size the last named "with their *débris*," may, he states, wholly compose the pale, loose, gritty deposits of oxalate of lime which are sometimes found in calculi.

He imagines that the spheres arise in the "clustering and blending of the dumb-bell crystals, attended with deposition on the surface of the aggregated particles." The tuberculated character he supposes due to the arched or wavy course of incipient laminæ corresponding to the contour of subjacent and enclosed spheroids.

He describes crystals occurring in the form of rhomboid plates or rhomboid prisms, in scattered groups, or disposed in one or more layers, which he regards as oxalate of lime from the fact that

[1] In regard to group 3 the author states that such forms are especially associated with uric acid laminæ and layers of urates.

Dr. Ord had obtained such crystals in his experiments made with gelatine.

W. Ebstein ('Die Natur und Behandlung der Harnsteine,' 1884) figures (Taf. iii) a thin section of a small portion of the body of a calculus of oxalate of lime, showing its radial and concentric striation.

He represents a certain number of more or less spheroidal bodies, yellowish in colour, embedded in its substance; these he suggests are calcified epithelial cells from the urinary tract. We have not ourselves met with similar bodies in any of our sections, and can offer no opinion on their nature, though we may observe that both Beale and Carter have described the presence of dumb-bells of oxalate of lime embedded in calculi of uric acid.

W. Ebstein ('Experimentelle Erzeugung von Harnsteinen,' 1889) has experimentally produced urinary calculi in dogs and rabbits by the administration of oxamide.

The excretion appeared as sand in all parts of the urinary track; in the renal pelvis the concretions attained a size of 2 cm. in length and 7 mm. in thickness. Like calculi of oxalate of lime, they had a warty surface, and were in section doubly striated.

The presence of an organic matrix, giving the reaction of albumen, was demonstrated by digesting the calculus in distilled water at 80°—90° C.

Dr. George Harley ('Proceedings of the Royal Society,' 1889), in regard to the structure of crystalline pearls, describes them as showing basalt-like prisms radiating from the centre to the circumference, and as presenting concentric markings as well: the prisms he describes as striated, and as branched and interlacing; but he imagines that the striation resides in the animal matter which he conceives to surround each individual prism.

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W. Ebstein and *Nicolaier.*—"Ueber die Experimentelle Erzeugung von Harnsteinen," 'Verhandlung des Congresses für innere Medicin,' p. 268, Wiesbaden, 1889.

May 7th, 1895.

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8. *Hydronephrosis, due to a stricture, apparently congenital, at the upper part of the ureter, at the point of its exit from the pelvis of the kidney.* (*Card specimen.*)

By W. W. Ord, M.D.

Taken from a boy aged one year, who died twenty-four hours after admission to the Victoria Hospital for Children of extreme anæmia, the cause for which could not be discovered. The other kidney was normal, except for hæmorrhages similar to those in the specimen; there were a few other hæmorrhages of a similar character elsewhere. The urine contained a small quantity of albumen. That in the dilated kidney was slightly turbid, and contained pus cells. *February 9th*, 1895.

9. *Primary carcinoma of the ureter.*

By Arthur Francis Voelcker, M.D.

[With Plate VI A.]

The specimen was obtained from a man aged 68 years, who was admitted into the Middlesex Hospital under the care of Dr. Cayley.

The patient stated that he had never been laid up before except on one occasion, two years previously, when he had an attack of influenza.

Four months before his admission to the hospital he noticed a discoloration of his urine.

He was seen on December 7th, 1894, by Dr. Pringle in the out-patient department at Middlesex Hospital, and noticed to have œdema of the left ankle. The urine was acid, sp. gr. 1014, and contained a clot of blood. The patient complained of pain across the loins and of nausea, and was unable to take solid food. He was admitted under the care of Dr. Cayley, and it was noted that the liver was tender, nodular, and enlarged, the liver dulness reaching to within two inches of the umbilicus. In the left iliac fossa there was felt to be some resistance to palpation.

A fortnight after admission much blood was noted in the urine, and the patient had lost $9\frac{1}{2}$ lbs. in weight in the last three months. Three weeks later the liver had enlarged, so that it now reached below the umbilicus; it was very tender. The patient had lost $14\frac{1}{2}$ lbs. in ten days. The patient died nine days later. There was no blood in the urine during the last week. At the autopsy the body was fairly nourished, and there was slight jaundice. Both legs were œdematous, the left more so than the right. The transverse colon was adherent to the liver, which was much enlarged, and weighed 8 lbs. 14 oz. The left lobe of the liver was almost entirely infiltrated by a pale, rather soft new growth. There were numerous nodules of new growth in the right lobe. The nodules were not umbilicated. The gall-bladder was natural.

The left kidney was small, only about one third the size of the right one. It showed distinct hydronephrosis. The right ureter was dilated and thickened. In the lower two inches of the left

ureter was a new growth in the walls of the ureter, which projected into the lumen of the tube in the form of delicate villous processes which were covered with blood. On the outer side of the ureter was a mass of new growth the size of a cherry, which was adherent to the pelvic brim.

The bladder contained a small blood-clot free in its cavity, and projecting from the vesical end of the left ureter was another small blood-clot. There was no new growth in the bladder.

The right kidney and ureter were natural. The lymphatic glands along the left side of the aorta were enlarged, being infiltrated with new growth.

One small nodule of new growth was present in the upper lobe of the right lung, but no growths were found in the testicles, vesiculæ seminales, rectum, or alimentary canal. The aorta was markedly atheromatous, and there was old adhesive pericarditis, with some hypertrophy of the left ventricle of the heart.

Microscopical examination of the growth in the left ureter showed it to be a villous carcinoma. A delicate branching stroma of nucleated fibrous tissue is clad with numerous layers of large pyriform epithelial cells having large nuclei. The growth invades the muscular layer, and shows as a fibrous alveolated stroma containing epithelial cells.

The secondary growths in the liver have a structure very similar to that in the ureter, the epithelial cells clothing the branching stroma having a distinctly pyriform or kite-shaped form.

The specimen is a rare one, and the 'Transactions' of this Society do not contain the record of any similar case, although there are records of secondary deposits of sarcoma in the ureters. I have been unable to find any reference to any case of primary carcinoma of the ureter.

In the twenty-first volume of the 'Transactions of the Pathological Society,' Dr. Murchison reported a case in which villous tumours were found in the pelvis of each kidney, and also in the bladder at the orifice of each ureter; and Mr. Bland Sutton calls attention to this case as a possible example of local infection. When we consider the similarity of the epithelium in the ureter and bladder, we cannot be astonished at the form the new growth has taken, and I should like to call attention to a point I have noticed in a case of a carcinoma of the cervix uteri which was invading the bladder. In this case projecting into the bladder was

DESCRIPTION OF PLATE VIa,

To illustrate the microscopical appearances present in Dr. Voelcker's case of Primary Carcinoma of the Ureter. (Page 133.)

Fig. 1 is drawn under a low power ($\frac{3}{4}$ inch) to illustrate the general arrangement of the growth. It shows numerous villous processes on the surface of the ureter, and the growth infiltrating the muscular coat.

Fig. 2 is a portion of one of the processes, showing the pear-shaped epithelial cells covering a nucleated fibrous stroma. ($\frac{1}{6}$ inch.)

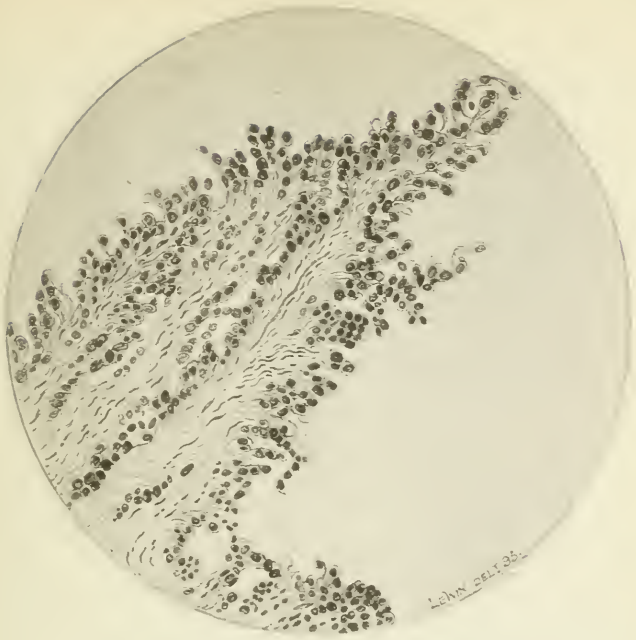

Fig 1.

Fig. 2.

a villous growth which had all the microscopical characters of a simple villous tumour, while the uterine growth was a malignant adenoma.

A striking feature in this case of primary carcinoma of the ureter is the large amount of secondary deposit in the liver, for it is rare to find secondary deposits in the liver after primary malignant disease of the bladder. In the last eleven years, at the Middlesex Hospital, there were fifteen autopsies made on cases of primary malignant disease of the bladder, and in none were there secondary deposits in the liver.

The points which make me regard the disease as primary in the ureter are—

i. The nature of the growth, and its similarity to primary villous carcinoma of the bladder.
ii. The want of any microscopical evidence of infiltration of the ureter from outside.
iii. The similarity of the secondary growths in the liver with the primary growth.
iv. The marked infiltration of the retro-peritoneal lymphatic glands on the left side only, and the marked infiltration of the left lobe of the liver.
v. The clinical history points to hæmaturia as the first sign of anything wrong.

It is noticeable that the left kidney is smaller than the right, and it is possible that a calculus may have caused some injury to the lower end of the left ureter, and that the malignant growth has developed at the site of this injury, but of this there is no evidence. *February 4th*, 1895.

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10. *Recto-vesical fistula due to tuberculous ulceration.*

By Stephen Paget.

This specimen was taken from the body of a man who died suddenly, the morning after his admission to the West London Hospital, on September 3rd. The history of his case is as follows:

A. B—, aged 50, but looking much younger: had been in the habit of taking a good deal of alcohol. His lungs had for a long

time been unsound, and he had suffered with hæmoptysis, and had latterly been losing flesh. About a year ago he had been under treatment for "obstruction of the bowels." Nine months ago he had been treated for "chronic cystitis." It is not certain when fæcal matter first made its appearance in his urine, but for some months his urine had been "suspicious." He was said to have a weak dilated heart.

He was admitted at once. The urine he passed that evening was heavy with large flakes of soft fæces, and was of a turbid brown colour and fæcal odour. No examination was made of him that evening, and he went to bed feeling as well as usual. At 7 the next morning he was found to be suddenly collapsed, but still conscious, and able to swallow. He quickly sank, and died a few hours later, with signs of primary failure of the heart's action.

Post-mortem.—Lungs: both lungs were affected with advanced tubercular phthisis. They were also adherent, and emphysematous in parts. There were two large tubercular cavities in the left upper lobe. *Heart:* advanced fatty degeneration; mitral valve incompetent. *Liver:* advanced fatty degeneration; advanced miliary tuberculosis.

The spleen was healthy. The kidneys were soft and congested, but showed no signs of tubercular disease.

Miliary tubercles were scattered over the lower part of the anterior wall of the peritoneal cavity. The upper and lateral parts of the bladder were fixed by old adhesions to the abdominal wall.

The right testicle was half destroyed by a tubercular abscess; the vas was greatly thickened.

Between the back of the bladder, close to the apex, and the rectum, about four inches up, there was a tortuous sinus. The vesical opening admitted a No. 10 English catheter; the rectal opening was rather larger and more ragged. The sinus ran a very crooked course through the thick, dense inflammatory tissue surrounding the parts. Another sinus, about four inches long, ran upward outside the front part of the rectum, opening into the rectum both above and below.

The rectum above the recto-vesical fistula was dilated. About the level of the fistula it was somewhat contracted; and here it was compressed by a tough mass of glands, broken down and matted together in dense scar-tissue, lying behind the rectum.

October 16*th*, 1894.

11. *Uterus didelphys.* (*Card specimen.*)

By Arthur Voelcker, M.D.

The specimen shows a double vagina, double cervix and body of the uterus. The Fallopian tubes and ovaries are natural. The recto-uterine pouch of peritoneum shows a median ridge dividing it into two lateral pouches. There were no other errors of development observed.

From an unmarried woman aged 28, who died from peritonitis following the perforation of a gastric ulcer.

November 6th, 1894.

VI. DISEASES, ETC., OF THE ORGANS OF LOCOMOTION.

1. *Specimen of osteitis deformans in which lengthening of bone is seen to have taken place.*

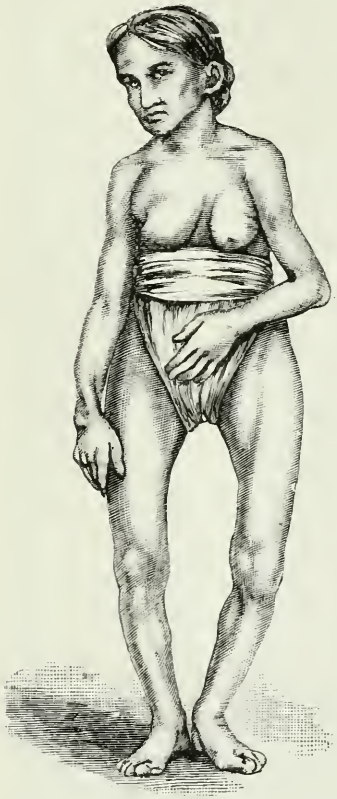
By H. H. Clutton.

The case was originally recorded in vol. xxxix of 'Path. Soc. Trans.,' 1888, p. 259, under the following title: "Case of Osteitis Deformans showing a want of symmetry and lengthening of some of the bones." The patient was in 1888 a woman of sixty-five years of age and was last seen alive in the autumn of 1894, when there was observed to be very little alteration from the condition described in 1888, except that the right humerus was just beginning to show a little curvature, and the right radius was still increasing in size. She died at home in January, 1895. The right upper extremity was removed after death with great difficulty, as no *post-mortem* examination was allowed. The specimen, which consists of the right humerus, radius, and ulna, is now shown to confirm the statement which was then made, namely, that the bones affected with this disease may be increased in length as well as in thickness.

The history, the original description, and the drawing (Fig. 8) of the patient during life all show that the case was one of osteitis deformans. The full length drawing (Fig. 8), which was executed in 1888 from a photograph, is introduced merely to show that the case was one of osteitis deformans, and requires no special description. Figs. 9 and 10, also taken during life in 1888, illustrate the unsymmetrical character of the disease in the upper extremities. It will be noticed that the left humerus is curved; it was also felt during life to be much thicker than the right. In spite of the curvature the left humerus, in measuring along the arc of the curve, was half to three quarters of an inch longer than the right. Of the two forearms the right only is affected, and is described in the following paragraph. Fig. 11 is the *post-mortem* specimen of the

right forearm shown to the members of the Society in May, 1895. The following description of the humerus, radius, and ulna was drawn up by Mr. Shattock for the museum of St.

FIG. 8.



Thomas's Hospital, where the bones are now placed:—"The right humerus with the radius and ulna from a woman who was the subject of osteitis deformans. The humerus presents scarcely any signs of disease except at the lower end, where the shaft is slightly thickened and less smooth than natural from osteoplastic periostitis. The olecranon fossa, which is deepened by the increased thickness of the bone, is rendered irregular by osseous outgrowths; the thickening of the bone is shown also by the formation of a distinct fossa above the capitellum in which the head of the radius has rested,

the elbow having been kept in the semi-flexed position. There is a slight abnormal curvature of the bone forwards, the part actually bent being the upper half of the shaft.

"The ulna (Fig. 11) is perfectly normal and quite straight; the

Fig. 9.

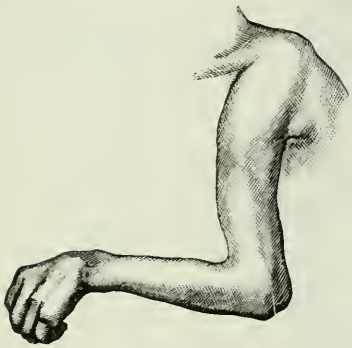
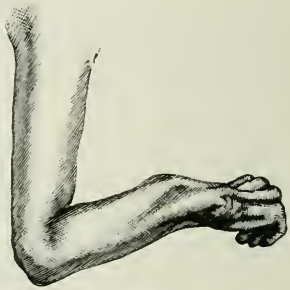


Fig. 10.

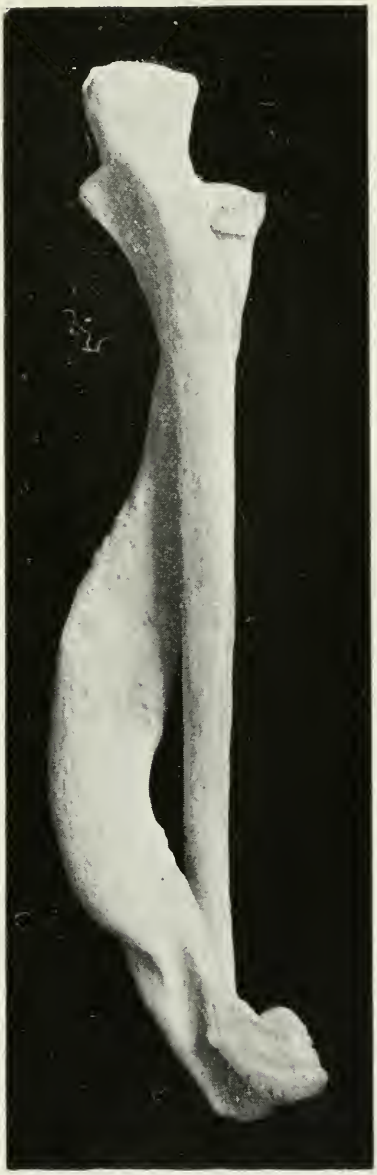


radius is extensively diseased. For its entire length the latter is increased in circumference, and irregular on the surface from chronic inflammation, the grooves for the extensor tendons being very deep. The most noteworthy feature, however, is the remarkable **S**-like curvature of the bone, due to its increase in length by the side of the unaffected ulna. The extreme length of the ulna from the olecranon to the point of the styloid process is $8\frac{3}{4}$ inches; that of the radius taken along its curvature is 9 inches.[1] When the forearm is held with the ulna vertical, the lower articular surface of the radius looks downwards and outwards, the elongation having affected the outer wall of the shaft to a greater extent than the inner. The bones of the forearm are themselves in a position of hyperpronation, the inferior extremity of the radius lying altogether behind that of the ulna."

The unsymmetrical character of the disease in the upper extremities in this case has enabled a comparison to be made as to the length of a bone. Without this opportunity it would be almost impossible to prove that lengthening could occur in this disease. The diminution of stature so commonly seen is probably

[1] Measured in this way, from the olecranon, the ulna should be at least an inch longer than the radius; whereas in this specimen the radius is the longer of the two bones.

FIG. 11.



Bones of right forearm, of which the radius alone shows evidences of osteitis deformans with marked lengthening. See further description in the text, p. 140.

entirely due to the stooping posture from curvature of the spine, so that if lengthening of the tibiæ and femora did take place in the ordinary symmetrical variety of the disease, it would be more than counterbalanced by the sinking of the spinal column.

The specimen is also interesting in another way, as was shown in the previous record of the case,—namely, that single bones may at times be affected. The patient showed undoubted evidences of osteitis deformans, but such a radius as this might not otherwise be accepted as due to this disease. And yet one must suppose, with such evidence before us, that some single bones affected in this way are of the class described even when the general characters are not so well distributed.

2. *Acute septic epiphysitis.*

By Stephen Paget.

The case was that of a boy aged 13, admitted to the West London Hospital on August 23rd, 1894, having fallen thirty feet. He had his scalp torn half off his head, and a double compound fracture of the lower jaw, and contused wounds on both legs. His general condition was so bad that it was impossible to take any immediate measures to ensure union of the fractured jaw. On the 26th his temperature rose to 102°; and on the 27th the left thigh was swollen, hot, and painful, with dilated superficial veins, and some effusion of fluid into the knee-joint. An incision was made down to the outer aspect of the femur, but no matter was found. Signs of septic absorption appeared (delirium, wild excitement, tympanites, temperature 103°, respirations 32, some dulness, and harsh breathing on right side of chest), but no diarrhœa, sweating, or rigors. The scalp wound was healed: there was suppuration round the fragments of the lower jaw. On the 30th the thigh, which had for a day improved after incision, was again incised; a quantity of pus and blood was let out, and a large irregular cavity was found, in which the front of the shaft of the femur lay bare of periosteum.

Two days later he had swelling of the left parotid; this was at once incised, and healed without suppuration. His general con-

dition became slightly improved; but bedsores formed, in spite of the most careful nursing, and there were signs of slight broncho-pneumonia. Then diarrhœa set in, with perspirations, restlessness at night, rapid loss of flesh, and constant high temperature; and on September 18th the thigh was amputated, as the knee-joint was plainly becoming disorganised. The interior of the femur was found infiltrated with pus almost as high as the neck of the bone: the knee-joint contained about two drachms of pus, and its cartilages were slightly eroded. The lower epiphysis of the femur was separated from the shaft by a gap half an inch wide, and the shaft of the bone was bare of periosteum for about four inches up, lying in a very large irregular abscess-cavity.

The boy lived for several weeks after the operation, but in the same septic condition. Abscesses formed in other parts of the body, he became slowly weaker, and died on October 19th. Abscesses were found after death in both lungs.

November 20th, 1894.

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3. *Endosteal sarcoma of the patella.*

Shown by D'Arcy Power for Robert Jones (Liverpool).

A longitudinal section through the knee-joint showing an endosteal sarcoma of the patella. The tumour in its shrunken condition measures 4 inches in length and $2\frac{1}{4}$ inches in thickness. It involves the whole substance of the patella, which is considerably increased in size. The bone appears to have disappeared completely, but the articular cartilage is healthy though it has become concave towards the cavity of the joint. The patella therefore presents very much the appearance usually seen in the tibia when its head has been expanded by an endosteal sarcoma. The tumour is solid, and microscopically consists of an ordinary myeloid sarcoma in which the multinucleated cells are very numerous.

The femur, tibia, and fibula, as well as the articular surface of the knee, appear to be quite healthy.

The patient was a girl aged 20, who fell upon her knee in the summer of 1890. She suffered pain and inconvenience for four or five days after the injury, but recovered completely. She again

fell upon the same knee, in the spring of 1891; although the fall was not a severe one, the knee-cap commenced to swell. She came

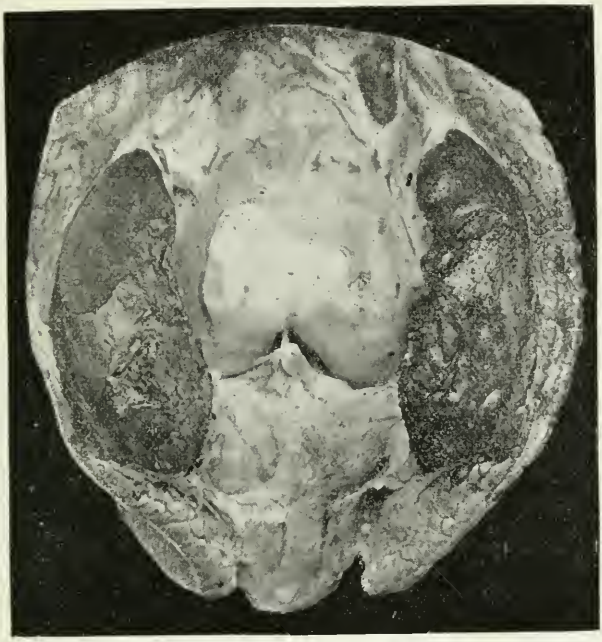
FIG. 12.

Photograph showing the enlargement produced by an endosteal sarcoma of the right knee-cap.

to consult Mr. Robert Jones in 1892, about twelve months after the second accident. She then appeared to be suffering from a chronic inflammation of the bursa patellæ; the skin, however, was blue and brawny, and the hollow around the patella was obliterated. Pressure was therefore applied over the knee-cap, and the patient was sent away with a back-splint on the affected leg. Six weeks later the knee was more swollen, and as the swelling appeared to fluctuate it was aspirated, but only blood was withdrawn. The patient would not allow an incision to be made into the tumour, and she was accordingly sent home again in a splint, but no further pressure was applied over the joint. This treatment was continued for a period of twelve months, during which the swelling steadily increased in size. The patient's permission to incise the tumour was at last obtained. It was found to be a sarcoma, and the thigh was amputated in its lower third.

The specimen is of interest, and must, I think, be rare. No growth from a patella has been shown at this Society, and there is none in the museum of St. Bartholomew's Hospital. The Hunterian Collection (No. 1637) contains an endosteal myeloid sar-

FIG. 13.



Section through the right patella, showing how greatly it has been expanded by the growth of an endosteal sarcoma.

coma of the patella. It was presented by Sir Astley Cooper. It differs from the present growth in being cystic.

The especial interest attaching to this preparation is the difficulty in recognising it, for so experienced a surgeon as Mr. Robert Jones was evidently for some time in the dark as to its true nature. Its solidity probably accounts for the absence of egg-shell crackling and pulsation.

The specimen has been presented to the Royal College of Surgeons, and it is numbered 1637A in the Hunterian Collection, and a thin section is in the museum of St. Bartholomew's Hospital, No. 453B. *February 19th*, 1895.

4. *Chondrosarcoma of right humerus.*

By Herbert Snow, M.D.

The specimen was removed in April last, by amputation at the shoulder-joint, from a well-developed young woman of 22. She had felt pain one year nine months, recently much more severe, but had noticed the tumour only five weeks. No family history of malignancy. Hard work as a general servant appeared to have been the sole exciting cause; there was no remembrance of any direct violence. The patient remains well to present time.

That gradual merging of well-organised tissue into the embryonic spindle-cells of malignancy, which is specially associated with the group of "cartilaginous tumours" (*vide* 'Paget's Surgical Pathology,' lecture xxvi), is well exemplified by the specimen, which presents three distinct zones; the upper of well-formed bone, the middle of cartilage, the lower of spindle-celled parenchyma mingled with cartilage nodules (slide exhibited).

These tumours grow more or less slowly to an immense size, always eventually passing into sarcoma. Sir J. Paget (loc. cit.) depicts one removed, after forty years' growth, from a naval surgeon, who shortly afterwards died apparently from chest metastasis. They are specially prone to attack the upper extremity of the humerus. The question of causation is interesting: traumatism or conditions involving chronic hyperæmia are the immediate antecedents. Of cases seen by the author, one of eight years' duration was in a sailor; two or three others in young girls who had been compelled to work hard at mechanical occupations. He believed that the growths were often primarily due to residual cells or nodules of unossified cartilage. For the multiple cartilaginous tumours on the hands and feet of children this explanation was almost certainly true. In the present specimen the tumour appeared to be of periosteal origin; but as the periosteum, when irritated, ordinarily develops spindle-sarcoma tissue only, some additional reason is necessary to account for the large masses of cartilage and bone found in this rather exceptional group of neoplasms.

December 4th, 1894.

5. *Tubercular disease infiltrating the tibia, and secondarily implicating the knee-joint.* (*Card specimen.*)

By William Henry Battle.

This specimen was removed by amputation from a discharged soldier aged 25. Admitted to the Royal Free Hospital on September 23rd. Amputation lower third of thigh October 3rd. Left hospital October 23rd, 1894. Fall at football in June, 1893, but no pain until a month later.

Section of upper end of left leg, showing interior of knee-joint, the capsule of which is the seat of tubercular deposit in an early stage. The head and part of the shaft of the tibia have been cut in two with a saw. The interior of the bone is changed into a soft yellow mass which extends across the bone within the compact tissue; in it is a canal made by the finger during a preliminary exploration. The disease extended into the joint through the external tuberosity, where it also caused most marked symptoms, including bulging. It extended four inches in a wedge-shaped manner down the shaft. *May* 21*st*, 1895.

VII. DISEASES, ETC., OF THE DUCTLESS GLANDS.

1. *A case of enlarged spleen in a child aged six.*

By William Collier, M.D.

The spleen was taken from the body of a female child aged six years, who was admitted into the Radcliffe Infirmary April 4th, 1894, and died there on September 7th. The mother stated that the child was a very fine and healthy infant up to the age of eight months, when she had a severe illness the nature of which is not known. When about two years old the abdomen was noticed to be enlarged and steadily increased in size. At the age of three she was for some months an inmate of the Wolverhampton Hospital, and the mother stated that she was assured that the child could not live many months. On admission to the infirmary the child was excessively emaciated. We found evidence of broncho-pneumonia and pleurisy, and tubercle was suspected, but during her stay the lung symptoms cleared up. Temperature was as a rule subnormal. The blood was carefully examined on several occasions, but no excess of white corpuscles found. The red corpuscles were misshapen, and did not form good rouleaux. Urine throughout contained a cloud of albumen. Beyond slight beading of the ribs, there was no evidence of rickets. Up to a few days before death, beyond being excessively feeble, the child did not seem to suffer much pain, and was exceedingly cheerful. Death seemed to be accelerated by an attack of epistaxis and sickness.

There was evidence of recent pleuritic adhesions on both sides. The bases were much congested, but no sign of tubercle was found anywhere. The spleen weighed 4 lbs. 2 oz., the child 23 lbs., therefore more than one sixth of the total body weight, the normal being 1 to 400. White irregular patches appeared on the surface of the organ, which on section corresponded with a whitish infiltration of the spleen substance. All the mesenteric glands were enlarged. On microscopic examination the splenic reticulum is seen to be replaced by very large endothelioid cells, in places packed closely

together and filling the whole splenic sinuses. In such places the blood-supply is almost *nil*, and the large cells show a tendency to degenerate. In such places also there is a slight increase in the thickness of the trabeculæ. The Malpighian corpuscles cannot be distinguished. Small arterioles are seen closely surrounded by the large cells. In some of the retro-peritoneal glands examined the adenoid tissue was seen to be largely replaced, especially at the periphery, by large cells similar to those in the spleen. Some small grey points like tubercles in smaller omentum found to be young lymphatic glands. The mother stated that she had had seven children, four of whom had died previously to this one,—one of inflammation of the lungs, two of consumption of bowel (tubercle), one in the infirmary six years previously.

On examining our *post-mortem* record I found that this child was admitted under my colleague, Dr. Brooks, October 4th, 1888, and died November 27th. She was admitted with bronchitis and enlarged spleen, and gradually lost strength and died of exhaustion. A soft cheesy mass was found in the posterior mediastinum, but no trace of any tubercular deposit in lungs or elsewhere. Spleen was found to be enormously and uniformly enlarged; weighed 25 oz. On section it seemed to be congested, and in substance was firm though somewhat friable. *January 16th*, 1895.

Report of the Morbid Growths Committee on Dr. Collier's specimen of enlarged spleen.—A longitudinal section through the middle of the spleen shows, towards its convex border, a zone occupying two thirds of its length of a mottled white colour. The rest of the section shows no abnormality. This zone varies in depth from a quarter of an inch to an inch, and in places is made up of wedge-shaped masses, with radiating processes of fibrous scar-tissue. There are no defined caseous foci, nor any evidence of thickening of the vessel walls. The capsule covering the affected zones is distinctly thickened. These appearances are similar to those commonly attributed to syphilis. The evidence is, however, insufficient to enable us to make any dogmatic statement on the subject. The scarring of the tissue is, however, against either of the suggestions which were made at the meeting, viz. that the condition might be lymphadenomatous or sarcomatous.

The existence of a similar fatal enlargement of the spleen in an elder sister should not be lost sight of.

We agree with the author in his statement that the most obvious feature in a microscopical section, taken from the central portion of the organ, is the presence of an enormous number of endothelial-like cells, while the leucocytes and Malpighian bodies are greatly diminished in number.

This appearance is similar to that which is not uncommon in the lymphatic glands, and was present in the lymphatic glands in the present case.

J. H. Targett.
G. Newton Pitt.
(Chairman) S. G. Shattock.

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2. *Fibro-adenomatous tumour of the supra-renal.*

By H. D. Rolleston, M.D.

In the upper part of the left supra-renal body, projecting from the anterior surface, there was a localised swelling, rather larger than a walnut. It arose somewhat abruptly from the remainder of the supra-renal capsule, which had on its surface a few of the collections of supra-renal cells, in an advanced state of fatty degeneration and yellow in colour, called adenomata.

On section this tumour was of a dark brownish-red colour, with a few hæmorrhagic spots, and so differed markedly from the large "adenomata" occasionally seen. The surface was not translucent, and there were no distinctly caseous areas.

It was removed from the body of a man aged fifty-four years, who died in St. George's Hospital of granular kidneys. There was no abnormal distribution of pigment on the skin, or any symptom suggesting Addison's disease. There was no tubercle or any sign of syphilis in any part of the body. The other supra-renal body was normal.

Microscopic sections were taken from various parts of the growth, and all showed the same changes, though varying in degree.

The supra-renal tissue, though altered, could be easily recognised; the normal arrangement of the layers in the cortex was somewhat

obscured, but not entirely lost. The columns of supra-renal cells were separated and compressed by strands of well-formed fibrous tissue, so as to produce an appearance homologous to cirrhosis of the liver. There was more fibrous tissue in the deeper parts of the tumour than on the surface. Running in this fibrous tissue were well-formed and large blood-vessels. The supra-renal cells were somewhat atrophied, but did not show any fatty infiltration. No caseous areas were found, and tubercle bacilli were not discovered.

The remainder of the supra-renal body showed no fibrous increase, so that this condition is not one of general cirrhosis, such as was described by Dr. Sidney Martin in the 'Illustrated Medical News' of December 15th, 1888, and no cause for a local cirrhosis, such as tubercle or syphilis, is forthcoming.

The appearances differed from that of the large adenoma or struma lipomatosa supra-renalis (Virchow) in two points:

(i) The presence of a large quantity of fibrous tissue, containing large and well-formed vessels; and

(ii) In the absence of any fat in the supra-renal cells.

The general resemblance of the columns of cells to those of a normal supra-renal body and the presence of well-formed vessels running in old fibrous tissue negatived the idea that the tumour was a carcinoma in any early stage.

The tumour may be considered as a fibro-adenoma of the supra-renal body. *October* 16*th*, 1894.

VIII. DISEASES, ETC., OF THE SKIN.

1. *Carcinoma arising in the bed of the thumb-nail.*

By Edgar Willett.

The specimen consisted of one half of a more or less spherical growth springing from and surrounding the ungual phalanx of the thumb the surface was nodular and uneven, and the skin

Fig. 14.

Section of the thumb and tumour. From a photograph. Natural size.

over the tumour was destroyed by ulceration; the nail, still embedded in the growth, had been displaced and pushed upwards from its bed. On the cut surface the tumour appeared strictly limited to the last phalanx, the whole of which was involved, so that the remains of the bone could not be made out.

Microscopically its structure was found to consist of irregular masses of deeply stained nucleated cells arranged irregularly in a meshwork of fibrous tissue; the cells appeared to be epithelial in character, somewhat similar to those forming a healthy nail; they did not grow from the surface; their arrangement recalled the structure of rodent ulcer; there was nothing at all resembling nest-cells to be seen. The tumour was considered to be a carcinoma.

The clinical history is interesting and as follows:—The patient was an old lady, eighty years of age at the time of the amputation of the thumb in November, 1892. The tumour had been growing for seven years, but had increased rather rapidly recently. It had been treated by the injection of methyl violet into its substance on alternate days for three weeks; the only effect was to produce a certain amount of shrinking from loss of substance by ulceration, but with much increased discomfort; the whole thumb was therefore removed. There was then no glandular enlargement, and a year later she was quite well. At the present time (April, 1895) she is still alive and in fair health, but there is a mass in the axilla as large as a hen's egg, also of slow growth.

A microscopical section was shown. *April 2nd*, 1895.

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2. *Cancer of axillary skin glands.*

By F. T. Paul.

[With Plate VII, figs. 1—4.]

In February of this year, 1894, Dr. Owen Bowen, of Liverpool, brought me a patient with a malignant growth in the right axilla. She was a young woman twenty-nine years of age, and the mother of five children. She first noticed a lump in her axilla

two and a half years ago whilst nursing her fourth child. It caused no pain, and she was not conscious of any wetness or discharge from it. In the course of a month or six weeks it subsided and disappeared without treatment. On the birth of her fifth child, sixteen months ago, the lump returned. This time it did not go away, but four months later became painful. However, she still took very little notice of it, and waited another six months before showing it to her doctor. He at once decided that the tumour was malignant, and advised its removal, but it was not until six months more had been lost that she consented to consult me.

On lifting the right arm a most typical-looking scirrhous carcinoma was revealed in the middle of the right axilla. It consisted of a bluish, shiny, prominent lump the size of a filbert, and beside it another smaller lump adherent to the skin, but not raised. Over the latter the skin was white and puckered, and had the characteristic "pigskin" appearance; whilst beneath the tumours hard cancerous glands could be felt extending in a diminishing chain to the apex of the axilla. There was no appearance of a nipple or duct opening on the surface, and the tumour had no connection whatever with the breasts, both of which were normal.

A week later with the help of Dr. Bowen I excised the growth, and dissected out all the axillary glands. The patient recovered quickly; but the tumour recurred, and five months afterwards I saw her with extensive internal secondary deposits, from which she died in September.

On cutting the tumour in halves the new growth was seen to have originated in some creamy white tough tissue, reminding one exactly of mammary gland. In parts there were small cysts or dilated ducts, particularly between the two lumps and near the surface; but just beneath the true skin all the ducts came to a sudden stop. However, upon carefully examining the surface above them minute pores were detected, though no visible communication between the two existed. The pores were apparently in connection with the hair-follicles, and were distributed over a space the size of a florin in the centre of the axilla. The secretion contained in the ducts was white, and resembled inspissated milk. The tumour had evidently originated in one of those "axillary lumps" described by Dr. F. H. Champneys, and regarded by him

as "tracts of skin in which the mammary function is developed in lying-in women."

In a paper by Dr. Charles Creighton on "Tumours arising from the skin glands of the dog," published in the 'Transactions of the Medico-Chirurgical Society' for 1882, he describes these structures as large convolute tubular glands, the ducts from which frequently open into the hair-follicles. They possess a very characteristic microscopical appearance, owing to the fact that the cubical epithelial lining rests upon a layer of unstriped muscular fibre, which gives to the gland tubes a marked longitudinally ribbed or striated character. He regards these dog glands as being of a special type, and states that they do not secrete the ordinary perspiration. At the same time he considers them identical in structure with certain patches of skin glands met with in the human axilla, breast-areola, and groin. Special axillary skin glands are described by many anatomists. They are met with in some subjects as a pad about the size and thickness of a florin, situated just beneath the skin in the centre of the axilla. The pad is composed of large convolute tubular glands having the structure of sweat-glands, and the fluid they secrete yields the peculiar axillary odour. Creighton regards them as obsolete accessory sexual structures.

The specialised muscular coat of large sweat-glands is a well-recognised anatomical observation. Schäfer, Henle, Stricker, and Kölliker all refer to it in their works; and Stirling notes the point referred to by Creighton that the ducts of the skin glands of the dog, which he calls sweat-glands, open into the hair-follicles a little above those of the sebaceous glands. Mansell Moullin has described a similar striated muscular coat as the membrana propria of the breast ducts. Henle has detected muscular fibres in the breast ducts, but their presence is not generally admitted, except in connection with the large ducts of the nipple.

Dr. Champneys has recently had the opportunity of examining microscopically two specimens of the milk-secreting axillary lumps previously described and published in the paper referred to. He has been kind enough to write me respecting their structure, and informs me that they are composed of a mass of overgrown sweat-glands. This being the case, it would appear that these peculiar tumours are derived from the special axillary glands, from which they differ more in function than structure. All the above obser-

vations seem to have an important bearing upon the specimen submitted this evening.

In describing its microscopical characters it will be well to consider separately the new growth and the equally abnormal gland tissue in which it originated. I will begin with the former. The tumour, as has already been stated, had the naked-eye and clinical features of a typical scirrhous cancer, indistinguishable from scirrhous mammæ. This appearance is quite borne out by its microscopical structure (see Plate VII, fig. 4). The cells are of the common breast cancer type, and are arranged in the usual manner; sometimes in large alveolar spaces, and sometimes in lines amongst a coarse fibrous stroma. In the older parts the cells have undergone fatty degeneration, and the coarse fibrous alveoli are almost empty. The same features characterise the infection of the lymphatic glands, and the mode of extension of the growth in both the ducts and acini of the deeper gland tissue is essentially the same as in true mammary cancer. Hence in both clinical and pathological features this tumour markedly resembles cancer of the breast; but at the same time it is important to bear in mind that Dr. Creighton's tumours of the skin glands of the dog also had scirrhus-like characters, which are well depicted in the engravings accompanying his paper.

Now to describe the abnormal gland tissue in which the tumour originated. In the deeper parts it consists of tree-like, branching ducts, terminating in breast-like acini, lined respectively with columnar and cubical epithelium (see Plate VII, fig. 3). The acini are embedded in fibrous and adipose tissue, and are grouped in small lobules very much like mammary gland. In places the encircling fibrous tissue is in excess, and then resembles the more delicate, translucent, and highly nucleated tissue of adeno-fibroma. In fact, the acini are so essentially breast-like in every detail that their nature hardly admits of question. The greater proportion of the gland tissue consists of duct-like structures. Some of these are very large, having been distended with fluid when fixed. Others are large ducts, but in a state of contraction, and amongst them are numerous smaller tubes, many of which are arranged in a convolute manner like very large sweat-glands, but others terminate in acini. In my judgment these are all varieties of the same structure. It is not easy to trace the small branches derived from the acini into these larger ducts; but here and there in a

DESCRIPTION OF PLATE VII.

(Reproductions in collotype of photographs taken by Mr. Paul.)

Figs. 1 to 4 illustrate the paper on "Cancer of the Axillary Skin Glands" (p. 153), and fig. 5 that on "Subcutaneous Horny Tumour" (p. 153).

Fig. 1 shows the duct of an axillary gland opening into a hair-follicle. × 20.

Fig. 2.—Coils of gland tubes with striated coat. × 80.

Fig. 3.—Breast-like gland tissue. × 20.

Fig. 4.—The new growth. × 150.

Fig. 5.—Section of the subcutaneous horny tumour. × 20.

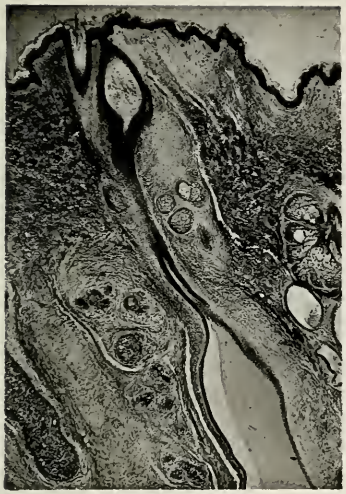

Fig. 1.

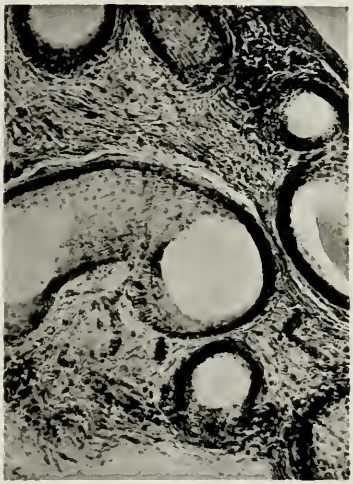

Fig. 2.

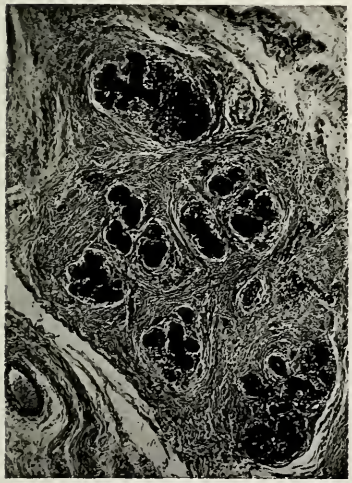

Fig. 3.

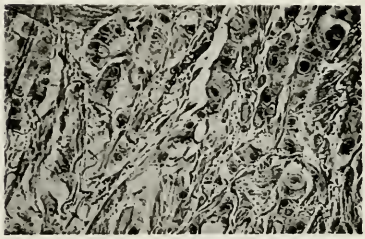

Fig. 4.

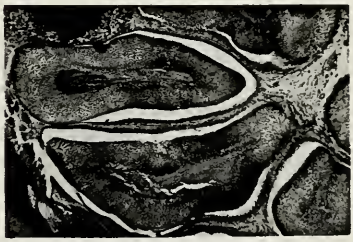

Fig. 5.

lucky section the connection may be distinctly seen, and is perhaps after all not much more difficult to follow than in the case of normal breast. The larger ducts have a dense fibrous sheath. Those which are dilated are spherical or oval on section, and are lined with a single layer of cubical epithelium. Empty ducts are lined with columnar epithelium, and are corrugated in section like the normal ducts of the nipple. In all, and especially in the smaller coils, one sees plainly through the clear, thin, cubical epithelium the delicate, elongated nuclei of unstriped muscular fibres, and the longitudinal striation due to them, and described by Creighton as characteristic of the special axillary and dog glands. This appearance is the most striking and peculiar histological feature present (see Plate VII, fig. 2).

The secretion in the ducts has generally the appearance of inspissated milk; but in some there are large round cells filled with fat, and containing one or sometimes two small distinct nuclei. They are like sebaceous cells, but are probably a sort of colostrum corpuscles, and exactly resemble cells which may be met with in the ducts of some breast tumours, or in the lactating gland.

The large dilated ducts a little below the level of the hair-follicles, and just beneath the layer of normal sweat-glands, suddenly contract to form a small, thick-walled tube with very little lumen, which passes upwards in the line of the hair-follicles to enter one of the latter a little below the surface, that is, rather above the entrance of the ducts of the sebaceous glands, as described by Stirling in the case of the skin glands of the dog (see Plate VII, fig. 1). So far as I can trace them, no ducts but those of normal sweat-glands open on the surface independently of the hair-follicles, an observation which has been rendered almost certain by the examination of numerous horizontal sections of the skin over the tumour.

Normal sebaceous glands are present, and are connected with the same hair-follicles as the special gland ducts; but they are neither very large nor very numerous. Normal sweat-glands of the usual size are also present in fair quantity. Their ducts discharge in the ordinary manner on the surface of the skin. Although some of the abnormal gland tissue resembles very large sweat coils, no transitional condition can be detected between it and the normal small sweat-glands; but, on the other hand, there are many intermediate states between the large convolute tubes and the very big ducts. Moreover the malignant growth invades

the large coils freely, as well as the large ducts and breast-like acini ; but it seems always to avoid the true sweat-glands, even although many of them are partly surrounded by it. All this tends to show that the peculiar glands present in this specimen in which the tumour originated are something different from sweat-glands, although they have some marked structural features in common with them.

The following is a summary of the chief points to which I have endeavoured to direct the attention of the Society.

1. The new growth in this specimen is like a typical scirrhous carcinoma of the breast.

2. It has not originated in a true supernumerary mamma, nor in a sequestrated portion of a normal mamma, but in a patch of axillary glands differing from both sebaceous and sweat glands.

3. These glands are complex in structure, the acini resembling breast, and the ducts sweat-gland tissue, whilst they discharge their secretion into the hair-follicles after the manner of the convolute tubular glands of the dog's skin.

4. The secretion is milk-like in character.

5. Normal sweat and sebaceous glands are present in the same tract of skin ; but there are no transitional conditions between these and the peculiar glands, and they are nowhere invaded by the new growth.

The conclusion at which I have arrived is that these peculiar glands are distinctly abnormal, that they occupy a position intermediate between breast and sweat-gland, and indicate a closer morphological association between the two than is ordinarily assumed. I fail to see why the sebaceous gland should be specially regarded as homologous with breast. There appears to be no stronger reason than because its secretion is always fatty. On the other hand, the sweat-gland has points of closer resemblance. It, like breast, can remain quiescent or secrete in large quantity as required, and without modification of structure its secretion may become fatty, as in the case of the ceruminous glands, the breast areola, and some other tubular skin glands. Moreover the sweat-glands, and in the human subject especially the large axillary glands, yield the characteristic odour of the animal, whilst the same odour may be detected in the milk. Yet another point is that the neoplasms of sebaceous glands do not resemble those of the breast, either in cancerous, adenomatous, or cystic formations;

whilst both Creighton's dog tumours and this specimen are indistinguishable from ordinary mammary cancer.

Finally it is interesting to me as an advocate of the sebaceous origin of rodent ulcer to note that a carcinoma derived from structures allied to sweat-glands has totally different histological characters, and it may be further experience will show that other cases of so-called scirrhus of the skin are really examples of true sweat-gland carcinoma. *December 6th*, 1894.

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3. *Subcutaneous horny tumour (so-called calcifying sebaceous adenoma). (Card specimen.)*

By F. T. Paul.

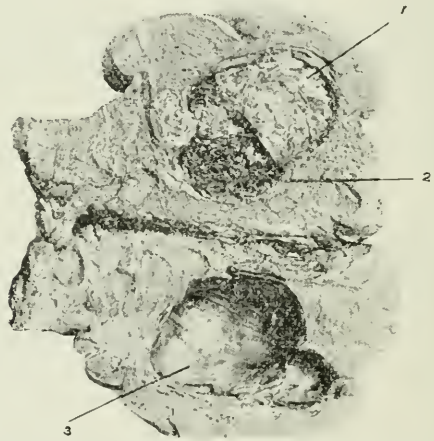
[With Plate VII, fig. 5.]

In January, 1894, Dr. Archer, of Liverpool, sent me a healthy young man, aged 23, with a very peculiar-looking tumour in the skin over the left deltoid muscle. It commenced eighteen months previously as a small pimple, which he was in the habit of emptying by pinching between his finger and thumb, when the discharge would shoot out as from a distended sebaceous follicle. For about six months he frequently used to squeeze it in this way, but it gradually got larger all the time. Subsequently pinching had no effect, so he left it alone; but it continued to grow all the same until it attained the size of a walnut about three months back, since when he thinks it has not increased in size. No other member of his family has suffered from a similar condition.

When seen the tumour projected from the surface of the skin, and presented a bright red angry appearance, though not inflamed. It consisted of a central kernel the size of a filbert as hard as bone, whilst the surrounding skin was swollen, and had undergone a mucoid degeneration so as to be quite translucent like very clear lineæ gravidarum. The translucency was such as to render the outline of the central hard tumour dimly visible, and was the cause of the angry appearance, owing to the visible redness of all the blood-vessels.

On January 29th the tumour was excised, and prepared for microscopical examination. The new growth was limited to the central hard part, the rest of the tumour being merely altered skin (see Fig. 15). The former was completely encapsuled and very hard, but could just be cut in the freezing microtome without decalcification; in fact, decalcifying agents had very little effect in reducing the hardness. The growth was composed of large, more or less spherical acini (see Plate VII, fig. 5), the oldest of which were whitish and very hard, whilst the more recent were smaller and quite soft. The appearance of the young growth reminded one at

Fig. 15.



Subcutaneous horny tumour from the skin of the deltoid region. The upper half shows the tumour *in situ*. The lower half the smooth-walled cavity occupied by it (3). (1) Older part of the tumour with advanced horny changes. (2) More recent soft growth. From a photograph of the hardened specimen.

once of an acinous form of rodent ulcer sometimes met with on the eyelids. These recently grown acini were round or oval, and were filled with polygonal epithelial cells with indistinct walls, but brightly staining nuclei. The peripheral layer were more distinct and sometimes cubical in shape, but not nearly so well differentiated as in skin or in rodent ulcer—a condition which was perhaps due to the pressure of the accumulated cells. In the older parts the centre of each acinus was occupied by a mass of

horny epithelium, in which the nuclei were clearly visible, though they remained unstained. In still older acini all but the outermost row or two of cells had undergone the horny change, and they were split up into crumpled layers amongst which were spots of small opaque, granular deposits of lime salts. In these older parts there was a tendency for the central horny cells to separate and change into *débris*, whilst the neighbouring interacinous connective tissue showed signs of irritation, and contained some giant-cells. One could imagine that in time ossification would have occurred here. As a further indication of the horny nature of the tumour it was observed that upon drying and burning thin slices of it a smell of burnt feathers was given off.

The history and general structure of this tumour shows that it originated in a sebaceous or hair follicle, and its histological and other characters prove that the primary and principal cause of its hardness was in a much larger degree owing to keratogenous than to calcareous change. This being the case, it must be erroneous to describe such a tumour as a calcifying adenoma. It seems to me that it is pathologically identical with the sebaceous horn, only in this specimen the horny growth has taken place beneath the skin instead of upon the surface. A similar tumour was exhibited at this Society by Mr. Eve in 1882, and is recorded in the 33rd volume of the 'Transactions,' p. 335. I had not the opportunity of seeing it, but he has seen my specimen, and tells me that they are identical. I have once previously met with a growth like this. It was about the same size, and had the same angry red look, and was situated on the forehead of a young man. Mr. Larkin undertook the microscopical examination, and found the structure to be similar to that described above. *December 4th*, 1894.

IX. MORBID GROWTHS.

1. *Malignant growth in the glands of the groin following the subsidence of a painful enlargement of the glands, with secondary growths in the skin at a distance from the primary tumour.*

By Charles A. Morton.

This case seems to me of interest as one of primary malignant growth of the glands—malignant both as to wide infiltration of the surrounding tissues and dissemination in distant parts—associated with a previous condition of temporary very painful enlargement of the same set of glands, the characters of malignant growth supervening on the subsidence of that temporary enlargement. Cases of lymphadenoma are described which present similar features. In this disease lymphoid growths may occur in distant parts, such as the testicle and omentum, as well as in the lungs, liver, and kidneys, where there is no lymphoid tissue, and in two of Professor Greenfield's cases recorded in the 'Transactions' of this Society (vol. xxvii, p. 275) nodules appeared in the skin at a distance from the primary growth. In the case in which the histology of these nodules is given they are described as lymphoid in structure.

But the chief interest of the growth in the case which I now record is that, although it was preceded by symmetrical, very painful gland enlargement, showing that it was not simply a case of primary sarcoma of the glands, yet there is no lymphoid reticulum in the primary growth, and the cells are larger than lymphoid gland cells, and the secondary growths in the abdominal wall at a distance from the primary growths, and the secondary growths in the lungs are exactly like sarcoma, for not only can no lymphoid reticulum be detected in them, but many of the cells are of the spindle form. Hence I think we have a growth exactly

analogous to sarcoma in structure, but affecting glands symmetrically after the subsidence of a painful enlargement. The vessels certainly, in most of the growths, have well-formed walls, thus differing from those in round-celled sarcoma; but in one lung growth they are quite like the vessels of round-celled sarcoma.

The relation between lymphadenoma and sarcoma is a very interesting one. The terms lympho-sarcoma and lympho-sarcomatosis have been used with such different meanings, that I will not employ them here. But the reasons for regarding Hodgkin's disease as distinct from disseminated sarcoma of the glands are, that in Hodgkin's disease the glands generally may be attached, the growth is simply hypertrophy of the gland tissue, and that lymphoid tissue even is reproduced in the secondary growths. Moreover there may be pyrexia or association with splenic leucocythæmia. On the other hand, besides being reproduced as secondary growths, it infiltrates like the most malignant sarcoma. In my case the resemblance to sarcoma is more striking than in most, as the microscopical examination of the secondary growths shows that they are not lymphoid, but sarcoma; yet the disease is evidently not simply primary sarcoma of the glands, for the malignant growth was preceded by the subsidence of a very painful enlargement, and the disease was symmetrical.

G. F—, aged 41, was first admitted into the Bristol General Hospital under my care in September, 1893, with enlargement of the glands in both groins of a month's duration. The glands were separate and not of any great size, but they were excessively painful. No cause for their enlargement could be discovered. There was no source of irritation, and he had not had any venereal disease. No other glands were enlarged. For some weeks they remained unchanged, and then the swelling and pain slowly subsided; but whilst they were steadily decreasing in size in both groins, and he had become an out-patient, the skin over the ones in the right groin became red, and I expected suppuration. At this stage he left Bristol, and I did not see him again until the beginning of April. He then looked better in health, but the glands in the right groin had increased in size until they formed a large hard mass, with the skin over it red and infiltrated, and breaking down here and there, with some slight purulent discharge from the surface. There was an area of induration extending from it towards the top of the scrotum, and much œdema of that

side of the scrotum. It could be moved on the deeper parts. The pain from it was very considerable. The glands in the left groin had not increased in size, nor had those in other regions. The spleen was not enlarged, and he was not anæmic.

On April 9th I attempted to remove the mass, but found it surrounding both the femoral artery and vein, and had to leave much of it behind. It infiltrated freely, and a separate nodule was found in the external oblique aponeurosis close to it. It resembled enlarged glands in some parts, but in others looked almost like fat, in lobules separated by dense fibrous tissue. There was no breaking down in the interior of the growth. He remained in the hospital for two months, and the glands in the left groin did not increase in size. After he left he lost much flesh, and died at the end of July. Fortunately I heard of his death, and was able to make a *post-mortem* examination.

Post-mortem.—The mass in the right groin had increased rapidly. It extended halfway down the thigh, and was continuous above with a similar mass around the iliac vessels and up the lumbar spine. In the left groin was a mass of similar firm white growth the size of a small orange, composed of separate round nodules, in the position of the glands, but not infiltrating the tissues. The left iliac and lumbar glands were affected in the same way. There were several growths exactly similar in appearance of the size of walnuts, in the subcutaneous tissue of the abdominal wall, quite away from the groin growths. One was umbilicated, with breaking down in the centre into a puriform fluid; all the others were firm. One was in the skin. There were similar growths in the transversalis fascia beneath the peritoneum.

The lungs, chiefly in their lower two thirds, were studded with minute hard white growths, both on their pleural surface and in their interior. There was some recent pleurisy at the right base.

There were no growths in the heart, liver, or kidneys, and the spleen was quite normal. The cervical, axillary, mesenteric, and mediastinal glands were not enlarged.

Sections of the primary growth show a small round-celled structure, the cells of which are a little larger than lymph-gland cells (some much larger), the nuclei not staining quite so deeply as lymph-gland cells, but in certain areas the cells exactly resemble those of lymph-glands. There is no definite lymphoid reticulum

to be discovered in brushed sections. The capillary vessels have well-formed walls. Here and there are tracts of coarse fibrous matrix between the round cells, with spindle nuclei and spindle cells in them.

The iliac gland growth on the same side and the groin gland mass on the left side show an almost exactly similar structure.

Sections of the growth in the transversalis fascia still more closely resemble sarcoma. The cells are all much larger than lymph-gland cells, and many are distinctly spindle-shaped. No lymphoid reticulum can be made out in brushed sections. The growths in the skin of the abdominal wall and the subcutaneous tissue are similar in character. The cells vary in size, and here and there are spindle in shape, and there is no lymphoid reticulum in brushed sections.

In sections of the lung studded with minute growth, the appearance of the growth was much the same as that already described. The cells in some parts were much larger than lymphoid cells. There was only a very imperfect lymphoid reticulum, and here the cells were many times larger than lymph-gland cells, and a few spindle-cells were present. In sections of another larger lung growth, where there were minute hæmorrhages, the vessels were quite like those of a round-celled sarcoma.

November 20*th*, 1894.

Report of the Morbid Growths Committee on Mr. Morton's case of malignant growth in the glands of the groin.—We have examined the microscopical specimens submitted to us, and find them all specimens of sarcoma, showing a great variety in size and shape of the cells, and a varying amount of original lymphatic gland tissue. With respect to the points emphasised by the author, viz. symmetry of the original growth, its temporary subsidence (? incomplete), and its superficial redness, we do not think these features inconsistent with the view that the growth was primarily sarcoma.

WALTER J. SPENCER.
S. J. SHARKEY, per Treas.
(Chairman) S. G. SHATTOCK.

January 30*th*, 1895.

2. *Epitheliomatous cyst of the neck.*

By Anthony Bowlby.

David I—, aged 58, was admitted under my care into St. Bartholomew's Hospital on September 3rd, 1894, suffering from a swelling in the right side of the neck.

He stated that the swelling first made its appearance only five or six weeks previously, and that it began as a small hard lump. This rapidly increased, and three weeks later was treated with Ung. Plumbi Iod., under the impression that it was of an inflammatory nature. He suffered a great deal of pain for a fortnight before admission, and had lost flesh. The past history and the family history were unimportant.

The patient looked ill and was thin. On the right side of the neck was a large swelling, covered by dark purple skin, which was tightly stretched and thinned. The swelling was oval, and lay with its long axis from above downwards; it measured 8 inches by 4 inches, and occupied almost all the right side of the neck. Further examination showed that the greater part of the tumour was fluid, fluctuation being very distinct; but the deeper part of the mass was hard and fixed, and the glands around appeared to be hard and enlarged. The glands on the left side of the neck also appeared to be larger and harder than normal. Careful examination failed to detect any disease in the mouth, fauces, larynx, or œsophagus, and there were no symptoms pointing to any affection of these parts. The viscera appeared natural.

Before the admission of the patient the swelling had been considered to be a large abscess, but the fixity of its base and its hardness seemed to point to malignant disease of an epitheliomatous nature. In the absence of any primary growth on the skin or mucous membrane in the neighbourhood it was further considered that the case was one of primary epitheliomatous cyst of the neck, for it resembled in almost every particular the tumours of this nature shown at previous meetings of this Society in the year 1887 (vol. xxxviii, pp. 360 and 374) by Messrs. Treves and Silcock.

It was unfortunately only too evident that no operation for the removal of the tumour could be entertained, and as the skin was

already involved and the cyst was threatening to burst, the patient was put under the influence of an anæsthetic, and the cyst was incised. It contained about half a pint of serous, blood-stained fluid; and when this had been evacuated the wall was found to be studded with tuberous masses of new growth, one of which was removed for further examination.

The cyst was drained, and gave rise to no further trouble; but the patient was very feeble, became wandering and delirious after a week or two, and, without any evidence of further disease, slowly sank, and died three weeks later. For the following notes of the *post-mortem* examination I am indebted to Mr. James Berry:

External appearances.—Rather thin, in left mammary region two deeply pigmented moles, the larger about a quarter of an inch in diameter. On right side of neck, one and a half inches above middle of clavicle, an opening large enough to admit a forefinger, leading directly into a large cavity; the edges were slightly thickened. No trace of branchial cleft, dimple, or supernumerary auricle or any other congenital malformation.

Head.—Brain and membranes normal.

Neck.—The right side of the neck was somewhat swollen, the swelling being due to a large malignant cyst occupying both anterior and posterior triangles of the neck. It measured three inches vertically, extending from the level of the hyoid bone down to the clavicle. It measured nearly as much transversely, extending from the side of the larynx and thyroid gland far back into the posterior triangle. It lay beneath the sterno-mastoid, but superficial (or external) to the sterno-hyoid and sterno-thyroid muscles. Posteriorly it just touched the edge of the trapezius. The omo-hyoid lay behind it, and projected as a prominent ridge into the cavity of the cyst. The prevertebral and sterno-mastoid muscles and the nerves of the cervical and brachial plexuses were more or less adherent to and infiltrated by the growth. About three inches of the interior jugular vein appeared to have been completely destroyed by the growth. The carotid artery, vertebræ, clavicle, larynx, trachea, thyroid gland, pharynx, and œsophagus were all unaffected, being neither infiltrated by nor adherent to the growth. The cyst was collapsed, containing only a small quantity of dirty pus and broken-down epitheliomatous material. There was also some dirty pus in the cellular tissue below and inside the tumour. The wall was about a quarter of an inch thick, and presented in-

ternally a somewhat rough tuberculated appearance; the exterior of the cyst was firmly adherent to neighbouring structures. It was composed of tolerably firm white new growth. Outside the cyst and close to it were a few small nodules of growth apparently glands, chiefly at the inner and lower part. The lymphatic glands of the left side of the neck and those of the thorax were quite free from disease. The growth did not present the appearance of a mass of epitheliomatous glands breaking down in the centre, but rather that of a cyst the wall of which had been converted into an epithelioma. The epitheliomatous wall was of about the same thickness everywhere. The mucous membrane of the *nasal passages*, *mouth*, *pharynx*, *œsophagus*, *stomach*, *intestines*, down to the anus, *larynx*, including the ventricles, *trachea* and *bronchi* were all examined carefully, and showed no sign of any primary disease. The lungs were both much engorged and œdematous; the right apex was firmly fixed by old adhesions. There were no signs of secondary affections of any other part of the thoracic or abdominal viscera. The left kidney contained a cyst as large as a hazel-nut, otherwise the abdominal viscera were all quite healthy. Microscopical examination of the cyst wall showed that the growth was a typical squamous-celled carcinoma.

The above case is in almost all respects similar to those already alluded to as described in a previous volume of the 'Transactions' of the Society. The presence of squamous epithelium in a tumour in such a position as that occupied by the cyst in question is, I believe, only to be explained satisfactorily by a growth from similar epithelium of fœtal origin in the branchial clefts—an explanation which has already been offered by Messrs. Treves and Silcock. It is quite certain that the growth was not secondary to any primary tumour in the face or neck, and it could not have sprung from the thyroid gland. I think, further, that the large collection of fluid which characterises tumours of this class, and which is immensely in excess of that which may complicate the development of other epitheliomatous growths, suggests that there is probably a potential cavity in the wall of which the tumour commences, and which is distended by the secretion from the affected lining membrane. It is to be noted that the cysts in all these tumours had a tolerably definite wall studded over with tuberous masses of epithelioma, and that none of them looked at all like cysts due to degeneration in the centre of a growth, for such cysts are in-

variably very ill-defined, their contents resemble thin sebaceous matter, and their surface is always ragged and shreddy. There appear, therefore, to be very good reasons for believing that these "epitheliomatous cysts of the neck" originate in the branchial epithelium. *November 20th*, 1894.

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3. *A case of cystic epithelioma of the neck.*

By F. C. Wallis.

The patient from whom the section was taken was a coachman of sixty years of age.

He came to my out-patient room, suffering from a swelling at the right side of the neck, early in January this year. His history was that he had noticed the swelling for about six weeks, and he was under the care of Dr. Farr, of South Kensington, who sent him to me.

The swelling was the size of an orange, situated over the anterior margin of the sterno-mastoid, on a line with the angle of the jaw. The skin over the tumour was red and adherent; the base was immoveable from the structures over which it lay; the margin was not well defined. The centre of the swelling was elastic, but the base was very hard. The neighbouring glands were enlarged and hard.

In many ways the swelling resembled an inflammatory one, but there was no history to bear this out.

Careful examination of the mouth, pharynx, and larynx did not reveal anything of the nature of a primary growth.

The patient's general condition was bad, and his tendency decidedly alcoholic. He was admitted into the hospital for ten days, but as no operation was proposed, he left, and became an out-patient again. I saw him a fortnight after he had left the hospital, when the growth had materially increased, and there was evident fluctuation. A small trocar was introduced into the fluctuating parts, and about three ounces of clear, light, straw-coloured serous fluid was drawn off. I examined several specimens

of this under the microscope, but saw only a few large, round, multinucleated cells and some epithelial scales. The patient did not return to the hospital again, but Dr. Farr informed me that the patient became much worse, the growth fungated and grew rapidly larger, and eventually killed him. No *post-mortem* was allowed, but Dr. Farr removed a portion of the growth, which he kindly sent me, and a microscopic section of it is in the next room. The drawing is taken from the most typical portion of the section, which shows very well the usual characters of a squamous-celled carcinoma.

This case resembles in all the main features those described by Mr. Silcock in vol. xxxviii, p. 374 of the Society's 'Transactions.'

November 20th, 1894.

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4. *A tumour of the pituitary fossa.*

By J. H. Targett, M.S.

Clinical History.—The patient was a middle-aged man, of no occupation except an occasional job at a public-house, where he seems to have spent most of his time. When first seen by a doctor he was in bed, and had been there for some days; it was, however, no unusual thing for him to remain in bed for two or three days at a time. He then presented the symptoms of Bright's disease; his face was generally œdematous, very little urine was passed, and he complained of headache. Questions were answered with difficulty as if from non-comprehension, the speech was thick, and most frequently the patient was found in a deep sleep, snoring loudly and continuously. The urine contained pus. Gradually he became more and more comatose, the left pupil was dilated, there was complete paralysis of the sphincters, and so he died. There had been no convulsions or localised paralytic symptoms in the extremities. Shortly before death a profuse discharge of pus from the left nostril occurred.

The autopsy revealed meningitis on the surface of the brain, but not of an extensive character. When the brain was raised for the

purpose of dividing the cranial nerves a tumour was found in the pituitary fossa, which seemed to be totally distinct from the cerebral substance. The upper surface of the tumour had a rounded outline, and no part of it looked as if it had been torn away from the brain. Further examination showed that the tumour completely filled the pituitary fossa and overlapped its margins, so that it rested on the clinoid processes. On removal of the growth it was seen that the clinoid processes were considerably eroded, and that a passage existed into the sphenoidal cells, thus establishing a communication with the nostrils. The growth was bathed with pus, and appeared to be attached to the dura mater lining the pituitary fossa, but its relation to the pituitary body was not determined. Unfortunately it was not observed whether that body or any portion of it existed, but no signs of acromegaly were noted during life. The liver was cirrhotic, and there were abscesses in both kidneys.

Description of the specimen.—The tumour removed from the base of the skull was kindly presented to the College of Surgeons' Museum (No. 3792 B), by Dr. C. J. Horner, of Walthamstow. It consisted of a solid mass, rounded in outline, measuring one inch and a half in diameter. Its surface for the most part was finely lobulated, somewhat like a cauliflower, and was covered with shreds of connective tissue like pia mater. No definite pedicle existed, but at one part of its circumference a small flattened area probably indicated its seat of attachment. The surface opposite this area was the most markedly rounded and nodular; hence it doubtless presented towards the brain. A vertical section showed that the tumour was composed of a white homogeneous and friable substance. The margin of the cut surface was irregularly indented in correspondence with the nodular aspect of the tumour; thus the appearance resembled in miniature the convolutions and sulci as seen in a section of the cerebral cortex.

Microscopical sections exhibited a very imperfectly alveolated structure; the spaces were large, and separated from each other by delicate strands of connective tissue permeated by thin-walled capillaries. This scanty material constituted the stroma of the growth, and in many parts the septa were so incomplete that the alveoli freely communicated with each other. The cells occupying the alveoli were chiefly spindle-shaped, small, and closely packed. Among them were numerous "pearls" or "nests," consisting of

concentrically arranged spindle-shaped cells, forming structures not unlike Pacinian corpuscles, but differing from them in size as well as in the greater abundance of nuclei. One, two, or more of these concentric bodies were met with in each alveolus, the remaining cells of the space being crowded around them, and thus holding them together. At the apex of such a body the nucleus of a larger cell was to be seen; it stained readily, and gave no sign of having undergone degenerative changes. In this respect the concentric bodies contrasted strongly with the cell-nests of a squamous-celled epithelioma. There was no evidence in any of the sections examined that these spindle-cells were concentrically arranged round a small or obliterated vessel. A few minute homogeneous particles were scattered through the section, but the substance of the tumour was not gritty. At one margin of the section there were several large, irregularly dilated capillaries filled with blood-corpuscles. They were lined with a single layer of flattened cells, and had no muscular coat.

The specimen may be regarded as an endothelioma, and in its minute structure it exactly corresponds with the illustration of that variety of tumour figured in Byron Bramwell's 'Intra-cranial Tumours,' p. 242. *December 18th*, 1894.

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5. *Malignant disease at the base of the skull, involving the pituitary fossa.* (*Two cases.*)

By Cecil F. Beadles.

Relation of the hypophysis cerebri to malignant disease at the base of the skull.—In a paper contributed by Professor Rubert Boyce and myself to the 'Journ. Path. and Bact.'[1] are recorded a number of tumours of the hypophysis cerebri, and collected together is an extensive literature on the subject, with references to more than one hundred cases. The records extend over the present century, but one dates back as early as the year 1679. Not half a dozen of these are recorded in the 'Pathological Transactions.' Few cases have since been published, and these

[1] "A Further Contribution to the Study of the Pathology of the Hypophysis Cerebri," February, 1893.

are almost limited to a more detailed report of the cases of Drs. Wills[1] and Waddell,[2] to which we referred. There have, however, appeared two important papers on the morphology and minute structure of the pituitary gland by Andriezen[3] and Berkley.[4]

We pointed out that the vast majority of pituitary growths were of the nature of an hypertrophy or a cystic glandular dilatation of the anterior lobe, and there appeared but few recorded instances of growths from the posterior lobe. Usually glandular tumours are of a non-malignant character, and but rarely of a carcinomatous nature; the latter, however, emerge by a slow process from the former.

We showed that the gland exhibits most functional activity in the boundary zone that lies between the two lobes. There is here a band of connective tissue containing the larger blood-vessels, which spread from thence forward into the anterior and backwards into the posterior lobe. The cells of the alveoli usually stain more deeply than do those elsewhere throughout the anterior lobe, and here cystic formation with colloid secretion within the alveoli is most marked. In fact, it may exist to but a slight degree elsewhere, but is rarely entirely absent from this neighbourhood, being carried sometimes to an advanced stage. Small and well-defined isolated portions of gland tissue (adenomata) are, moreover, not uncommon at the lower extremity of this band of connective tissue, which is directly continuous above with the peduncle of the gland. It is from this portion of the hypophysis, and it may be from such more or less isolated portions of the gland, that I am inclined to believe neoplastic development generally starts. When this is of a benign character, such as simple hypertrophy or cystic development, it expands gradually outwards and upwards in the direction of least pressure, giving rise to the slow development of cerebral symptoms from compression of the brain, intercranial pressure, and symptoms referable to atrophy from pressure on the optic or other nerves. In addition there is a thinning of the bone and a hollowing out of the cavity of the sella turcica, as is almost invariably found in fatal cases of acromegaly. These tumours often have extensive hæmorrhages into their substance.

[1] 'Brain,' vol. xv, 1892, p. 464.

[2] 'Lancet,' 1893, vol. i, p. 921. See also paper by Dr. Blackburn.

[3] 'Brit. Med. Journ.,' 1894, vol. i, p. 54.

[4] 'Brain,' vol. xvii, 1894, p. 515, and 'Johns Hopkins Hosp. Rep.' (Neurology II), 1894.

When the growth is of a malignant character and of rapid progress—probably too rapid to be accompanied by the characteristic signs of acromegaly—the growth will usually be found to be situated below the gland, and extend by eroding the bones at the base of the skull, and often associated with deposits in other of the cranial bones. The two cases of malignant disease which I now bring forward were thought at first to be of this nature. They both appeared to have arisen from the anterior glandular lobe. The one is a large localised tumour, situated in the greatly expanded and hollowed-out body of the sphenoid bone, and having the pituitary body situated upon its upper surface, with a second deposit external to the temporal bone; while the other formed no marked tumour, but the growth has eaten away the bone of the middle fossa on the left side of the skull. In each case the pituitary body is intimately connected and blended with the growth beneath, but the major portion of both its lobes remains unaffected, and still presents its normal appearance. In both instances the symptoms and the external signs of disease were very similar, but, as will be seen, the character of the intercranial growth differs very markedly in the two cases.

In the previous paper we called attention to the large proportion that hypophysial tumours seem to bear to the number of intra-cranial growths in the insane, and we gave the notes of eight cases. One of the specimens now shown was from a man who died insane. It is impossible to believe that this was the cause of the insanity in this person, as his mental symptoms were of forty-five years' duration, whereas the signs of disease were present only a few months, and histologically the growth was of a very malignant and rapidly growing form. In the other insane cases the tumours were limited in extent, and all were apparently non-malignant, except one which was presumed to be secondary to cancer of the breast. In all but one, where symptoms had lasted five years, the mental state had existed for less than four years, and, in most instances, the intra-cranial growth did not seem to be the cause of the insanity.

Sarcomata and other connective-tissue growths, which arise either from the posterior lobe or the membranes covering the gland, form but a very trifling percentage of the neoplasms in the site of the pituitary body. The number recorded, so far as we were able to discover, is less than a dozen, including those from

the infundibulum. From the nature of the tissues there represented such growths might take the form of fibromata, gliomata, myxomata, sarcomata, or endotheliomata. The posterior lobe is largely composed of spindle-shaped cells which are arranged in more or less distinct bundles; but there are also present cells similar to those of the neuroglia. At times the cells are much degenerated, at other times more embryonic. They are often much pigmented, and there is a variable amount of colloid material present between the cells. In the boundary zone may occasionally be seen large solitary cells.

In the posterior portion of many pituitaries, numerous small capillary blood and vascular spaces exist, often surrounded by a variable number of spindle-shaped cells, and there may be collections of round or elongated nuclei in the connective tissue. It is from such cells that growths probably arise, and are most likely to start in proximity to the boundary zone. The specimen that Mr. Targett shows to-day from the College of Surgeons may possibly be an instance of the rare but pure connective-tissue growths that take origin from the posterior lobe of the hypophysis cerebri. But the peculiar structure of the tumour, characterised by the formation of dense whorls or circles of cells, often with a small vessel through the centre, is one frequently seen in connection with the brain membranes, and is occasionally met with in the insane. Byron Bramwell[1] describes a tumour of this nature, under the term "endothelioma," that was situated beneath the left frontal hemisphere; and J. W. Blackburn[2] has lately illustrated a number of similar growths arising from the dura mater, to which he applies the name "endothelial sarcoma."

Case 1. *Malignant growth at the base of the skull, probably arising from the epithelium of the tympanic cavity.*—The death of this patient occurred in the asylum at a time when I was making a special study of the hypophysis cerebri in the insane, and the pituitary body, of apparently normal size and form, was handed to me for examination. On making a vertical antero-posterior section in the median line I found its lobes distinctly smaller than usual,

[1] 'Intra-cranial Tumours,' Byron Bramwell, 1888, p. 242; and 'Journ. Ment. Sci.,' April, 1884.

[2] Pathological Supplement to 'Report of the Government Hospital for the Insane, U.S.A.,' 1894.

and surrounding it on its lower and hinder aspect was a greatly thickened covering, which was soon seen to have been cut away or separated from the tissue beneath. Both the anterior and posterior lobes were of a rounded shape, but they were of practically normal structure. There was but little colloid secretion, with scarcely any cystic condition even in the boundary zone.

With a low power of the microscope the thickened investing membrane was found to be the seat of malignant growth of a carcinomatous nature—large and irregular cell-masses, staining far more deeply than the glandular epithelium of the anterior lobe, and a stroma of a fibrous nature with but few nuclei, intimately connected with the capsule of the gland of which it seemed to form a part. The epithelial cell-masses came into close contact with the normal structure of the hypophysis, and completely surrounded the inferior and posterior portion of the gland. Under a higher power, the cells forming the new growth presented closely the appearance of a glandular carcinoma; in places where the spaces were large they were spheroidal, with uniform round nuclei about equal to those of the normal secreting cells of the hypophysial alveoli; but in other parts, more especially where the spaces were small and slit-like, the cells were compressed and their nuclei larger, elongated, and irregular, and presented a more malignant aspect. In the centre of the anterior lobe was a strand of fibrous tissue, containing a few small alveolar spaces enclosing malignant-looking cells of a similar nature, which proceeded from thence into the vascular spaces of the gland in the immediate neighbourhood.

Here I believed was a clear case of glandular carcinoma, arising from the anterior lobe of the hypophysis, but on inquiry I found the hypophysis was associated with the piece of skull which had fortunately been preserved and is now shown. An examination of the specimen and a review of the history of the case precludes the possibility of such a conclusion as that indicated above.

History.—The patient (1948) was removed to Colney Hatch Asylum on July 8th, 1859, from Grove Hall Asylum, where he had been an inmate for eleven years. He was suffering from a recurrent attack of insanity of unknown duration, was then in fair health, of weak intellectual capacity, incoherent in speech, and had aural hallucinations, but was not subject to epilepsy. After admission he became more demented, but health remained fair.

In March, 1873, it is noted that he was imbecile, quiet, in good bodily health, and was employed in the kitchen. A few years later he remained in the same mental state, but found work on the farm. In October, 1888, it is reported: "dull, apathetic and incoherent, face expressionless, memory impaired, does not readily converse; habits tidy. In fair health, aortic sound accentuated, works in the kitchen garden." Up to March 15th, 1892, he had remained in the same condition, when he had a fainting fit and looked ill.

On May 23rd, 1893, it is said his health was much impaired and that he was quite demented. There was then a swelling on the left side of the face with partial facial paralysis. Some discharge from the left ear pointed to suppuration in the middle ear, and it was suggested that he had a malignant growth. During the past twelve months his sight had been failing; but he was not completely blind, and there was no prominence of the eyeball and no difficulty in swallowing or breathing. He died the following June, seventy years of age, having been insane over forty-five years.

At the *post-mortem* the body was fairly nourished. The only lesion of importance presented by the thoracic and abdominal viscera were some atheroma of the aorta and of the valve, and some secondary growths scattered throughout the right lobe of the liver, aggregated at the lower portion.

On examining the head the pia mater was found thickened and congested, the brain soft, and the ventricles dilated and filled with fluid. When the brain was removed, the bony floor of the left middle fossa at the base of the skull had entirely disappeared, and its place was occupied by a firm, ragged, malignant-looking growth. Nearly the whole of the left temporal bone, the left side of the sphenoid, and a portion of the frontal were found eroded and eaten away, and the growth had invaded the posterior fossa. The bone was brittle, and broke through under slight pressure. The growth passed into the body of the sphenoid where it was in contact with the lower part of the pituitary body, the upper portion of that gland appearing normal, and separated with the brain on its removal. Above the zygoma the growth had completely ulcerated through the squamous portion of the temporal bone, and a large opening existed between the cavity of the skull and what appeared an abscess beneath the temporal muscle. The pericranium was

much thickened here, but was intact, and there was no connection between the outer and inner side of that structure.

The cranial nerves involved in the growth were the third, fourth, and sixth of the left side; the ophthalmic division of the fifth, the other two divisions of which nerve also passed through

FIG. 16.

Diagram of the base of the skull showing the areas involved by the growth. *a*. Layer of growth extruding over the bone. *b*. Trigeminal nerve lying on the surface of the growth. *c*. Area over which the bone has been entirely destroyed by the growth. *d*. Area over which inner table of bone is eroded. *e*. Projecting masses of growth.

the growth, while the Gasserian ganglion rested upon it. The seventh and eighth nerves of the left side evidently came into contact with the growth, as the whole of the anterior portion of the petrous bone had disappeared.

The nature of the growth.—On making a section from the anterior portion of the new growth it had a gritty feel, and is seen under the microscope to contain small spicules of bone. The stroma is made up of a well-formed connective tissue with a scarcity of cell nuclei. Large alveolar spaces exist, and are occupied by cells of an epithelial nature, but the character of these cells differs much from that composing the portion of malignant growth connected to the hypophysis which has already been described. Instead of resembling a glandular carcinoma in appearance, it in many parts far more closely assumes the form of a neoplasmic growth that has taken its origin from squamous epithelium. The cells vary much in size, their nuclei being round or oval and often of very large size. Although the smaller cells are not unlike those of the pituitary, both in size and form, yet there are in places cells of great size which are keratinoid in nature, as are seldom found except in squamous-celled epithelioma, while here and there may be seen more or less well-formed cell-nests which it is impossible to believe could have arisen except in such a growth. Other sections are mainly made up of small groups of large squamous-like cells. The presence of these cells makes it difficult to believe that the growth is derived from the anterior lobe of the hypophysis, and we must look elsewhere for a likely site from which it could have originated.

Is it possible for the disease to have started either in the nasal cavity or in the upper part of the pharynx, and eaten its way upwards to the cranial cavity? A review of the history of the case and a thought as to the nature of the epithelium lining the cavity of the nose and naso-pharynx makes such a site impossible as the point of origin of the primary growth.

The mucous membrane of the naso-pharyngeal division of the pharynx (viz. down to the level of the soft palate) is lined with cylindrical and ciliated epithelium, while the mucous membrane of the nasal chamber proper is continuous with that of the upper pharynx, lines the walls of the accessory cavities, and extends into the Eustachian tubes. The epithelial layer is of the columnar variety, ciliated in the lower or respiratory portion, but devoid of cilia in the upper or olfactory region. Such epithelium does not give rise to large keratinoid cells, and glandular carcinoma is very rare in this situation, sarcoma being the most common form of malignant disease.

Squamous epithelium covers only the lining membrane of the vestibular portion (the part formed by cartilage) of the nasal fossæ, and exists in the pharynx only below the level of the uvula. The first of these sites is extremely rare for malignant growths, whereas the middle and lower pharynx are particularly liable to this form of neoplasm. But both these regions are at some distance from the disease, which could scarcely have existed without becoming recognised during life, and it seems highly improbable that the growth would spread thence to the base of the skull.

We must therefore turn our attention elsewhere. The only other conceivable spot is the epithelium of the auditory apparatus, the external auditory canal or that of the drum cavity. Malignant disease of the ear occasionally takes place in consequence of chronic purulent otitis media. In such cases the mastoid is usually attacked, and openings occur in it and in front of the auricle, and the maxillary with both occipital joints are destroyed. Instead of these outward manifestations of the disease, symptoms of intracranial lesions only may be found. The disease attacks persons between forty and sixty years of age, and generally lasts a year and a half.[1]

Here I believe is to be found an explanation of our case. The patient had suppuration from the middle ear for several months, and although the external signs of disease were limited to a swelling in the temporal region, there were signs of injury to the nerves in proximity to the petrous bone, which is seen to be greatly destroyed by the disease. We must conclude, therefore, that the malignant disease started within the temporal bone and spread thence forwards and inwards, destroying the bones as it went, and although the growth beneath the pituitary body differs much from the growth elsewhere, we must, I think, look upon it merely as a modification of the latter, which is involving the pituitary and has actually invaded the anterior lobe of the gland.

Case 2. *Malignant tumour at base of brain of doubtful origin.*—Two years ago I was asked to examine a large oval tumour as big as a medium-sized orange, that was found situated in the greatly hollowed-out sella turcica and occupying the site of

[1] 'Diseases of the Ear, Nose, and Throat,' Burnett, 1893, vol. i, pp. 463, 565.

the hypophysis cerebri. It was a definitely localised tumour, moderately firm, and quite white both externally and on section, resembling macroscopically a round-celled sarcoma. Situated on its upper surface at its anterior extremity was the pituitary body firmly attached by its under surface to the growth, apart from which the gland was of normal colour but slightly enlarged.

A vertical section through the centre, cutting the pituitary body in its antero-posterior median line, showed the growth of a uniform nature throughout, with no cystic spaces visible to the naked eye and no hæmorrhagic extravasations; it blended with the under surface of the pituitary, the limits of which were easily recognisable owing to the buff colour of the gland. The anterior and posterior lobes could also be more or less differentiated. This tumour had the appearance of being a primary growth, and looked as though it had originated from the pituitary body.

History.—Before proceeding to describe the histological structure of the tumour, it may be as well to give the history of the case as far as I am able. The patient was a man aged 20, who was admitted into the Cancer Hospital on October 28th, 1892, where he died three days later, being under the care of Mr. Elam, to whom I am indebted for the following facts.

There was no family history of cancer. The man had been a sailor in the Royal Navy, and eighteen months before had met with a severe fall on his head, since which he suffered much cephalic pain, gradually becoming worse. Two months ago he first noticed a swelling forming on the left side of his head, and another in the parotid region, and shortly the left eyelid began to swell. Previous to this he complained of some loss of sight on the left side.

When admitted to the hospital he was unable to give any expression to his feelings or to answer questions. His face and left side of head were much swollen. Optic neuritis in the right eye existed, while no examination of the fundus of left eye was obtainable. Proptosis of left eye with ptosis of eyelid. There was no paralysis of limbs. A soft fungating growth sprang from the roof of nose and pharynx. He was extremely restless, noisy, and very pugnacious, although very weak, which condition lasted to within a few hours of death. At the autopsy the head lesions were as follows:—Externally to the bone an extensive cavity existed beneath the scalp on the left side of the skull, covering an area

from the outer extremity of the eyebrow to a line with the external auditory meatus, and from the zygoma to an inch from the vertex. It was occupied with fungating growth, and was associated with profuse suppuration, the pus having burrowed downwards beneath the cheek.

Internally, on removing the brain, a pale homogeneous mass of growth, about half the size of a cricket ball, occupied the sella turcica (the tumour previously described). This appeared to have commenced in the pituitary body, and involved the whole of the sphenoid; extending downwards to the left and slightly forwards, it had replaced the normal structures such as the large wing of the sphenoid and the mastoid cells, and had pushed forwards the eyeball. The bone was much thinned, but no communication existed into the pharyngeal or nasal cavities. The growth was believed to be a mixed-celled sarcoma.

The patient was previously in St. Thomas's Hospital under Mr. Makins from December 4th, 1891, to January 31st, 1892. The resident medical officer, Mr. G. R. Box, has kindly informed me that he had a firm naso-pharyngeal polyp, of doubtful nature, blocking the posterior nares, and giving rise to a discharge from the left ear. There were then no cerebral symptoms, and the optic discs were normal. He gave a six months' history, and had had his tonsils removed when six years old.

The nature of the growth.—In thin antero-posterior sections taken through the pituitary and a part of the growth and then stained, a difference can be readily detected with the naked eye between the anterior and posterior lobes and the growth. The glandular portion stains the most deeply, the posterior lobe to the slightest extent, and the growth occupies a degree between the two.

Under the microscope the anterior lobe is found to be of a normal structure. There is no marked colloid secretion, and cystic dilatation is not marked. In the boundary zone, however, there are several distinct cystic cavities and slit-like spaces filled with colloid, which extend down to the very limit of the gland beneath, and distinctly separate the two lobes from one another. The posterior lobe is large. Its upper part is little altered from the normal, but the lower portion has a more myxomatous structure than is usually to be found in man, and more closely resembles that seen in some of the lower animals. It presents a loose appearance, with branching cells and much ground substance. Both

these lobes are for the most part distinctly separated from the tumour below by a band of fibrous tissue, and it is only at the lower extremity of the connective-tissue band which forms the boundary zone between the lobes that a more intimate connection appears to exist with the new growth. This band of connective tissue spreads out, and is continued into the tissues of the neoplasm, where it blends with the sarcomatous elements of the stroma. The tumour is composed to a large extent of a young connective-tissue growth formed of spindle- and round-cells, and has at first sight the appearance of a rapidly-growing sarcoma. The cells run in bundles in various directions, and numerous thin-walled blood-vessels and vascular spaces exist, some filled with blood, but others seemingly contain colloid matter. Throughout the growth, however, are to be seen a few epithelial-like cell masses contained in alveolar spaces. The cells are deep staining, spheriodal and irregular, and their nuclei take various forms. Some of the cell-masses have a central lumen which suggests a glandular origin. Owing to the existence of these epithelial cells, it would seem necessary to class this tumour amongst the carcinomata, but I would point out that the great bulk of the growth is composed of connective-tissue elements, and might quite as readily be defined as a mixed round- and spindle-celled sarcoma.

It now remains to decide the seat of origin of the disease in this case. The growth, both from its situation and histological structure, might very well be a neoplastic tumour of the pituitary gland. There exists, however, the history of a previous naso-pharyngeal growth, and the nature of which is at doubt. It is conceivable that it was a malignant growth—a carcinoma arising in the glands that normally exist in that region. Direct spread of the disease from the original site is, moreover, out of the question, for no perforation or infiltration of the bones at the base of the skull was present, and no communication of any kind existed between the sella turcica through the sphenoid bone with the pharyngeal cavity, the bone being sound and free from disease, although much thinned. The large tumour resting on the centre of the skull must therefore be a secondary deposit similar to that external to the parietal bone, otherwise it is a primary malignant growth of the hypophysis cerebri, probably of the nature of glandular carcinoma.

The relation of the previous injury to the new formation is very

close, and little doubt can exist that it acted as a causative agent of the malignant disease in this case. *December* 18*th*, 1894.

Report of the Morbid Growths Committee upon Mr. Beadles's tumours at the base of the skull.—The appended report refers to the second case described in the paper.

After careful examination of the sections submitted to us, we have come to the conclusion that the growth is a spindle-celled sarcoma which in many places is constructed on an alveolar type. We regard the epithelial-like cells referred to by the author as of connective-tissue origin; these do not lie in definite alveoli, and there is no demarcation between such cell-groups and the contiguous parts of the growth. At one edge of the section we find a small area of hyaline cartilage, and one or two trabeculæ of calcified or ossified material.

This shows that the growth is of a complex character; but as the sections referred to us are of one small area only, the general structure of the new growth cannot be properly determined. The other deficiencies, moreover, in the observation of the case do not allow of any decision as to the source of the tumour, or even whether it is primary or secondary.

The committee consider it possible that the growth is a teratoma arising within the cranial cavity in connection with some residue of the pharyngeal diverticulum.

The looseness of its connection with the bone is opposed to its being a chondrosarcoma of subperiosteal origin.

RICHARD G. HEBB.

January 3*rd*, 1895. SAMUEL G. SHATTOCK.

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6. *Myeloids* (*giant-corpuscles*) *in some rare specimens of malignant disease, with their seeming rationale.*

By HERBERT SNOW, M.D.

CASE 1. *Myeloids in spindle-celled sarcoma of the mamma.*—Betsy W—, aged 62. Whole of left breast occupied by a large, rapidly-growing sarcoma; the axillary glands slightly enlarged

and fixed. Excision in November, 1886; microscopic phenomena as above; the growth extremely vascular. The lymph-glands found to be converted into small cysts filled with black, grumous fluid, but devoid of malignant tissue. Rapid recurrence in the muscular substance of the pectoralis; this removed in August, 1887; the same microscopic appearances.

Case 2. *Myeloids in thick wall of breast cyst.*— Mary H—, aged 44, a tumour of left breast of fourteen years' duration. Two months previously a blow, followed by pain and rapid increase. Removal in December, 1888. A single cyst as large as an orange, containing some recently-developed vegetations of embryonic spindle-celled tissue, and filled with a blackish fluid. The wall of the cyst very thick, composed of well-organised fibrous tissue, containing myeloid corpuscles. No subsequent trouble.

Case 3. *Myeloids in scirrhous carcinoma of mamma.*—Eliza P—, aged 45. In left breast a hard, nodular, scirrhous kernel of one year's duration, as large as a bean, with an axillary gland of equal size. Excision in October, 1885. On removal the cut surface of the tumour was of a uniform reddish black, suggestive of melanosis; that of the gland was whitish, as in ordinary carcinoma deposit; the section, however, of another gland, not enlarged, exactly resembled that of the primary lesion. Under the microscope well-marked scirrhous acini, with abundant myeloids in the connective tissue around, but no pigment. In February, 1887, a recurrent nodule was removed from the inner end of the cicatrix, with a still remaining axillary gland. In October, 1887, two nodules as large as hazel-nuts were dissected out of the muscle substance. All these presented the same macroscopic and microscopic characters. The patient remains perfectly well up to date. She is a little spare woman, of very dusky complexion and irregular distribution of skin pigment, a point suggestive of idiosyncrasy.

Although huge multinucleated cells are not especially rare, the author believed that true myeloids had not previously been described in association with mammary or any other local form of carcinoma, and that the last case was unique. He had not met with any parallel to Case 2. One or two corresponding to No. 1 had been reported some twenty-five years previously, but he believed not to the Pathological Society, as he had been unable to find any record of such in the 'Transactions.'

In addition to malignant new growths, myeloids (or bodies per-

fectly indistinguishable by the microscope) are found associated with tubercle, and with processes of bone absorption or of bone repair. In some of these conditions they have been regarded as macrophages; there is no evidence, as regards cancer, in favour of such a view. Of malignant parenchyma they seem to be purely passive elements. The so-called "myeloid sarcoma" of the text-books differs clinically in no respect from a spindle-celled sarcoma devoid of giant corpuscles, and is not entitled to rank as a distinct species. Although typical myeloids contain very numerous leucocytes, yet a fair number are perfectly amorphous; and these offer the key to a comprehension of their nature. They are simply microscopic fragments of fibrin—minute blood-clots, in short. The one condition essential to their development is undue vascularity, with probably some idiosyncrasy in addition. It need hardly be said that they have no connection with the bone-marrow.

November 6th, 1894.

Report of the Morbid Growths Committee on Dr. Herbert Snow's specimens of giant corpuscles.—We have carefully examined the preparations handed over to the committee by Dr. Snow, and report as follows:

Case 1.—In regard to the first case, we concur with the author, and hold the tumour to be a spindle-celled sarcoma containing a considerable number of multinucleated myeloid or giant-cells. These cells are indeed so numerous that the growth might equally well be classed as a giant-celled sarcoma.

Case 2.—The number of giant-cells in the cyst wall of this case is inconsiderable, and forms no important feature. We have no comment to make on the author's description, except that we consider the use of the term "spindle-celled tissue" ambiguous, and should substitute that of "granulation tissue," the tissue being of inflammatory origin.

Case 3.—This the author describes as a scirrhous carcinoma in which there are numerous giant-cells. It is upon the latter that the interest of the specimen turns. By taking particular examples of such, the conclusion that the structures so named are giant-cells might certainly be arrived at. After carefully examining the whole of each of the different sections, however, we think the appearances are either accidental or artefact: if the former, they are due to the sections of compressed and misshapen cell-columns;

if the latter, they are due to age or imperfect preparation. In favour of the latter view is the fact that in none of the sections is there any evidence of a cell margin, even where there would be no dispute as to a real epithelial column being in question. This universal absence of cell-demarcation renders it equally impossible to say whether any of the bodies under consideration are cell-fusions of epithelium such as are encountered in certain carcinomas.

The view of their artificial character is further supported by the fact that similar elements can be occasionally seen not only side by side with the cell columns, but also in their midst. We may observe that there is nothing in the general structure of the tumour which which would render the presence of macrophages probable, *i. e.* there is no extravasation of blood, and nowhere any necrosis of tissue.

RICHARD G. HEBB,
January 30th, 1895. SAMUEL G. SHATTOCK.

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7. *The malignant reversion of mammary "cystic fibroma."*

By HERBERT SNOW, M.D.

CASE 1. *Reversion into carcinoma.*—Mrs. S. K—, aged 64, had her left breast excised in February, 1887, for a tumour of uncertain duration, but known to have existed several years at least. It was as large as a well-sized orange; there was no gland enlargement. The mass was found to consist of firm white fibrous tissue, studded with minute acinar dilatations lined by columnar epithelium; a cyst as large as a hazel-nut occupied the centre; there was nowhere any trace, microscopic or macroscopic, of carcinoma structure. In March, 1888, reappearance of disease in the scar, in the corresponding axilla, and in the viscera ensued, with a quickly fatal result. The autopsy revealed typical scirrhous carcinoma in all these tissues.

CASE 2. *Reversion into true sarcoma.*—In April, 1893, E. M—, aged 42, had her right breast excised for a large, prominent, bossy tumour, in size that of a "child's head," noticed by the patient

four years, and therefore doubtless of much longer duration. There had been rapid increase during the previous two months; pain had been felt for three weeks only; there was no gland enlargement; the woman was ruddy and robust-looking. The greater part was found to consist of well-organised fibrous tissue; a thin section displayed to the naked eye that peculiar cribriform appearance which denotes the cystic fibroma; the little meshes were seen under the microscope to be lined by columnar epithelium.

Amid the white and firm tissue base was, however, a small region not larger than a hazel-nut, of greyish colour and soft consistence. Microscopically this was seen to be constituted of embryonic spindle-cells ranged in bands (true sarcoma); the appearances were wholly distinct from those in the remainder of the tumour, and were unmistakably malignant in character. In September the disease "recurred" under the cicatrix, this time showing sarcoma tissue only. It was removed with very temporary success. In April, 1894, another tumour had formed above the scar and close to the sternal edge; as there was no gland enlargement, and the growth still appeared to be strictly local, an attempt was made to remove it, but the whole parietes in the neighbourhood were found extensively infiltrated, and the patient speedily succumbed.

Remarks.—In text-books the connective-tissue hypertrophies which attend the evolution of the female breast (*i. e.* from fifteen to twenty-five years) are usually confounded with those incidental to the period of devolution or permanent degeneration (that is, from the age of thirty-four onwards). There can be no greater error, pathological or clinical; and though, as in most similar lesions, intermediate examples may occur, yet the great majority fall into two extremely distinct classes. The "lumps" we commonly encounter in the mammæ of young girls, and which I prefer to designate the "fibroma of adolescence," are hardly ever associated with cyst formation; the "cystic fibromata" of middle-aged or elderly women is invariably studded with cysts, macroscopic or microscopic. The minute are, of course, but an early stage of the large; confer on the section its characteristic cribriform appearance; are the normal acini dilated. The "fibroma of adolescence" is commonly multiple, involving both breasts simultaneously or successively; the "cystic fibroma" is always single.

But of the gravest importance is the relation of the two lesions to malignancy. The fibroma of young girls rarely grows beyond the size of a walnut; commonly disappears under local treatment, or under the stimulus of pregnancy; has none but a casual association with cancer; although often the site of subjective ill-sensations, is, so far as I know, a perfectly harmless lesion. On the other hand, the "cystic fibroma" grows slowly for a term of years as a benign tumour, but as surely in the end becomes associated with malignancy in one of two modes, illustrated by the above cases.

The *modus operandi* appears to be as follows. We have in these growths two principal elements—the hypertrophied fibrous tissue, and the epithelium of the acini which this includes. Each of these may be the source of the inevitable malignancy. The former slowly grows until, with advancing age, portions fail to undergo proper organisation; then an embryonic development of spindle-celled tissue—in effect, a spindle sarcoma. The latter element, again, the acinar epithelium, is harmless so long as it continues bounded and, so to speak, "encapsuled" by the thick masses of enveloping fibrous tissue. But sooner or later the cells gain access to the softer fatty or other tissue beyond, and there proliferate. Then ensue the phenomena of ordinary carcinoma.

May 21*st*, 1895.

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8. *Primary melanotic sarcoma of clitoris.* (*Card specimen.*)

By William Henry Battle.

The specimen exhibited was removed during life from a patient aged 79. This was done on account of the offensive sloughing condition of the growth, which caused much annoyance and discomfort. The clitoris is much enlarged and clubbed at the extremity. The section has been carried through the centre of the organ and skin over the pubes, from before backwards. The clubbed portion is pigmented, and covers the organ like a cap; it is about a quarter of an inch in thickness, and of a brownish black appearance. The stalk of the mushroom is without pigmentation, and presents striæ, and a complete infiltration with growth of a yellowish

appearance and firm consistency. In the subcutaneous tissue over the pubes the section shows a series of circular pigmented patches varying in size from a crow quill to a cedar pencil; these are the infiltrated lymphatic vessels, full of pigmented growth. As a rule the section of these is quite clearly defined, circular, and isolated; but in one or two places there is a blackish discolouration, and near the base of the clitoris on the upper aspect the pigmented growth extends between the upper part of the clitoris and the largest lymphatic. The surface of the main growth is ulcerated.

The growth had been noticed in October, 1893. She came under care April 23rd, 1894, and died May 18th, eighteen days after operation.

Necropsy.—Hypostatic congestion of the lungs, and cardiac failure. Secondary deposits universal—skin, lymphatics, glands, bones, heart, viscera, including ovaries. Heart: left ventricle markedly hypertrophied; aorta and cardiac valves extremely atheromatous. Microscopically, an alveolar sarcoma.

May 21*st*, 1895.

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9. *Adeno-fibroma of the lip.* (*Card specimen.*)

By L. A. Dunn.

This tumour, measuring $1\frac{1}{16}$ by $\frac{3}{4}$ by $\frac{1}{2}$ inch, was removed from the upper lip of a young adult man, W. F—, in Guy's Hospital, December, 1894. The swelling had existed the greater part of the patient's life, but had lately grown more rapidly. It was perfectly encapsuled, and projected towards the mucous aspect of the lip. On section it appears fibrous looking, and contained one small cyst in the centre. It is of a flattened ovoid shape, slightly nodular on the surface. It shelled out with the greatest ease through an incision on the mucous aspect of the lip. The microscopic specimen shows much fibrous tissue with numerous glandular spaces. *February* 19*th*, 1895.

10. *Sarcoma of lung, secondary to sarcoma of tibia.* (*Card specimen.*)

By H. Morley Fletcher, M.D.

Description and Remarks.—From Florence J—, aged 16. Right femur amputated by Mr. Marsh on February 2nd, 1894, for malignant growth in middle third of leg. Primary growth was a subperiosteal spindle-celled sarcoma, and contained cartilage, in parts calcified. Patient readmitted to St. Bartholomew's December, 1894, suffering from pain in left leg, right arm, and cough. Died December 31st, 1894.

Post-mortem.—Small secondary growths on stump of right femur, left radius, left knee, ribs, &c. Both lungs uniformly infiltrated with secondary growth, the pericardium being buried in the growth occupying the anterior mediastinum. Right lung more affected than left. Growth hard at outer portions of lung, while central part was soft, and in fresh condition contained dark-coloured semi-gelatinous fluid. Great vessels not compressed or affected. Bronchial glands natural. Body not emaciated, very abundant subcutaneous fat. *May* 21*st*, 1895.

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11. *On the identity of so-called duct-cancer with ordinary carcinoma.*

By Herbert Snow, M.D.

A brief communication on this question was brought before the Society. *January* 15*th*, 1895.

X. MISCELLANEOUS COMMUNICATIONS.

1. *A note on variola and vaccinia.*

By J. Jackson Clarke.

[With Plate VIII.]

Many years ago Lionel Beale [1] described cell-forms he had observed in active movement in vaccine lymph. The corpuscles assumed a stellate form, and the peripheral processes exhibited a streaming movement in their granular protoplasm. In 1886 Van der Loeff described as parasites similar bodies he had found in the pustules in six cases of smallpox. The same author described motile flagellates in the blood of vaccinated children and calves. These organisms are half the size of a human red blood-corpuscle, and are provided with one or more nuclei and a single flagellum. They are free in the blood-plasma or attached to red corpuscles (L. Pfeiffer), but are not found within red corpuscles after the manner of the parasite of malaria. They make their appearance when the areola forms about the inoculated spot—that is, when the fever develops ; and they gradually disappear from the blood with the subsidence of the fever.

L. Pfeiffer, in 1887, described as sporozoa certain structures he had observed in the course of the histological examination of the lesions of variola.

In 1892 Guarnieri, who was led by the observations of Van der Loeff and L. Pfeiffer to investigate the subject, published the results of experimental inoculation of the cornea of rodents with vaccine, and with the contents of smallpox pustules. Guarnieri's observations are of the greatest interest and importance, and as the writer has been able to repeat them they will be given in some detail below.

L. Pfeiffer [2] confirmed the observations of Van der Loeff and

[1] 'Quart. Journ. Micr. Sci.,' vol. iv, old series.

[2] L. Pfeiffer, "Behandlung und Prophylaxe der Blattern," Penzoldt and Stintzing, 'Handbuch der speciellen Therapie, &c.,' Jena, 1893, vol. i.

Guarnieri, and embodied his own and their work in a complete account of variola and vaccinia, in which the whole of the literature concerning these affections is fully collected. Doehle ('Centralb. für Bakt.,' 1892) confirmed Van der Loeff's description of flagellates in the blood during the fever of vaccinia and the early fever of variola, and described similar flagellates in the blood in measles, scarlet fever, and in the febrile stage of syphilis.

The writer will now give the results of his own observations on the histology of the vaccinated cornea of rabbits and guinea-pigs. If a rabbit is killed forty-eight hours after the cornea has been inoculated with calf-lymph, sections of the cornea show in the neighbourhood of the seat of inoculation peculiar changes in the epithelial cells (see fig. 1, Plate VIII). In the protoplasm of the epithelial cells, generally in a small cavity which indents the nucleus, minute (1—3 μ), slightly irregular, dense, highly refracting particles are present. These bodies are readily visible in unstained preparations, and they are deeply stained by acid hæmatoxylin and picro-carmine. A few appear to be entirely surrounded by nuclear matter, as at *b*, but this may be due to the plane of the section having passed through the deepest part of a depression in the peripheral part of the nucleus; others, as at *c*, appear as if they were undergoing subdivision into two; others are elongated and appear to be undergoing gemmation, *d*. It is to be noted that the epithelial cells containing these bodies are slightly swollen. These appearances the writer first saw in a preparation made by L. Pfeiffer in 1893, and subsequently in the cornea of every rabbit (four or five) which he (J. J. C.) experimented on. Guarnieri and Pfeiffer have described amœboid movements in the small adnuclear bodies of the vaccinated cornea; thus L. Pfeiffer (loc. cit.) has written, "If a portion of the corneal epithelium near the seat of inoculation is sliced off and is placed on the warm stage in some of the aqueous humour slightly tinged with methyl blue, quite definite amœboid movements are discernible in the foreign particles which lie in the epithelial cells. The movements cease when the parasite dies, an event which is known by its assuming a spherical form and becoming stained by the methyl blue." The cell-inclusions shown in fig. 1 are absent from the normal cornea, and from healing wounds of the cornea. Thus if the cornea is scratched without being inoculated no cell-inclusions are present. L. Pfeiffer has found that when the cornea is anæsthetised by cocaine before inoculation the disease is not

contracted; thus it would appear the parasites of vaccinia are killed by this drug. Moreover at the forty-eighth hour after vaccination leucocytes have not reached the injured spot, nor have noteworthy changes occurred in the connective-tissue cells; indeed, there is not the slightest evidence to support the idea that the cell-inclusions may have come from leucocytes or connective-tissue cells. Chemical irritants do not produce the peculiar appearances of the vaccinated cornea (L. Pfeiffer). It appears to the writer that evidence of the parasitic nature of vaccinia is to be obtained by comparing sections made from the vaccinated cornea on the third and fourth days with those taken at the end of the second day. For this purpose the guinea-pig's cornea appears to be more suitable than the rabbit's, for the reason that the process is more rapid and the forms assumed by the parasites more varied in the guinea-pig. Fig. 2, Plate VIII, represents a portion of the epithelium of a guinea-pig's cornea taken seventy-two hours after vaccination. The epithelial cells are more swollen than at the forty-eighth hour. Clefts (*a* and *b*) have appeared in the epithelium, and in these clefts are bodies which have the high power of refraction and staining reactions which recall the bodies by many regarded as parasites in molluscum contagiosum, cystic ureteritis, cancer, &c. The cell-inclusions as at *c* are larger, stain more with eosin than hæmatoxylin, and present stiff peripheral processes which remind the observer of certain bodies in cancer. In the clefts some of the free bodies present a distinct zone of peripheral granules, but no nucleus (*d*); others have a nucleus with several masses of chromatin (*e*); others again a "flame-nucleus (*e'*). Of the cell-inclusions which have the high refractive power and staining reactions of these free bodies, some present a peripheral layer of nuclear granules; others, as at *f*, present nuclear changes like those which have been more fully noticed in connection with sarcoma; lastly, some of the cell-inclusions possess peripheral granules of the characters of the "corps albuminoides" of coccidia (*g*). If any doubt remained of the nature of the intra-cellular and free bodies of the vaccinated cornea, it would, in the writer's opinion, be removed by a somewhat closer study. Thus examination of the free nucleated bodies under a higher magnification reveals in some cases a structure closely resembling that seen in some of the parasites of cystic ureteritis. In some of the highly refracting cell-inclusions of vaccinia beaded threads of chromatin or minute mitoses are present

DESCRIPTION OF PLATE VIII.

Illustrating Mr. Jackson Clarke's communication on Variola and Vaccinia. (Page 192.)

The drawings were made under Zeiss's $\frac{1}{12}$ oil immersion, and oc. 3. Figs. 1 and 2 × 750 diams.; the rest × 1000 diams.

Fig. 1.—*Part of a section of a rabbit's cornea forty-eight hours after vaccination. a.* Seat of inoculation; *b*, parasite subdivided into two; *c*, parasite in process of fission; *d*, minute parasite in a depression in a nucleus.

Fig. 2.—*Part of a section of a guinea-pig's cornea seventy-two hours after vaccination. a* and *b* are clefts between the epithelial cells; *a* contains two parasites; one round and reticulated in the centre, and presenting a peripheral granule layer; the other elongated with clubbed extremities; *b* contains eleven parasites, two of which (spores) are very small; *c*, large dense intra-cellular parasite, with stiff radial processes; *d*, intra-cellular parasite; *e*, free parasite, with peripheral granules; *e'*, nucleated free parasite; *f*, nucleated intra-cellular parasite; *g*, free parasite, with flame-nucleus.

Fig. 3.—*From a vaccinated guinea-pig's cornea, third day.* Parasite with central clearing (*a*), containing masses of chromatin; *b*, dense ectosarc.

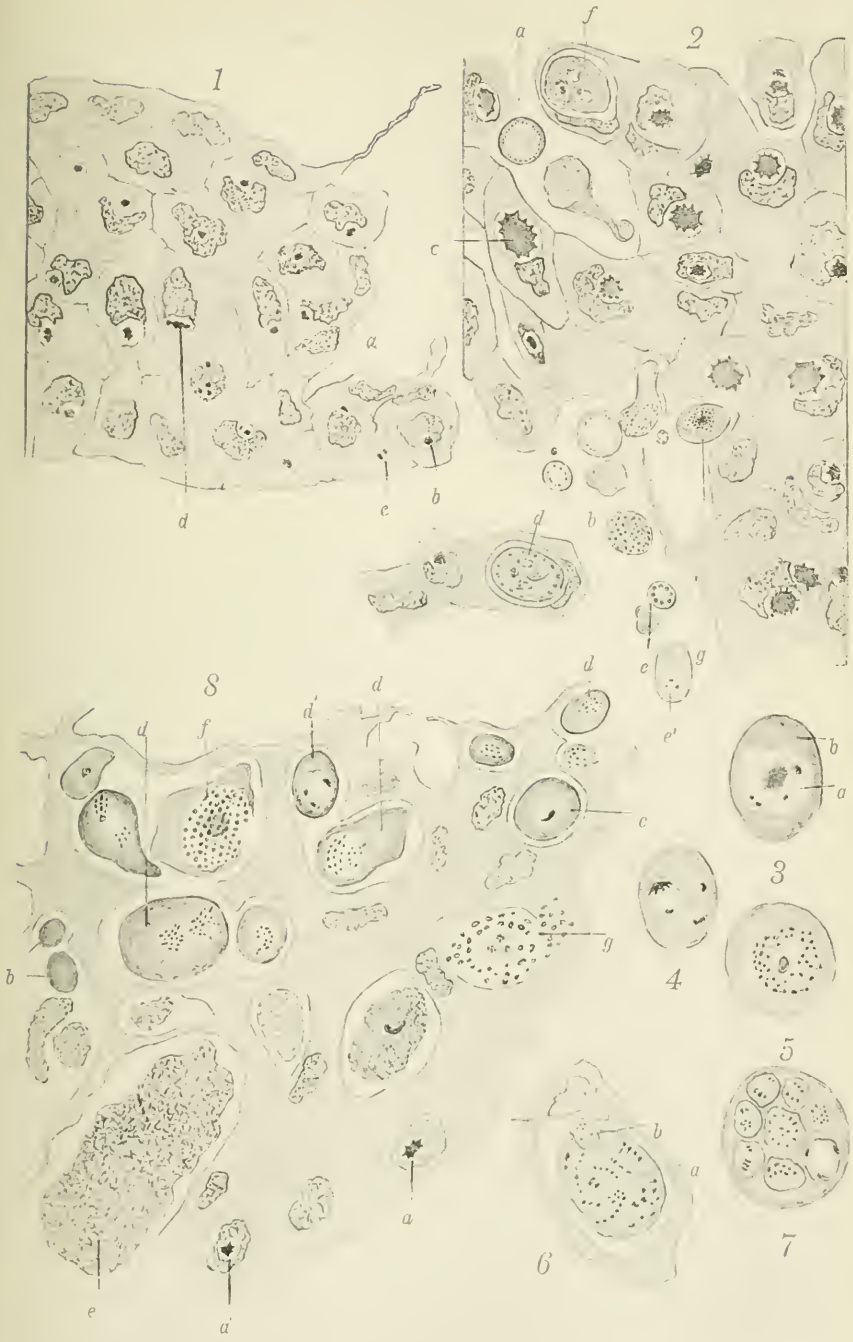
Fig. 4.—*Ibid.* Free parasite, with several irregular mitotic figures.

Fig. 5.—*Ibid.* Parasite, with dense central body and nuclear reticulum, of which the nodal points were stained blue by acid hæmatoxylin.

Fig. 6.—*Ibid. a.* Parasite, from which a portion (*b*) has separated as a potential sporogonium. The parasite contains numerous particles of chromatin, and lies within an epithelial cell.

Fig. 7.—*Ibid.* Free parasite in process of sporing. Eight sporogonia are shown in optical section. The sporogonia all contain nuclear particles (blue with hæmatoxylin). The chromosomes are extremely minute.

Fig. 8.—*Part of the epidermis, near the margin of a primary syphilitic sore.* At *a* and *a'*, intra-nuclear parasites; *b*, dense homogeneous parasites; *c*, bodies similar save in that they have a dense nuclear body, which stains blue with hæmatoxylin; *d*, *d*, free parasites, with chromatin arranged in beaded filaments; *d'*, parasite, with vesicular nucleus which contains three masses of chromatin; *e*, large reticulum; *f*, free parasite, with a central nuclear body, and at the outermost part of the nuclear clearing a hollow sphere of granules; *g*, parasite, subdividing into spores.


1
2
3
4
5
6
7
8
a
b
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(figs. 3—7), as is the case in many sporozoa. Again, among the free bodies of the peculiar characters mentioned above there is evidence of simultaneous subdivision into smaller particles, which in many cases present nuclei with minute chromosomes comparable with those of the sporogonia of sporozoa, with molluscum bodies, and with some of the structures regarded by the writer as parasites in cancer.

Ruffer and Plimmer ('Brit. Med. Journ.,' 1894, vol. i, p. 1412) have accepted the bodies shown in fig. 1 as intra-cellular parasites, confirming the previous descriptions of Guarnieri and L. Pfeiffer. They, however, make some statements with which the writer cannot agree. In the first place, they state that the parasites of vaccinia differ from those of cancer. According to the writer's experience, every parasitic form which occurs in vaccinia occurs also in cancer. Again, Ruffer and Plimmer state that the parasites described by Guarnieri have nothing in common with those described by L. Pfeiffer. Such a statement is incomprehensible, since L. Pfeiffer accepts the parasites as seen in the rabbit's cornea as the earlier phases of some of the cell-inclusions originally described by him. Finally, Ruffer and Plimmer state that they have been able to find no evidence of sporing. This contradicts their statement as to their accepting the position of Guarnieri, who described in the vaccinated cornea parasites undergoing simultaneous subdivision into radial segments, a process which is accepted as sporing in the well-known parasites of malaria. S. Monckton Copeman[1] refuses to accept experiments on rodents, because in these animals vaccinia does not cause exactly the same lesions as it does in man. Now, since many observations serve to show that vaccinia is but modified variola, the following observation made by the writer seems to render such objections valueless. Some variola lymph kindly supplied by Dr. F. J. Ricketts was rubbed into a rabbit's ear. Seven days later the animal was killed. The scratch healed, but a scab formed over it and spread for two millimetres on each side of the scratch. Examined histologically and compared with scabbed vaccination lesions from a child's arm, and with variola lesions from a man who died of smallpox, the lesion on the rabbit's ear was found to present characters in every way corresponding to those in the human subject. And, moreover, a smallpox lesion does not always assume a pustular character in man. It may be confidently

[1] Copeman, 'Brit. Med. Journ.,' 1894, vol. ii, p. 157.

asserted that in vaccine lymph there is a protozoon which determines in the cornea of rodents a definite series of pathological changes, and that the study of variola and vaccinia[1] in man shows that a morphologically identical protozoon is present. The early intra-cellular stage of the parasites of the vaccinated cornea and human variola goes to show that they are probably both necessary parasites. The conclusion is that the parasites are identical in the two conditions. There is, in the writer's opinion, as much evidence that vaccinia and variola are caused by the protozoon described above as that malarial fever is caused by the protozoa first described by Laveran.

It has been mentioned above that Doehle described nucleated flagellate bodies in the blood of persons suffering from primary syphilis, a disease which in some aspects has a considerable resemblance to the specific fevers, and, as is suggested by the vulgar name of the disease, it is sometimes a difficult matter to distinguish between pustular syphilitic lesions and those of smallpox. When some syphilitic sores of the skin and of mucous surfaces covered by stratified squamous epithelia are examined microscopically they frequently present epitheliomatous characters, long processes of epithelium being found to penetrate deeply into the subjacent supporting connective tissue. It becomes thus a matter of interest to compare syphilitic lesions with those of smallpox and cancer. When spreading primary or secondary lesions are excised and at once placed in Foà's solution, hardened in the usual way, and cut into sections, these present appearances closely resembling those of the vaccinated cornea and some cancers. In Plate VIII, fig. 8, is depicted a portion of the superficial epithelium about three millimetres from the edge of a primary sore. At *a*, *a*, within the nuclei of epithelial cells, are bodies resembling the young parasites of vaccinia; whilst at *b* are shown dense homogeneous bodies closely resembling some of the parasites of cystic ureteritis. At *c* is a larger body similar to those marked *b*, except in that it has within a central clearing a nuclear bar which stained blue with hæmatoxylin. At *d*, *d*, are other bodies showing radiating strings of chromatin granules. At *f* is another of these bodies, presenting a central dense body around which a hollow sphere of granules, some of which stained blue with

[1] For further observations on this subject see Jackson Clarke, 'Med. Press and Cir.,' 1893, vol. ii, p. 233; 'Brit. Med. Journ.,' 1894, vol. ii, p. 869; 'Lancet,' 1895, vol. i, p. 139; 'Centralblatt für Bakt.,' 1895, B. xiii, p. 300.

acid hæmatoxylin, has formed, recalling a form of the parasites in cystic ureteritis. The appearance shown at *g* in fig. 8 is strongly suggestive of sporing. The reticulated bodies, as at *e*, are produced by a change in the denser structures, and seem to precede a subdivision into minute bodies similar to those represented at *g*. In a previous article the writer [1] first made the comparison between the parasites of variola and the bodies now under consideration. At that time he had not been able to make out karyokinetic processes in the bodies, and consequently was unable to express a definite opinion as to their nature; but on comparing structures such as those represented in figs. 3—6 with those shown in *d* and *d'*, fig. 8, the writer is of opinion that the syphilitic lesions contain parasitic protozoa akin to those of variola and vaccinia.

Material obtained from the mortuary twenty-four hours or longer after death loses many of the appearances which are present when it is fixed whilst still warm and alive. In spite of this, some gummata of the liver present a few dense structures comparable with those shown at *b* in fig. 8, as well as less definite bodies which are comparable with the reticulated formations shown in fig. 8, as at *e*.

In conclusion it may be stated that there is ground for further research, and it may prove that the common infective fevers as well as syphilis produce lesions long after the first effects of the infection have passed away—lesions comparable to the tertiary lesions of syphilis. It may even prove that among such lesions are some of those known as cancer and sarcoma. Further, it may prove that when a chronic syphilitic lesion assumes a cancerous character, this is but a modification of the syphilitic process.

October 16th, 1894.

[1] Jackson Clarke, 'Centralblatt für Bakt.,' 1895, B. xiii, p. 300.

2. *Absorption and metabolism in obstruction of the pancreatic duct.*

By Vaughan Harley, M.D.

It being of particular interest to investigate what changes occur in the absorption of food as well as metabolism in that diseased condition in which so important a juice as the pancreatic is prevented from entering the alimentary canal, I venture to bring forward the following facts:

As early as 1832 Bright[1] stated that in diseases of the pancreas large quantities of fat were found in the stools.

In 1862 Dr. George Harley[2] pointed out that the solidification of oil taken by the mouth in the stools was a reliable sign of occlusion of the pancreatic duct.

Experimentally von Mering and Minkowski[3] showed that in dogs in which the pancreas had been entirely extirpated, and the animals thus rendered diabetic, large quantities of fat occurred in the stools.

Subsequently Abelmann[4] investigated the metabolism of dogs from which the pancreas was either partially or totally extirpated; in this research he showed that von Mering's and Minkowski's observations were perfectly correct, and that animals thus operated on were unable to absorb as much fat as normal animals. In fact, while olive oil was entirely unabsorbed, milk fat was only absorbed in small quantities. He further found that while the absorption of proteids was very much diminished, carbohydrates were not absorbed in the normal quantity.

In September, 1893, while working in the Physiological Laboratory of Turin, I found that in a dog from which almost the entire pancreas had been removed, the body weight fell from 8·5 kilos. to 5·05 kilos. in the space of two months; at the same time the urine contained no sugar. The fæces of all the animals that I have experimented upon

[1] Bright, 'Med.-Chir. Trans.,' 1832.

[2] George Harley, "Complete Obstruction to the Bile and Pancreatic Ducts," 'Trans. Path. Soc.,' vol. xiii, 1862, p. 118.

[3] Von Mering and Minkowski, 'Arch. f. exp. Path. u. Pharm.,' vol. xxvi, 1889, p. 371.

[4] Abelmann, 'Inaug. Diss., Dorpat,' 1890.

had a most peculiar foul smell; this fact, trifling as it may appear, is nevertheless of importance, as I have found it invariably to occur when the dogs were fed on raw meat, which even often reappeared in the stools apparently unaltered; when fat was given it also reappeared in large quantities in the stools. Before describing a human case, I shall give, for the purpose of comparison, the results of the analyses in a dog which lived for two months after an almost total extirpation of the pancreas. The dog lost considerable flesh, although the urine at no time contained any sugar, for which it was repeatedly examined by fermentation, phenyl-hydrazine, and Fehling's tests. The urine, on the other hand, contained not only acetone, but also aceto-acetic acid in small quantities. The fæces always contained undigested food, and had the remarkably foul odour above described.

TABLE 1.—*Showing the absorption of nitrogen in a dog in which the pancreas had been almost extirpated; the animal lost flesh considerably, but the urine never contained sugar, owing to some very small portions of the tail of the pancreas having been left.*

Day.	Weight.	Food.	Urine.	Fæces.			P. cent. of N. absorbed.
	Kilos.	N. in grams.	N. in grams.	Quantity in grams.	N. in grams.	Total N. for 4 days.	
1	5·700	No food	1·945	None			
2	5·700		2·193	80·2	5·900		
3	5·500	17·618	2·260	60·3	3·100	14·469	17·88
4	5·450		3·013	66·4	2·221		
5	5·300	No food	1·147	67·0	3·248		
6	5·150		1·520	18·7	0·644		

On the first day, as shown in Table 1, no food was given, while during the next three days the animal was given meat containing 17·618 grams of nitrogen. With the first and last meal charcoal was given to indicate how long the fæces passed, belonged to this diet; the black colour disappeared on the sixth day. The stools passed on the sixth day, which did not contain any charcoal, are therefore not reckoned in calculating the total quantity of nitrogen unabsorbed.

That even fasting animals pass fæces we know from the experiments of Voit, and that the same holds good in human beings has been further shown by observations made on various fasting individuals. The fæces passed on the sixth day correspond in all probability to

the fasting stool, which is supposed to be derived from an excretion into the alimentary tract, as described by Hermann, Ehrenthal, Bernstein, and F. Voit.

It is interesting to note that when food was given on the second morning the animal passed some of the black-coloured stools in the evening. The stools were each day collected in the morning before giving the food, but for the purpose of convenience they are entered in the above table as if passed during that day.

It is seen in Table 1 the quantity of nitrogen given in the meat was 17·618 grams, while the quantity eliminated from the alimentary canal was 14·469, consequently only 17·88 per cent. of the nitrogen given was absorbed. In reality, in all probability somewhat more was absorbed, as some of this nitrogen found in the fæces would correspond to that which is normally eliminated in a fasting animal.

In the analysis of the urine we find that during the three days on which the animal was fed the quantity of nitrogen eliminated was almost uniform; at the same time the animal could not be said to be at nitrogen equilibrium, as it continuously lost weight.

The quantity of nitrogen eliminated in the urine and fæces was more than was really given to the animal in the diet, so that some of the nitrogen contained in the urine was derived from a breaking down of the tissues themselves, and hence the source of the loss of weight.

The loss of weight in this experiment can be partly explained by the diminished absorption of food from the alimentary canal, but this alone does not seem a sufficient explanation.

Abelmann found that when he removed the entire pancreas, from 22 to 58 per cent. of the proteids given to his dogs was absorbed, while when the gland was only partially removed, the absorption ratio rose from 40 to 83 per cent.

It is therefore shown by these experiments that the absorption of proteids from the alimentary canal is markedly affected in pancreatic disease, and that, as will be seen later, it is in reality not much less affected than the absorption of fat which has hitherto been generally believed to be, if not the only, at least the principal kind of food affected.

If we now turn to the effects on the absorption of mutton fat produced by extirpation of the pancreas in dogs, we find that the

proportion varies with the period which has elapsed since the operation.

TABLE 2.—*Showing the absorption of mutton fat, after almost complete extirpation of the pancreas; one twentieth of the tail of the pancreas being left. The experiment begins fifteen days after the operation.*

Day.	Weight.	Fat in food.	Fæces.		Per cent. absorbed.
	Kilos.	Grams. Total.	Quantity. Grams.	Fat. Grams.	Fat.
1	7·670	36·40	19·3	26·71	26·62
2	7·600		106·0		
9	6·850	75·81	116	47·05	37·94
10	6·830		174		
11	6·720		53		
15	6·500	46·95	none	44·885	4·4
16	6·350		9·620		
17	6·250		8·037		
18	6·100		9·914		
19	5·900		10·936		
20	5·900	no food	6·378		

Charcoal was given as indicator in this case in the same manner as previously described. In the above table it is seen that in the first two periods of two and three days respectively 26·62 to 37·94 per cent. of the fat given was absorbed, the largest absorption taking place when the largest quantity of fat was given; while during the third period, when the animal was in a weaker condition, and would not take so much food, the quantity of fat absorbed was much less, being only 4·44 per cent.

Abelmann found that after the total extirpation of the pancreas in his dogs no fat was absorbed, whereas in partial extirpation from 25 to 59 per cent. of the quantity given was absorbed. Milk fat, however, proved an exception to this rule, for he found in total extirpation from 28 to 33 per cent. of the milk fat was absorbed.

In other experiments in which I have endeavoured to ascertain the amount of fat absorbed from the intestinal canal of dogs after either partial or total extirpation of the pancreas, I have in all cases found a very marked decrease from the normal amount of fat absorbed, but the above samples are the best of them.

In a paper on the absorption of milk fat recently published in the 'Journal of Physiology,'[1] I showed that while a normal dog fed on milk absorbs from 21 to 46 per cent. of the fat given in seven hours, in a dog from whom the pancreas had been entirely removed no absorption of milk fat whatsoever could be definitively found to have occurred in this space of time.

With these preliminary remarks I will proceed to narrate an exceptionally characteristic case of pancreatic duct obstruction in which, through the kindness of Dr. Auld, of Wimborne, I had the opportunity of making a series of analyses while the patient was on a fixed diet.

The patient was a boy aged thirteen, who, after recovering from scarlet fever, was attacked by severe gastritis in February, 1894. He had previously suffered from an attack of acute nephritis. Two months after the scarlet fever an offensive smell was noticed by persons coming near him, and this was found to be due to an oily excretion which collected on the seat of his trousers.

On examining his fæces Dr. Auld found them of a light brown colour, soft, and containing undigested food. A large quantity of oil floated about them; on cooling, the oil solidified into a hard beeswax-like cake. A motion followed immediately upon each meal, associated with pain in the rectum, which was found to be due to an inflammatory congestion of the mucous membrane and an appearance of villous growths.

When Dr. Auld brought the boy to Dr. George Harley on the 4th October, 1894, he was passing every tenth day or so a large quantity of more or less bright orange-coloured oily fluid, which immediately gave rise to the supposition that he was labouring under some form or another of pancreatic disease. His abdomen was consequently carefully examined, without any pain, tenderness, or swelling of any kind being found in the pancreatic region. The oily stools were, however, so characteristic of the absence of pancreatic juice that he was put under the appropriate treatment for that affection.

When I examined the urine in June it contained 1·51 per cent. of urea, no acetone or aceto-acetic acid, nor any sugar. At this time the boy weighed 78 lbs. Some of the oily matter he passed was sent to me for analysis in July, and I found it consisted of small quantities of neutral fat and soap, and large quantities of fat acids.

[1] Vaughan Harley, 'Journal of Physiology,' vol. xviii, 1895, p. 1.

During December, 1894, all medicines were stopped, and he was placed for four days entirely on milk diet.

On this diet the fæces were of a yellowish-white colour, and of the consistence of a soft cream cheese. They contained a few yellowish lumps like beeswax, and smelt like extremely bad cheese. They contained a small quantity of bile acids and urobilin. From this, and the absence of any jaundice or bile in the urine, the bile-duct was evidently pervious. The results of a quantitative analysis are given below in a tabular form.

TABLE 3.—*Boy, age thirteen, suffering from probable obstruction to the pancreatic duct.*

Date.	Weight.		Milk diet.			
	Kilos.	lbs.	Quantity. c.c.	N. Grams.	Proteids. Grams.	Fat. Grams.
December 13	37·8	84	Ordinary diet	—	—	—
„ 14	37·8	84	3976	13·12	82·5	196·85
„ 15	37·6	83·5	3976	13·12	82·5	196·85
„ 16	37·4	83	3976	13·12	82·5	196·85
„ 17	37·4	83	3976	13·12	82·5	196·85
„ 18	37·6	83·5	Ordinary diet	—	—	—
„ 19	37·8	84	Ditto.	—	—	—

Date.	Urine.				Fæces.			
	Quantity c.c.	Re-action.	Sp. gr.	N. Grams.	Quantity. Grams.	N. Grams.	Proteids. Grams.	Fat. Grams.
December 13	—	—	—	—	—	—	—	—
„ 14	1680	acid	1007	10·017	—	—	—	—
„ 15	1960	acid	1007	10·272	257·84	1·149	8·931	19·98
„ 16	2240	acid	1008	12·096	688·02	5·631	35·194	149·72
„ 17	1960	acid	1009	10 027	576·40	4·859	30·368	137·87

The analysis of the four days given in Table 3 show that, as far as the urine is concerned, the quantity of nitrogen excreted is comparatively equal. During the first two days on a milk diet he lost a pound in weight (14th and 15th), the next two days (16th and 17th) his weight remained the same, and the nitrogen eliminated in the fæces and urine was practically the same. In calculating the absorption and metabolism in his case the results of the 16th and 17th of December only are employed.

As regards the absorption of nitrogen and fat from the alimen-

tary canal I will compare the average results of these two days with that found by Rübner[1] in a healthy man on a milk diet.

TABLE 4.—*Comparing the quantity of nitrogen and fat absorbed from the alimentary canal on milk diet in a healthy man (Rübner) and the patient suffering from probable obstruction to the pancreatic duct.*

Condition.	Milk contained			Fæces contained				Absorbed.			
	Quantity. c.c.	N. Grams.	Fat. Grams.	N Grms.	%	Fat. Grams.	%	N. Grams.	%	Fat. Grams.	%
Health	3075	19·4	119·9	1·5	7·7	6·7	5·6	17·9	92·3	112·9	94·4
Pancreatic obstruction	3976	13·12	196·85	5·25	40·0	143·80	73·05	7·87	60·0	52·05	26·95

In Table 4 it is seen that in the healthy man the fæces contained 1·5 grams of nitrogen, *i. e.* 7·7 per cent. of the total nitrogen given, consequently 92·3 per cent. of the total nitrogen given had been absorbed. When we compare this with the unhealthy boy's case it is seen that in an average of two days, during which the patient was on nitrogen equilibrium, the fæces contained 5·25 grams of nitrogen, so that 40 per cent. of the total nitrogen given was eliminated in the fæces, and 60 per cent. only had been taken into the system to be made use of in metabolism.

As regards the fat, in Rübner's healthy man only 6·7 grams were excreted in the fæces, *i. e.* 5·6 per cent.; whereas in our boy's case (of probable obstruction to the pancreatic duct) the fæces contained 143·80 grams of fat, *i. e.* 73·05 per cent.,—so that only 26·95 per cent. of the fat given was absorbed from the intestines and rendered capable of being made use of in metabolism.

The two cases seem fair ones to compare, as the quantity of food given was about equal in both; the only difference being that while the boy received a larger quantity of fat in his diet, Rübner's received a larger quantity of nitrogenous food.

Turning now from what the results given in these tables show as regards absorption to the actual nourishment of our case, it may be as well to express it in the form of calories,—that is to say, the quantity of heat necessary to raise one kilogram 1° C.

[1] Rübner, 'Zeit. f. Biol.,' 1879, vol. xv, p. 115.

From Rübner's[1] calculations we obtain the following results:

1 gram proteid converted into urea, uric acid, ammonia, &c. . = 4·1 calories.
1 gram fat converted into carbonic acid and water . . = 9·3 „
1 gram carbohydrate converted into carbonic acid and water . = 4·1 „

In metabolism experiments it is customary to reckon that 100 grams of proteids contain on an average 16 per cent. of nitrogen, so that if we multiply the quantity of nitrogen by 6·25 we get the quantity of proteid it represents.

As in our boy's case we did not estimate the quantity of carbohydrates, an average of the other analyses has been taken.

If the quantity of food given to our patient be converted into calories we find—

	Grams.		
Proteid . . .	82·51 × 4·1	=	338·25 calories.
Fat . . .	195·85 × 9·3	=	1830·71 „
Carbohydrate . .	198·75 × 4·1	=	814·87 „
			2983·83 „

Consequently the boy had received in his diet 2983·83 calories, and as he weighed 37·4 kilos. (78 lbs.) during the days of observation, he received 78·9 calories per kilo. in his food.

Numerous observers have found that a normal man on an average requires from 30 to 40 calories per kilo. to maintain his weight according to the muscular work he is doing, and that 32 calories per kilo. is sufficient for most people doing an ordinary amount of muscular exercise. So our boy received in his diet twice the quantity of nourishment necessary to maintain his bodily weight, and yet, notwithstanding this, he lost weight.

The loss of weight is partly explained by the greatly diminished absorption of food which we found by the analysis of the fæces to have occurred, from which is seen the importance of analysing both the urine and fæces before formulating a diagnosis in a case like his.

If from the quantity of food given we now subtract the quantity we found by analysis to have remained unabsorbed from the alimentary canal, we get the following results. From the carbohydrates having in our case not been calculated, I have taken as my standard the results found by Abelmann. He found in partial extirpation of the pancreas that only 71·78 p. c. of the carbohydrates given in the food were absorbed from the intestines.

[1] Rübner, 'Zeit. f. Biol.,' vols. xix—xxi, 1893–5.

Consequently in the case of the boy we find—

	Given.	Unabsorbed.			
Proteid .	82·5	− 32·75 =	49·72 × 4·71	= 203·85	calories.
Fat .	196·85	− 143·80 =	53·05 × 9·3	= 493·37	„
Carbohydrates	198·75	− 43·00 =	155·75 × 4·1	= 638·58	„
				1336·80	„

From these calculations it is seen that, instead of the boy absorbing into his system 2983·83 calories, he only absorbed 1336·80 calories; that is to say, only 36 calories per kilo.

On turning to Table 3 we see that he weighed 37·8 kilos. while on ordinary diet. On the first day of milk diet (Dec. 14th) his weight remained the same, while on the third day (Dec. 15th) it fell to 37·6 kilos., and on the fourth day (Dec. 16th) to 37·4 kilos., and remained so (on the 17th); whereas on resuming ordinary diet (on the 18th) it rose to 37·6 and (on the 19th) to 37·8 kilos.

The results of our analysis show that during the boy's milk diet, while taking a large quantity of food, he only absorbed a small part of it, but at the same time he absorbed as much as 36 calories per kilo., and in spite of this he lost weight; from which it appears, that although from 32 to 34 calories per kilo. per diem would have been ample for him to keep up his body weight if in health, it was insufficient under the abnormal circumstances under which he laboured.

We must, therefore, conclude that not only was there in his case a disordered absorption of food from the alimentary canal, but there was also a defective assimilation of what was absorbed.

The following table shows the changes the milk fat underwent during its passage through the alimentary canal in the case of the boy under observation.

TABLE 5.—*Showing the composition of the fat in the fæces of a boy suffering from probable obstruction of the pancreatic duct, and the composition of fat in the milk given.*

	Total fat.	Neutral fat.		Free fat acids.		Fat acids as soap.		Cholesterin.	
		Total.	p. c.	Total.	p. c.	Total.	p. c.	Total.	p. c.
Milk	196·85	191·000	97·02	5·690	2·89	0·121	0·06	0·160	0·08
Fæces :									
16th	149 72	59·051	39·44	54·348	36·30	26·270	17·55	10·051	6·71
17th	137·87	49·149	35·65	61·355	44·50	16·135	13·15	9·231	6·70

In Table 5 we find the quantity of neutral fat taken has diminished from 191 grams to 59·051 and 49·149 grams respectively, so that a large quantity of it has either been absorbed during its transit along the alimentary canal, or, in spite of the absence of the pancreatic secretion, it has been broken up into fat acids, &c.

In the milk given, although there were only 5·690 grams of free fat acids, yet 54·348 and 61·355 grams were found in the fæces. From this it is seen that we can at least account for the disappearance of part of the neutral fat from the alimentary canal by its having been split up into free fat acids in its passage along the intestines, seeing that they were increased tenfold.

As regards soaps, their quantity in the milk was only 0·121, while in the fæces it was no less than 26·270 and 18·135 grams.

Thus, in spite of the pancreatic secretion being absent, the neutral fats have not only been split up into free fatty acids and glycerine, but the fat acids have been able to find in the intestines an alkali wherewith to form soap.

The amount of cholesterin in the milk was only 0·16 grams, while the quantity found in the fæces was 10·051 and 9·231 grams respectively. This increase cannot be regarded as being due to a chemical change in the milk, but is in all probability due to a quantity of cholesterin being eliminated by the bile, or perhaps due to intestinal secretion.

That the above chemical changes should have taken place in the milk fats during their sojourn in the alimentary canal in the boy might argue against the idea of the absence of the pancreatic juice really occurring, had not other experiments shown that the same thing occurs in animals when we have undoubtedly not only hindered the flow of pancreatic juice into the intestines, but removed the entire gland.

I shall now give a table showing the results found in the case of the boy with supposed obstruction of the duct, and those I found in the fæces of dogs which had had their pancreas extirpated.

TABLE 6.—*Showing average composition of fat in the fæces of a normal dog on milk diet, compared with one from which the pancreas had been removed, placed side by side with the average result obtained in the two days' analysis in the case of the boy supposed to be suffering from obstruction of the pancreatic duct.*

	Total fat.	Neutral fat.	Free fat acids.	Soap as free fat acid.
	p. c.	p. c.	p. c.	p. c.
Normal dogs	100	34·17	58·65	7·19
Pancreas extirpated . . .	100	33·90	55·25	10·84
Boy with obstructed pancreatic duct	100	37·55	40·40	15·35

It is seen in Table 6 that, if we take the total ether extract of the fæces as representing 100, the quantity of neutral fat contained in it is in normal dogs 34·17; while in those from whom the pancreas was artificially removed, as well as in the boy, we get respectively 33·90 and 37·55 per cent.

In the normal dogs, while the free fat acids are 58·65 per cent., in dogs without the pancreas and in the boy they are respectively only 35·25 and 40·40 per cent. On the other hand, the soaps as represented as free fat acids are in normal dogs only 7·19 per cent., while after pancreatic extirpation they are increased to 10·84 per cent., and in the case of the boy they are 15·35 per cent. Consequently these cases very closely resemble each other in as far as neutral fat and fat acids are concerned. In fact, from merely the analysis of neutral fat and fat acids one would be unable to say whether the pancreatic juice was present or absent. In the case of the soaps we see that there is a slight tendency to excessive formation, or, I should rather say, an excessive excretion of soap in the stools when the pancreatic juice is hindered from reaching the intestines. This may be regarded as most remarkable, since when the pancreas is either entirely removed, or its secretion is merely prevented reaching the alimentary canal, there is either a non-absorption or a greatly diminished absorption of fat from the intestines.

According to former ideas, this non-absorption would have been attributed to the fat-splitting-up action of the pancreatic juice no

longer coming into play, and from the fats not being broken down, no emulsification taking place, and therefore no absorption.

In the case of the dogs, as well as the boy, it is seen from the above analysis that, in spite of the absence of the fat-splitting ferment of the pancreas, the fats during their passage through the alimentary canal are, by some means or another, broken up, and not only form free fat acids, but also soaps. Yet, in spite of this fact, they are for some reason or another not absorbed.

It may be as well to try and explain by the light yielded by the analyses what is the probable state of affairs in the case of the boy.

The results of the analyses show us that large quantities of fat appeared in the stools, no less than 73·05 per cent. of the total quantity given. And, still further, that the proteids excreted in the fæces are far above the amounts normally found, so that 40 per cent. of the nitrogen given has been excreted in the stools.

The foul odour of the stools which was a constant feature in the case of my dogs, was at the same time specially marked in the case of this boy, so that it is worthy of note. For this fact led me to believe that for some reason or other the pancreatic secretion was not reaching the alimentary canal. Yet that this is not due to an absence of the pancreas, or its destruction by disease, is shown by the fact that at no time was sugar present in the urine, and therefore the evidence is only in favour of an occlusion of the pancreatic duct.

Moreover, the morbid anatomical condition which has led to this obstruction appears to be some chronic inflammatory stricture of the duct. For as the analyses have shown us that bile reached the intestine, the common bile-duct must have remained free. We cannot therefore suppose that the common orifice of the bile and pancreatic ducts can even be partially obstructed. For seeing that bile and pancreatic juice are secreted at the same pressure, namely, 260 mm. of water, it is hardly possible that one only should be hindered reaching the intestines if both were implicated. As the pancreas is, however, known to have very frequently accessory ducts, and in some rare cases the ducts enter the duodenum separately from the common bile-duct, the accompanying diagram will, I think, assist in explaining what seems to have occurred.

As the commonest form of accessory duct is one entering the duodenum nearer the stomach (*d*), and we know from the history of the case that the boy suffered from gastritis previous to the appearance of the foul-smelling motions; it is conceivable that

either the main duct of the pancreas (*a*) may be absent, and only the accessory duct present, and if so that an inflammation spreading from the stomach down the duodenum may have involved it, without having extended far enough to have likewise involved the orifice of the common bile-duct (*c*). In this way there might be complete obstruction of the pancreatic and not of the bile duct. Or

Fig. 17.

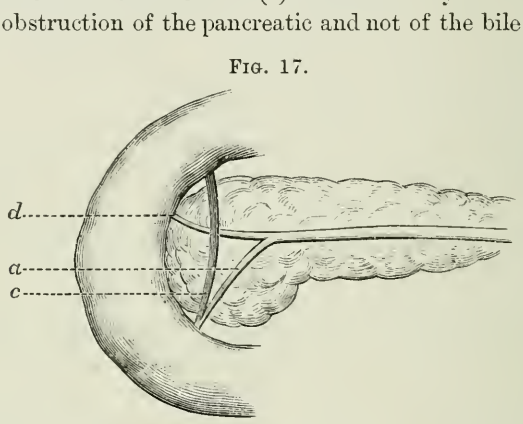

Diagram to show how an accessory pancreatic duct may open away from the main duct, the latter opening as usual into the duodenum with the common bile-duct.

we may even imagine that both the main (*a*) and the accessory pancreatic duct (*d*) are present, and that the inflammation has extended up the accessory duct so far as to involve the main duct also. The diagnosis being obstruction of the pancreatic duct, and it being impossible to give any drug which could with any probability cure such morbid condition, it became necessary to consider what could best be done in the case, and the following was arrived at.

Abelmann having found that feeding dogs after removal of the pancreas with raw pancreas caused an increased absorption of fat, I recommended Dr. Auld to give the boy raw pancreas. From February 28th until March 10th, 1895, this was done, and during this time the quantity of oil passed with the stools was very markedly decreased, although it did not entirely disappear. The foul smell was also absent, but as the boy was taking at the same period calomel and potassium benzoate, both powerful intestinal antiseptics, we can hardly put this last fact down to the effect of the raw pancreas. The parents then refused to continue the pancreas treatment, in consequence of the boy's having been ill after eating

a supposed bad pancreas. And since then oil has again been present off and on in the stools, and Dr. Auld has unsuccessfully endeavoured to get the parents to allow the boy to resume taking the pancreas.

During the last four months, what with careful dieting and treatment, the patient has increased 2 lbs. in weight.

In conclusion it may be said, from the results of the analyses in this boy's case, and of the dog's from which the pancreas was either partially or completely removed, that the pathology of the absence of pancreatic juice from the intestines is much more complicated than what was formerly supposed. Seeing that not alone was there diminished absorption of fat, so that only 26·95 p. c. of the total given was absorbed in the case of the boy, and from 4 to 37 p. c. in the case of the dogs I experimented on, but at the same time the proteid absorption was greatly diminished, so that in dogs only 18 p. c. and in the boy 60 p. c. was absorbed.

The results of the analyses of the fæces in the boy show that the non-absorption of fat in pancreatic duct obstruction is not due, as is generally supposed, to any want of the splitting up of the neutral fat into fat acids, glycerine, and the formation of soaps; but, on the contrary, is dependent on some as yet unexplainable cause.

When the quantity of food given is increased to above the quantity necessary for a healthy individual, so that the quantity absorbed may be equal to the number of calories necessary to maintain the body weight in health, it is nevertheless owing to improper metabolism insufficient to keep the body weight up to the normal standard when the pancreatic duct is obstructed. By still further increasing the quantity of food, however, the body weight can be maintained, and not only so but we see that, in the case of this boy, careful dieting, together with treatment, not only kept up his body weight, but even sufficed to cause a gain of 2 lbs. in the space of four months.

Appendix.

Methods employed in this investigation.—With the first meal a quantity of charcoal was given, so that the fæces of that meal might, by their dark colour, be distinguished from those belonging to the previous one. With the last meal charcoal was also given for a similar purpose.

In the case of the dogs, they were given charcoal but otherwise kept fasting before commencing the dieting.

The quantity of nitrogen was always estimated by the method of

Kjeldahl. And in the case of the food and fæces at least four samples were analysed, and the quantity of nitrogen calculated from the average. In the case of the urine, on the other hand, two analyses were found sufficient.

In analysing the fats some of the fæces were first extracted with alcohol and then with ether in a Soxhlet's extractor, and the two extracts, after being dried, were again treated with absolute ether, and the extract then weighed. The residue, after complete extraction with ether, was heated with dilute hydrochloric acid, dried, and again extracted with ether, so as to obtain the fat acids liberated from the soaps. The quantity found in the first ether extract, together with the soap, is in the above tables termed total fat.

In order to separate the neutral fat, fat acids, and cholesterin, the first ether extract was warmed with a solution of sodium carbonate, to saponify the free fat acids, and, after drying, the neutral fat and cholesterin were extracted with absolute ether. The free fat acids were calculated by the loss of weight.

The new ether extract was then treated with a freshly prepared alcoholic solution of metallic sodium (NaOH), and, after drying, extracted with ether to separate the cholesterin. It was often found in practice necessary to repeat the process several times before pure cholesterin could be obtained, and in all cases it was repeated until there was no longer any loss of weight. By subtracting the quantity of cholesterin from the neutral fat and cholesterin the quantity of neutral fat was obtained.

In order to study the absorption of milk fat and proteids in the case of the boy a quantity of milk was sterilised, and a litre of it analysed to form a standard of comparison. The method of analysis was exactly similar to that employed in the case of the dogs.

May 21*st*, 1895.

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3. *Extensive perirenal hæmorrhages.*

By Francis H. Hawkins, M.B.

The specimen now shown is one of extensive perirenal hæmorrhage. The left kidney is smaller than the right, and is embedded in a mass of blood which has in parts become organised.

The hæmorrhage, while surrounding the kidney, is more extensive over the anterior surface and the upper, outer, and lower border, being smaller in mass over the posterior surface. The capsule strips off easily, and has no communication with the hæmorrhage. The lower part of this hæmorrhagic mass communicates by a narrowed neck with a hæmatoma, which was situated on the inner surface of the transversalis.

The right kidney, apparently somewhat enlarged, shows over the anterior surface a similar though much smaller hæmorrhagic mass, which is also entirely outside the fibrous capsule of the organ.

The other pathological conditions were cardiac hypertrophy and dilated mitral orifice, with retraction and thickening of the mitral cusps. There were no vegetations or fungating masses on the valves. Also an infarct in the anterior border of the right lung, recent pleurisy, and an infarct in the spleen. There were also numerous small hæmorrhages in the bladder.

The patient from whom this specimen was removed—a man aged 31 years, who had always been a sober and steady man—was admitted into the Royal Berkshire Hospital, under my care, on September 11th, 1894, with peripheral neuritis, œdema of legs, and mitral regurgitation; and there was, in addition, a swelling which was firm and immoveable, situated about one inch above the left superior iliac crest in the continuation of the mid-axillary line: there was also some resistance over the left renal region. I must also add that there was no bleeding from the gums, no epistaxis or signs of purpura or scurvy. There was some slight hæmoptysis, which was attributed to the pulmonary œdema. The history of the case previous to coming under my care is as follows:—Six years ago the patient had rheumatic fever, but remained quite well until about fourteen weeks before admission, when he had a second attack of rheumatic fever, and shortly after its onset, in addition to the peripheral neuritis, he had acute pains in the abdomen—shooting in character, but not confined to any particular part. I am told by my surgical colleague, Mr. W. J. Maurice, who had seen the case some time before he was transferred to my care, that there had been a fluctuating swelling over the region of the left kidney, as also a similar swelling in the right lumbar region, which were neither painful nor tender. The swelling above the left iliac crest, however, had been red, tender, and distinctly fluctuating. There had also been some extravasations of blood over the back.

Remarks.—I have brought this specimen before the Society because, in looking through works on pathological anatomy, as also treatises on medicine, I cannot find any description of or reference to any such condition. Then the specimen is of some practical interest, as perirenal hæmorrhages have in no work which I have yet read been suggested as a possible cause of a renal tumour. The cause of the hæmorrhage is in this case not quite clear. At no time was there any sign or symptom suggestive of purpura hæmorrhagica or scurvy, otherwise I should be inclined to suggest such a condition as the cause. Failing this, I would suggest—although I have no proof of such—that a lumbar artery or arteries became blocked, small aneurisms formed, ruptured, and produced the hæmorrhage. *November 6th*, 1894.

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4. *Actinomycosis of the cheek.*

By H. J. Waring, M.S.

Actinomycosis which is limited to the tissues of the cheek is a rare disease in man. In the majority of cases in which the cheek is involved the disease commences in connection with the upper or lower jaw, or in or around the base of a carious tooth. In the following case the pathological process appears to have been primary in the tissues of the left cheek, and not to have arisen in connection with a similar affection of the jaws.

Case 1.—G. W—, aged 20, by occupation a laundryman, was first seen on March 9th, 1895, when he was suffering from a localised swelling of the left cheek. The swelling was first noticed by the patient in November, 1894, after which date it gradually increased in size, and in the middle of December it burst internally into the mouth, a certain amount of purulent matter being evacuated. After the rupture the swelling for the most part disappeared. In January, 1895, the swelling again became apparent in the same situation, and since then it has slowly increased in size. Recently the skin over it has become reddened.

In April, 1894, the patient was in the London Hospital on account of a swelling of the right cheek immediately below the orbit. This

was incised, purulent matter evacuated, and according to the account of the patient it was called a "chronic abscess."

The patient suffered from diphtheria when he was five, otherwise he has had no other illnesses. He has never worked among animals of any kind, nor has he had to do with grain or straw.

Condition on admission.—The patient is a strong and fairly healthy working man. Upon the outer side of the left cheek, a short distance behind the angle of the mouth, there is a hard and irregularly shaped swelling about the size of a half-crown piece, which involves the whole thickness of the tissues of the cheek. The skin over it is reddened and scaly, and upon the internal surface there are several small soft areas which fluctuate. Here also are to be seen a few small puckered scars which appear to be the remains of former communications with the oral cavity. These scars are situated around the opening of the duct of the parotid gland. This duct appears to pass through the swelling, but there does not seem to be obstruction to the lumen of the duct, as saliva passes along it into the mouth without any difficulty. Underneath the ramus of the lower jaw on the left side there are one or two enlarged lymphatic glands, and also the parotid lymphatic glands of the same side are distinctly larger than normal. No other signs of disease were detected in any of the viscera. The temperature was normal. A small incision was made over the largest of the fluctuating spots upon the internal aspect of the cheek. From this there exuded a purulent fluid in which were noticed numerous small oval-shaped bodies which were whitish in colour. Under the microscope these were found to have the typical structure of the actinomycotic fungus. In addition *Staphylococcus pyogenes aureus* was found to be present. These were demonstrated by Dr. Kanthack, of St. Bartholomew's Hospital, who kindly examined the fluid for me.

After the diagnostic incision had been made on the inner aspect of the cheek the swelling diminished somewhat in size. A definite diagnosis of actinomycosis having been made, the patient was advised to come into the hospital and have the disease locally removed. This he consented to, and the following operation was done a few days later. During the interval before the operation the incision on the inner aspect of the cheek quite closed up, and the swelling again increased in size, chiefly on the outer surface. The patient was anæsthetised, and an oval piece of skin which comprised nearly the whole of the reddened area was removed. The

underlying tissues, which were very much infiltrated, were then thoroughly scraped with a sharp Volkmann's spoon, care being taken to avoid the duct of the parotid gland. In this way the involved tissues were freed from the disease as far as possible. The infiltration extended upwards for some distance, but no dead or diseased bone was met with, and in no place could it be seen that the inflammatory process had extended to or involved the jaw. The mucous membrane lining the cheek was left intact, as, if any portion had been removed, the part which surrounded the aperture of the duct of the parotid gland must have been taken away. After all diseased tissue had been removed the entire wound was irrigated with a solution of perchloride of mercury. Next, narrow strips of iodoform gauze upon which iodoform paste had been spread were packed into the wound, the margins of which were then approximated with strips of Leslie's strapping. On the following day the packing was removed, the wound irrigated, and then filled with iodoform paste and dressed with gauze and strapping as before. This method of dressing was repeated daily, and in a few days the wound began to close. In about three weeks after the operation the wound had completely closed and healed. The only sign which remained of the disease was a small puckered scar a short distance above and outside the angle of the mouth.

The presence of the small oval white bodies (which have been mentioned above) in the purulent matter which exuded when the diagnostic incision was made first suggested the true nature of the affection, and the succeeding microscopical examination made it clear. Usually these oval bodies have a distinct yellow coloration, but in this case there was no sign of it. From the history it is not easy to see how the patient contracted the disease. The occupation does not throw any light on the matter. In all probability the actinomycotic fungus was introduced into the mouth along with the food, and obtained an entrance into the tissues of the cheek through an abrasion upon the inner surface. The presence of carious teeth upon the affected side suggests that one of these may have been the point of inoculation, but against this there is no evidence that the jaws have been affected during any stage of the disease. In most of the recorded cases of actinomycosis of the cheek the jaws or the region of the gums have been first the seat of the disease, and then the infective inflammatory process has spread to the surrounding tissues. In these cases the lower jaw has most commonly been

the seat of the commencement of the affection. In the above case, however, the disease did not extend downwards as low as the ramus of the lower jaw, but involved chiefly the tissues of the cheek above the level of the angle of the mouth. The fungus is usually introduced into man along with some variety of grain or vegetable matter to which it clings. Actinomycotic meat has been said to be the vehicle of infection, but there does not appear to be much evidence in favour of this. The present case, however, suggests that this may have been the manner of infection. In a case which was in St. Bartholomew's Hospital a few weeks ago, in which the jaws and cheeks and the skin of the neck and chest were the seat of actinomycotic infiltration, the infection could apparently be traced to raw barley, which the patient had eaten a few weeks before the onset of the disease.

Treatment.—Iodide of potassium has been said to cure the disease when it is given in large doses. In a former case I have seen this method of treatment carried out without any improvement in the condition of the patient. In the above case there was distinct evidence of suppuration, and as the seat of the disease was easily accessible for surgical measures it was decided to remove it locally at once. Iodoform paste was used, with the idea that it would destroy any foci of disease which had not been removed by scraping, and in this case appears to have been successful. Possibly iodoform may have a destroying action on the actinomyces.

The enlarged lymphatic glands were not interfered with, as it was thought that the enlargement was due to a simple inflammatory process. The *Staphylococcus pyogenes aureus* was found in the purulent material which was removed from the swelling, which fact may have been the cause of the enlargement of the glands. It has not been shown that the fungus spreads by means of the lymphatics.

May 21st, 1895.

5. *Observations concerning the repair of tendons.*

By J. Jackson Clarke.

An explanation is due to the Society before I begin to take up some of the time of the meeting with so well-worn a subject as the repair of tendons, more especially as this matter was so lately as last session brought forward in an able paper by Mr. Tubby. My reasons will appear if the chief points to which your attention is sought are at once enumerated.

First, the histological examination was made of aseptically divided tendons forty-eight hours after division, with a view of tracing the histogenesis of the new tissue which joins the divided and widely separated ends of the tendon; secondly, the question of "Schlummerzellen," first raised by Grawitz, will be touched upon; and finally, phagocytosis, as seen in the material of repair, will be briefly examined with the view of ascertaining how far this phenomenon may be made to account for certain cell-inclusions, much discussed of late years.

The material was derived from two rabbits, in which the tendo Achillis had been subcutaneously divided on one side under antiseptic conditions. The rabbits were killed at the end of forty-eight hours, and the tendons were at once excised and placed in Foa's solution. After the usual paraffin process they were found to give satisfactory sections both of the old tendon and the soft uniting material. The latter, in the recent state, consisted of a straw-coloured firm gelatinous formation which ensheathed the separated ends of the tendon, and at its narrowest central part was about as thick as the original tendon. There was but little effused blood, which was confined to the cut surfaces of the tendon. It may here be added that in another rabbit the tendon was divided on a director through incisions in the skin and in the tendon-sheath. This rabbit was killed after twenty-four hours, and the uniting material had the same volume and naked-eye appearance as that of tendons examined at the end of forty-eight hours. No histological examination was made of the tendon at the end of twenty-four hours, the specimen being kept intact for the museum.

Sections of the structures taken at the end of forty-eight hours showed that every part of the connecting material was occupied by

young branched connective-tissue cells, which have all the characters of those described by Sherrington and Ballance, under the name of plasma-cells,—a term first, I believe, employed by Waldeyer—found within Ziegler's chambers placed under the skin in aseptic surroundings. Referring to fig. 1,[1] it will be seen that these cells are joined together by slender ramifications, and thus a meshwork is formed, the interstices of which are filled with a finely granular material. I was not able to find definite fibrin reticulum, save about the blood-clot, close to the divided ends of the tendons. The nuclei of the young branched cells everywhere showed signs of activity, and many of them contained mitotic figures, even in the part of the uniting material farthest removed from the blood-vessels.

On examining the sections to ascertain the origin of the young connective-tissue cells, as estimated by mitotic figures, they were seen to be derived from two sources. First, from the connective-tissue cells of the loose fibrous tissue of the sheath. A series of three such cells is shown in fig. 2, where one of the three conjoined cells is undergoing mitotic division. The chief source of the young cells seemed to be in the endothelial cells of the capillaries of the sheath, fig. 3, and of its interfascicular prolongations between the bundles of tendon-fibres, fig. 4. The tendon cells proper, at the forty-eighth hour, show no evidence of proliferation. This is in harmony with the experience of Tubby[2] and of Viering.[3] Sections stained with the Biondi-Ehrlich reagent showed an absence of Mastzellen.[4]

The theory of Schlummerzellen seems to have arisen with Grawitz:[5] as applied to repair of tendon it has been taken up by Viering (loc. cit.); in fat, and again by Hermann Schmidt,[6] in regeneration of the cornea, by Kruse,[7] and in the stroma of cancer by Heidemann,[8] and in the latter place opposed by Hansemann.[9] It is

[1] The various drawings mentioned in this paper were shown at the meeting of the Society.

[2] A. H. Tubby, 'Guy's Hospital Reports,' 1892, p. 109.

[3] Wilhelm Viering, 'Virch. Arch.,' 1891, p. 252.

[4] Westphal, 'Ehrlich Gesammelte Mittheilung,' 1891.

[5] Grawitz, 'Virch. Arch.,' 1889, p. 73.

[6] H. Schmidt, ibid., 1892, p. 59.

[7] Alfred Kruse, ibid., 1892, p. 251.

[8] W. Heidemann, ibid., 1892, p. 77.

[9] D. Hansemann, ibid., 1893, p. 147.

not my purpose to discuss this matter fully, but I can affirm that in aseptically divided tendons there is no evidence that new cells arise in any other way than by mitotic subdivision of pre-existing cells. The process of vacuolation of the ramifying and anastomosing young connective-tissue cells appears not to have begun at the forty-eighth hour. This process results in the formation of new capillaries, and has been fully described most recently by Yamagiwa.[1]

With regard to the leucocytes, I can fully confirm Tubby's conclusion to the effect that they take no part in the formation of new tissue in tendon repair. Two kinds of white corpuscle are readily detected in the sections (see fig. 5). The more numerous corpuscles, when stained with Biondi, present in the protoplasm orange-coloured granules and a subdivided nucleus, when stained with hæmatoxylin and eosin (Grübler's Wasserlöslich in 60 per cent. alcohol) have a purplish but not markedly granular protoplasm. These are termed by Ehrlich amphophile cells, and by Kanthack and Hardy[2] finely granular oxyphile cells. They seem to take no part in phagocytosis. Much less numerous are the lymphocytes. These are the microphages of Metschnikoff. Three of them are represented in fig. 6. One of these has engulfed one of the granular leucocytes, and the other two contain red corpuscles. Finally, the young connective-tissue cells afford ample evidence of phagocytosis. One of these cells (drawn in fig. 7) contains a granular leucocyte and a red corpuscle. In conclusion I would say that none of these appearances of phagocytosis can be mistaken for cell-infection by sporozoa. *December 18th*, 1894.

[1] K. Yamagiwa, 'Virch. Arch.,' 1893, p. 446.

[2] Kanthack and Hardy, "Wandering Cells of Mammalia," 'Journ. of Phys.,' August, 1894, p. 91. See also Everard, Demoor, and Massart, 'Ann. de l'Inst. Pasteur,' 1893, p. 165.

6. *Lymphangiectasis Intestini.*

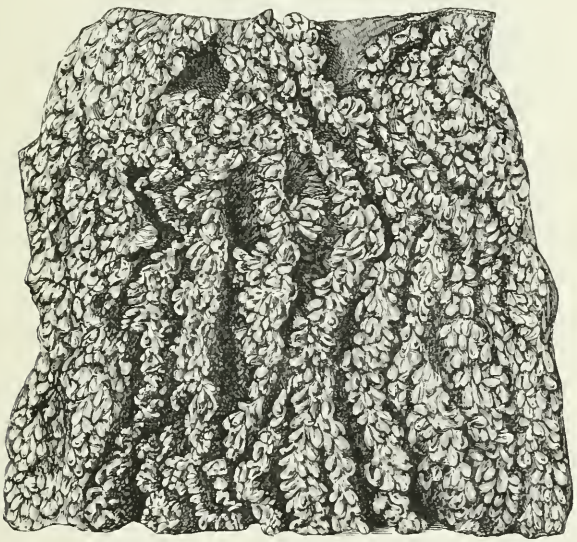
By W. H. Allchin, M.D., and R. G. Hebb, M.D.

[With Plate IX.]

F. J. A—, male aged 38, admitted into Westminster Hospital under Dr. Allchin, August 24th, 1894.

Was a policeman and previously quite healthy, except that for some months he had suffered from an increasing diarrhœa, for which he had been under treatment outside the hospital for three months, and during the same period had lost flesh considerably. He had,

Fig. 18.



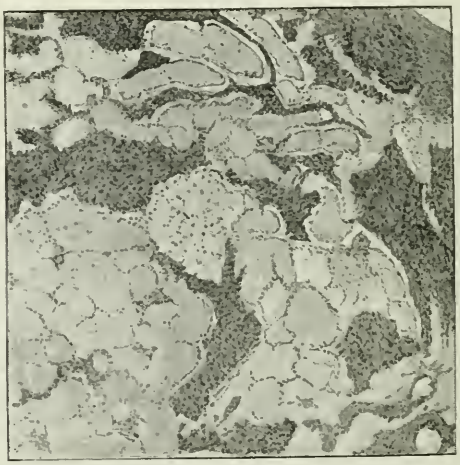
To show the naked-eye appearances of the mucous surface of the small intestine, which is covered with small villous processes produced by the distension of the lymphatics.

however, so much improved as to be able to return to duty, but after twenty-four hours profuse diarrhœa and vomiting set in, and he was admitted in a state of collapse. The motions were of a

"pea-soupy" appearance, and the vomit dark green. Temperature 101° F. Urine contained bile, but no albumen. He gradually sank, and died within twenty-four hours of coming into hospital.

The *post-mortem* examination was made twenty-nine hours after death. Body much emaciated. No special abnormal indications externally. Peritoneum smooth and glistening. Disposition of abdominal organs normal. Small intestines, especially upper half, distended and walls thickened, though not indurated. The thickening of the gut chiefly due to tumefaction of mucosa (in great measure congestion), which is of a dark red-purple hue throughout. The entire mucosa is beset with myriads of whitish flocculi, which give it a shaggy, coarsely villous appearance. The villosities are of the mucosa, and not in it. This condition is strictly limited to the

FIG. 19.



Section of a mesenteric gland showing dilated lymph channels. Obj. $\frac{2}{3}$, oc. 1, reduced one third.

small intestine, the stomach and colon being normal, and affects the iliac and not the cæcal side of the ileo-cæcal valve; it is most marked in the duodenum and jejunum. The upper part of the small intestine is five inches in circumference. Peyer's patches depressed and wasted. No ulceration of intestine.

The intestinal contents fluid and of a dark drab colour, not offen-

DESCRIPTION OF PLATE IX.

Illustrating Drs. Allchin and Hebb's case of Lymphangiectasis Intestini. (Page 220.)

FIG. 1.—Vertical section of duodenum, showing the distended lymphatics on one of the valvulæ conniventes. The photographic print, which was taken from a drawing, brings out the distended spaces, but does not differentiate them sufficiently from the adjacent normal tissue. (Obj. 1 in. oc. reduced one third.)

FIG. 2.—A portion of the same under a higher magnification. The distended lymphatic spaces stand out clearly.

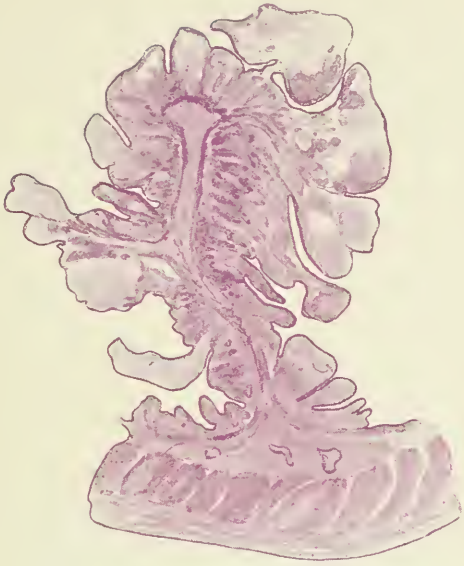


Fig. 1.

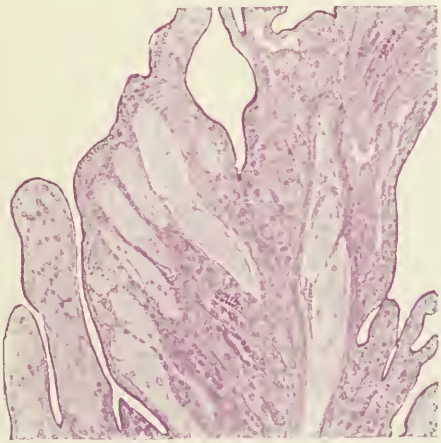


Fig. 2.

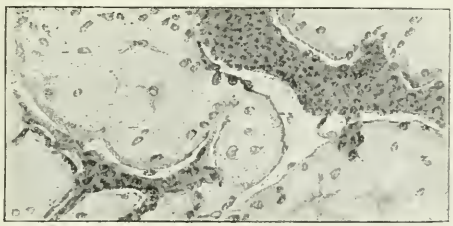
sive, and deposited on standing a considerable whitish sediment, which on microscopical examination was found to consist chiefly of oil-globules, débris, and cells.

The mesenteric glands much enlarged, tough, yet flabby; some pinkish, others of a whitish colour, similar to the intestinal villi. White dilated lacteals are seen to pass along mesentery from the intestine to the glands. Beyond the glands there was no discoverable affection of the lymphatic system. The pancreatic duct patent.

The thoracic and rest of the abdominal tissue do not present any abnormal appearance.

Microscopical examination of the intestine confirms the view that the appearances are due to dilatation of the lymphatic vessels. Sections show large coarse villi containing varicose lacteals, which are distended with an amorphous, finely-granular substance containing a few cells. This material only gives a slight reaction with osmic acid. There was considerable loss of the intestinal epithelium.

FIG. 20.



The same under a higher power. Obj. $\frac{1}{6}$, oc. 1, reduced one third.

The lymphatic vessels in the mesenteric glands present an identical appearance to those in the villi. The other tissues of the villi and glands normal; no indications of any new growth. The pancreas and kidneys quite normal in structure.

The appearances seen in the villi, the lacteal vessels, and mesenteric glands, together with the absence of any apparent lesion in the lymphatic system beyond the glands, suggest a varicosity of the vessels from obstruction, but the nature and cause of the obstruction is quite obscure. *May* 21*st*, 1895.

7. *Observations and experiments on the pathology of Graves's disease.*

By Walter Edmunds, M.C.

[With Plates X—XIII.]

Microscopic examination of the enlarged thyroid constituting an ordinary goitre shows various changes; there are found—

1. A tissue differing from the normal thyroid only in being somewhat coarser.

2. Cysts, some containing colloid material, and some a papillomatous ingrowth.

3. Nævoid or erectile tissue (explaining the expansile pulsation felt in some goitres).

4. Myxomatous changes of the interacinous tissue: this tissue then stains of a pale colour, and thus contrasts with the colloid contents of the vesicles. Sometimes the vesicles contain in their centre normal dark-staining colloid, and external to this, next the lining cells, a layer which stains much more palely.

5. Tissue of an embryonic type, consisting mainly of secreting cells, and not containing either vesicles or colloid.

The goitre of Graves's disease does not differ greatly from others, but a remarkable hypertrophy of the blood-vessels is sometimes found, and the presence of the "embryonic" (small-celled) tissue is fairly constant (Plates X and XI).

This tissue resembles that of the parathyroid glands.

These glands are most easily recognised in rabbits, for in them they are situate quite apart from the thyroid proper; they are of a bright red colour, and lie one on each side of the trachea below and at a considerable distance from the thyroid. They consist mainly of secreting cells arranged more or less in columns; there are no vesicles and no colloid; these glands were first described by Sandström in 1880.

In rabbits it has long been noticed that excision of the thyroid gland is not followed by the same fatal result that attends the operation almost (though not quite) invariably in dogs and cats; but Gley has recently shown that in rabbits, if, as well as the thyroid, the parathyroid glands are removed, the animal, as a rule,

dies. These experiments of Gley's have been repeated by myself, and it was found (1) that if both the thyroid and the parathyroid glands are removed the animals die: out of a batch of seven rabbits on whom this operation was performed, five died within eight days, the other two surviving for months. (2) That when the thyroid gland only is excised, the parathyroid glands being left, many of the animals also die: in a batch of seven operated on, five died within forty-two days, and two survived for months; in another set of seventeen operations two were killed while in good health (at the fifty-second and the fifty-ninth day), and the remaining fifteen all died within ninety-seven days: in four of them there was noticed a condition resembling myxœdema in man; the general health failed, the hair fell out, and there was a remarkable œdema of the lower part of the face. (3) If the parathyroids are alone extirpated, the animals, as a rule, live, and do not undergo any obvious change, at least not for a long time. In a batch of seven, one died at the thirty-fifth day, a second the eighty-second day, and a third the one hundred and fifty-sixth day; the other four survived, but two of these now, after six months, are weak and emaciated.

The appearance of some of these parathyroidless rabbits gave rise to the suspicion that the operation caused exophthalmos, and a fresh series of experiments (with controls) was made to test this point; the result seemed clear, the operation did not cause exophthalmos,—indeed, after the lapse of six months the eyes in two or three of these operated rabbits looked sunken, as if they were suffering from the opposite condition of enophthalmos. It is therefore proposed to make another series of experiments to decide as to this.

The parathyroids after extirpation of the thyroids do not undergo any marked changes, but they may hypertrophy somewhat; under the microscope, too, there is no pronounced alteration of minute structure, they do not develop into normal thyroids, no vesicles and no colloid form.

In dogs, also, there are parathyroids, but in them these small glands lie half embedded in the substance of the thyroid itself; consequently, in excision of the thyroid lobes, the parathyroids have been removed as well. Gley found that if the parathyroids are separated and left, the animal will live, notwithstanding the removal of the rest of the thyroid lobes. The present writer's experiments (six in number) show that if the whole of one lobe of

the thyroid, including its parathyroid, and also the greater part (two thirds or more) of the other lobe be removed, the animal will live or die, according as the parathyroid is or is not left.

The parathyroid and also the portion of thyroid that is left in these experiments hypertrophy considerably.

The hypertrophied parathyroid consists only of new columns of secreting cells, and has not developed into thyroid proper: no vesicles nor colloid formed in the two specimens I examined.

The hypertrophied portion of thyroid proper contains a considerable growth of new tubules lined with a single layer of secreting cells; there also appears to be less colloid in the vesicles, as if it had been absorbed: in one case many vesicles were empty. Further, the cells lining the vesicles are greatly hypertrophied, as described by Hürthle; they have become much larger than natural, and generally both in normal and enlarged thyroids the larger cells seem the more active cells, and this throws some light on the "vacuoles" which are found in both normal and diseased thyroids in the periphery of the colloid in the vesicles. The so-called "vacuoles" are to be seen in alcohol-hardened specimens; and, from the fact that they are not present after osmium fixing, it has been supposed they are due to shrinking from the action of the alcohol: but they seem too regularly disposed for this, and their absence from the vicinity of flat (non-acting) cells points to their probably consisting of tiny portions of recent secretion which has not yet become mixed with the rest of the colloid (Plates XII and XIII, and Fig. 21, p. 234).

Greenfield has described in the thyroid of Graves's disease (1) a similar change of the secreting epithelium "from a cubical to a columnar form;" (2) "an absorption of the colloid, it being replaced by a more mucilaginous fluid;" (3) an enormous number of newly formed tubular spaces lined by a single layer of cubical epithelium.

Parathyroids also occur in the sheep, monkey, and in the human subject. Cresswell Baber has found them in the seal.

The parathyroid gland is, it is clear, of considerable importance—it is not quite so important as the thyroid gland, but, bulk for bulk, it probably is more so, as it is considerably the smaller. In a rabbit weighing 1800 grammes the thyroid weighed 220 mg., and the parathyroids together 19 mg., or about one twelfth of the thyroid.

Although the tissue of the parathyroid gland does not at all resemble that of the thyroid in its adult form, there can be little doubt that they are closely connected, not only on account of one

being able, to a great extent, to replace the other physiologically, but also because (1) the parathyroid resembles the embryonic form of the thyroid; (2) the two tissues are occasionally found side by side in the parathyroid of the dog; and (3) because they are closely connected anatomically; in the monkey the parathyroid is embedded in the substance of the thyroid.

Now it has been supposed that the symptoms of Graves's disease (other than the goitre) are due to the action of the internal secretion from the enlarged thyroid: there does not, however, exist any evidence that thyroid secretion can produce exophthalmos. The eating of the thyroid of sheep, or the receiving of the subcutaneous injection of the extract, has produced unpleasant symptoms in healthy persons; in the subjects of myxœdema an excessive dose has produced grave and, it is stated, even fatal symptoms; but it does not appear that the eye symptoms of Graves's disease are among these effects.

In animals, thyroid feeding produced, in my hands, no very obvious results, certainly no exophthalmos. To a healthy dog were given, in one day, the thyroids of sixteen sheep, without any apparent result; and to another dog were given sheep's thyroids, two per diem, for some days without effect. Also monkeys were treated daily with large doses of the extract subcutaneously without the production of obvious symptoms, except that in one case, about the time of stopping the treatment, suddenly an area of baldness appeared on each temple, extending downwards to the shoulder: this hair gradually grew again, but an attempt to reproduce the result in the same monkey by the re-application of the supposed cause, *i. e.* the administration of thyroid extract in large doses and then suddenly stopping it, failed.

If it be argued that the thyroid of Graves's disease is not merely an enlarged one, but is also altered in structure, and that therefore the secretion is also probably altered, it must be answered that that may well be, but that no evidence has yet been brought forward that this altered secretion can produce exophthalmos.

The apparent contrast between the symptoms of Graves's disease and myxœdema, coupled with the brilliant success which has attended the treatment of the latter, and also of cretinism[1] by thyroid taking, certainly helps the secretion theory. But there are one or two considerations that go against it.

[1] Plate XII, fig. 4.

1. The contrast between Graves's disease and myxœdema only holds good with chronic myxœdema: in the acute myxœdema as seen in dogs, and sometimes in monkeys, there are tremors, with attacks of dyspnœa resembling those of Graves's disease.

2. Two cases have been described (by Sollier) of the co-existence in the same patient at the same time of Graves's disease and myxœdema.

3. Thyroid feeding does not as a rule make cases of Graves's disease worse. Dr. Mackenzie tells me he tried the treatment in a series of cases without marked result in either direction. Auld has, however, recorded a case in which injurious result followed and appeared to have been caused by the treatment.

4. The difficulty of saving by thyroid treatment animals deprived of their thyroids tells against the secretion theory. Twenty dogs, whose thyroids were excised, were treated by thyroid feeding, or by the administration of the extract of thyroid: the details of the treatment were varied, and also of the operation; the thyroid in some cases was removed in stages. The total result was that only two out of the twenty were saved: [1] this is, however, more than could have been expected without treatment, judging from the experience both of myself and others. The survivals are stated to be less than five per cent.; moreover the dogs lived a few days longer than without the treatment they would have done, and the symptoms were much modified, for the acute attacks of dyspnœa and rapid breathing were absent, the animals dying of emaciation and asthenia.

In monkeys, eight were treated with thyroid extract administered subcutaneously in all cases but one; they all died in from twelve to one hundred and twenty-eight days, the average time of survival being forty-four days. The symptoms from which they suffered were those of myxœdema in monkeys as described by Horsley; they lost weight, became less lively, respiration became slower, hair fell out in places, œdema appeared in the face, and the pupil was somewhat dilated; tremors occurred, and sometimes convulsive attacks, with rigidity of limbs.

Stanley Kent's results in cats are in accord: of five submitted to thyroidectomy and treated he saved only one; and of four in which the thyroid, and also one or both testes, were removed, and the treatment followed, two died, one was killed while ill, and only one survived.

Another argument for the secretion theory is found in the cure

[1] The treatment was in both cases stopped after a few weeks without ill effect.

or amelioration of Graves's disease which now many times has followed the removal of the whole or part of the enlarged thyroid. The last to review these cases is Dr. Oppenheimer, of Baltimore, who finds a total of sixty-eight on record: of these, eighteen are said to have completely recovered; twenty-six were more or less improved; in nine there was no change either way; in five there was immediate death; and in four death followed the operation within twenty-four hours.

One case of improvement, amounting practically to cure, has come under my own observation. The case was seen almost from the commencement of the symptoms, and treated, but without success; it gradually became worse, the patient at last being very ill, with the usual symptoms, including the paroxysmal attacks of palpitation and rapid breathing. The only course that seemed left was to operate on the goitre, but before undertaking this step a consultation was held with Dr. Hector Mackenzie. He agreed in the advisability of the operation, and also in considering the spasmodic attacks to be due to the effects of the disease itself, and not to the mechanical pressure of the goitre on the trachea. The attacks resembled those which occur in thyroidless dogs. A considerable portion (but not all) of the goitre was removed; the patient was much benefited, and the symptoms gradually passed off, so that the patient was practically well, though the pulse, if counted, was found too fast, and a little exophthalmos might still have been detected on critical examination (at no time was it a prominent symptom).

It is argued that the improvement must be due to the diminution of the thyroid secretion, following the removal of a portion of the thyroid, and that therefore the symptoms are due to that cause; but it must be remembered that for these cures to take place it is not apparently necessary that the whole or nearly the whole of the goitre should be removed; in some cases only one lobe has been excised, the remainder atrophying in time. This, too, is only what occurs in operations on ordinary goitre. In a case in which about half of a considerable goitre (which was compressing the trachea) was removed, the remaining portion gradually atrophied, so that in about a year the thyroid could not be detected, and the patient was well. These latter cases can only be explained by the breaking of some vicious circle, and the same explanation may apply in the cases of Graves's disease. Moreover the improvement, as we have seen, does not always follow: Dr. Mackenzie informs me of a case

under his care of ten years' standing, in which a considerable portion of the goitre was excised in the hope of benefiting the exophthalmos, which was extreme: the patient was not improved, certainly not in the exophthalmos.

The fact that the eye symptoms of Graves's disease can be produced by a chemical poison (cocaine) may be held to support the view that a poison secreted by the thyroid might do the same.

The effects of cocaine in this connection were first pointed out by Koller, and have since been carefully studied by Jessop; the latter found that by dropping cocaine into the eye there was produced (1) proptosis, (2) absence of winking, (3) Graefe's sign, (4) local anæsthesia, (5) dilatation of pupil, (6) widening of the palpebral fissure, (7) paralysis of accommodation, (8) diminution of ocular tension.

In a case of complete facial paralysis cocaine still caused widening of the palpebral fissure, and he argues that the cocaine must act on the unstriped muscular fibres (which are supplied by the sympathetic). His experiments also show that stimulation of the sympathetic in the neck could further dilate a pupil already as fully dilated as atropine could make it; and that cocaine could also dilate a pupil fully dilated with atropine. In a case of Graves's disease he found that cocaine administered cautiously produced increased proptosis, further dilatation of palpebral fissure, and halting in the descent of the upper eyelid.

Jessop also found that in the rabbit, if the cervical sympathetic be divided, after a few days cocaine will not produce dilatation of pupil, nor proptosis, nor widening of the palpebral fissure.

The effects of cocaine injected subcutaneously in monkeys, both with and without division of the cervical sympathetic, have been tried by myself. The results in monkeys of division and stimulation of the cervical sympathetic are described by Sherrington in the 'Journal of Physiology,' and represented in the figure here reproduced.

Division of cervical sympathetic causes (1) recession of eyeball; (2) contraction of pupil; (3) narrowing of palpebral fissure; (4) œdema and flushing of skin round eye; (5) swelling of caruncle; (6) projection of pinna from side of head; (7) puckering of skin of muzzle; (8) flattening of certain hairs on forehead, which cannot then be elevated by the emotions which will raise the corresponding hairs on the opposite (normal) side of the head.

Stimulation of the cervical sympathetic, on the other hand, produces (1) proptosis of the eyeball; (2) dilatation (well marked) of pupil; (3) widening of palpebral fissure; (6) lying back of pinna; (8) erection of certain hairs on forehead.

The solution of cocaine used was the hydrochlorate, and it was found that two grains of the salt (= 0·13 gramme) was fatal to a monkey. Immediately after the injection he jumped about in an excited manner; then his movements became less precise, and soon

FIG. 21.

Shows effects on division of right cervical sympathetic nerve. Sketch by Lapidge, *ad nat.*

he had to hold on to the side of his cage to retain the erect attitude; then his hold relaxed, and he collapsed on the floor of the cage, and had a succession of attacks of clonic spasms, during which the arms were extended and the hands clenched, the head partly thrown back, and the upper eyelids retracted. These attacks lasted about four seconds, with intervals of fifteen seconds. Gradually the respiration became feebler, and notwithstanding artificial respiration he died in twenty minutes or half an hour from the time of injection. After death it was noticed that the eyelids were unusually widely open, the upper eyelid being retracted, and that the eyes were prominent

(as shown by comparison with a normal monkey). Half an hour after death the cornea was still clear and convex instead of hazy and flaccid, as it usually becomes.

The cocaine experiments were made on twelve monkeys altogether. The drug was injected subcutaneously in half-grain doses (= 0·032 gramme) once a day, but it being found that this when continued produced death, the dose in the later experiments was reduced to a third or a quarter of a grain. Five of the monkeys died certainly from the effects of the injections, and three others probably from the same cause; two of the five died in convulsions.

The effect of the injections caused the animals to seem dull and to lie down,—indeed, they appeared unable to stand. Sometimes there ensued an attack of convulsions; these effects passed off in about an hour, and there remained exophthalmos, dilatation of the pupil, and widening of the palpebral fissure, and (as was thought) increased intra-ocular tension.

In three cases thyroid extract was injected as well as cocaine, but its addition made no difference that could be detected. When the cocaine injections were stopped the symptoms at once ceased: it seemed impossible to start a disease in any way resembling exophthalmic goitre by administration of cocaine or thyroid extract, either separately or together.

In seven of the monkeys, a few days before commencing the cocaine injections, a long piece of the sympathetic nerve in the neck was excised. The effects of the excision were to produce contraction of the pupil (which came on as the effects of the anæsthetic passed off) and retraction of the eye; the effect of cocaine subcutaneously on such a monkey is to greatly dilate the pupil on the normal side, and to cause proptosis there. On the operated side the pupil is somewhat dilated, but not so much; apparently no proptosis is produced, but it is not easy to be absolutely certain of this, as the opposite side is no longer normal for comparison; if there is any proptosis it certainly is not much, for the eye is not nearly so prominent as on the unoperated side. This effect of division of the sympathetic is very important, for it affords an indication for treatment in these cases of Graves's disease, in which the prominence of the eye is so great as to cause ulceration of the cornea. The usual treatment is to partially or wholly close the palpebral opening by suturing the eyelids together, but this is not always successful: sometimes, notwithstanding this, and also strapping the lids toge-

ther, the cornea sloughs and the eye (or even both eyes) is lost. The effects of paralysis of the sympathetic in man are not serious—contraction of pupil and absence of perspiration on that side; the affection is generally only discovered accidentally.

The effects of cocaine, then, it must be admitted, show the possibility of a poison being secreted by the thyroid which might cause symptoms like those of Graves's disease.

The real issue is whether the goitre of Graves's disease is primary, and by its secretion the cause of the other symptoms, or whether the disease is primarily of nervous origin.

In favour of the latter view it may be said that the relations of the disease are not so much thyroidal as neurotic.

It seems to be generally agreed that it is not more common in goitrous districts than elsewhere. On the other hand, it has many nervous connections. Solbrig relates the case of a boy aged eight (the son of a woman who suffered from the disease), who, after a disappointment at school, was seized with palpitation and profuse sweating: the next day the thyroid was large, the eyes prominent, and the pulse 180. Two days later the symptoms gradually disappeared, and in ten days he was well again. Putnam cites from Coggeshall an exactly parallel case. The patient was a young girl, and the symptoms followed immediately on great excitement attending a whipping, but subsided in a few days.

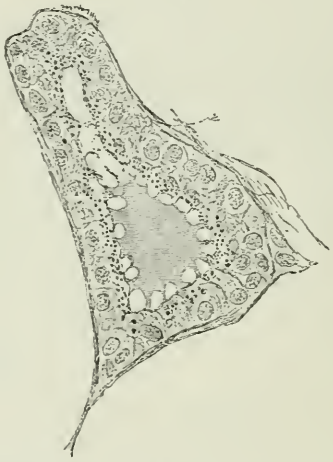
Again, certain experimental lesions of the central nervous system (of the restiform bodies) have been stated by Filehne and Bienfait to be capable of causing the symptoms of Graves's disease, namely, tachycardia, exophthalmos, and hyperæmia of the thyroid (but not a definite goitre). Further, Mendel found *post mortem*, in a case of Graves's disease, atrophy of one restiform body.

The disease, too, has some relations with diabetes. Dr. Acland had recently under his care in St. Thomas's Hospital a patient suffering from diabetes, and passing between four and five ounces of sugar in the twenty-four hours. Eighteen months previously the patient had been admitted with Graves's disease, suffering from a considerably enlarged thyroid and palpitation; on his second admission the thyroid was much smaller, though still enlarged, and the palpitation absent though the pulse was still quick.

An irritation of the sympathetic nerve, either applied to its origins in the central nervous system (brain or cord) or to its prevertebral ganglia, would readily enough account for both the cardiac and the

ocular symptoms: as to the hypertrophy of the thyroid, it has been shown that stimulation of the sympathetic causes an increased secretion of the solid constituents of the saliva; the thyroid closely resembles the salivary glands, differing from them mainly in not draining through a duct, and it may be conjectured that prolonged stimulation through the sympathetic might cause the hypertrophic changes. The thyroid contains similar granules to those found in the secreting cells of the parotid gland (see Fig. 22).

Fig. 22.



Vesicle of thyroid, showing granules near inner side of secreting cells, resembling salivary glands. The vacuoles in the colloid are also shown.

Again, occasionally the eye symptoms are unilateral, and then the hypertrophy of the thyroid is generally greater on the same side as the affected eye. It was so in a case recorded by Maher, of Sydney.

The recovery in which Graves's disease in many cases terminates seems to negative any pronounced central lesion, and we need not therefore be surprised that none has been with certainty yet established.

Somewhat against the secretion theory is the fact that no poison can be found in the blood or spleen in experimental athyroidea. The blood from a dog dying of acute myxœdema, following thyroidectomy, was drawn and defibrinated, and injected into a normal dog: no effect—certainly no permanent effect—was produced. This experiment was tried five times. Also the albumoses

DESCRIPTION OF PLATE X,

Illustrating Mr. Walter Edmunds' Observations and Experiments on the Pathology of Graves's Disease. (Page 224.)

Fig. 1.—Section from the goitre of Graves's disease. A portion of the hypertrophied goitre was removed by operation; it is the second case referred to in the text. The large amount of young tissue between the vesicles will be noticed; also the great hypertrophy of the nuclei of the secreting cells, and the multiplication of these cells. (× 380.)

Fig. 2.—Section of the goitre in a fatal case of Graves's disease. A drawing under a low power. On the right and also on the left above is seen capillary ingrowth into the enlarged vesicles. Below, in the centre, is a lobule, which in the absence of colloid-containing vesicles resembles accessory thyroid tissue. (× 25.)

Fig. 3.—The portion of the section marked with a square in Fig. 2, more highly magnified. (× 225.)

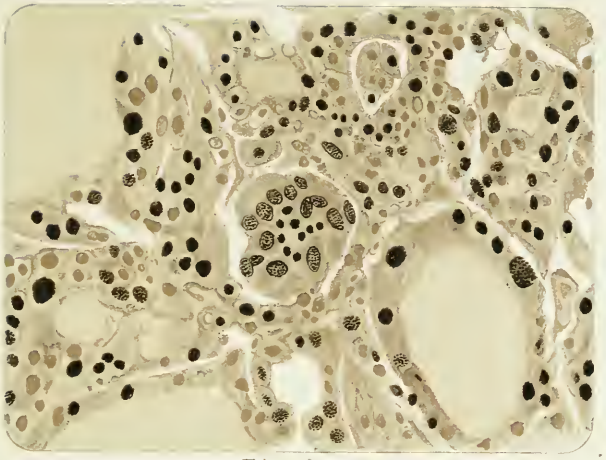


Fig 1

Fig 2.

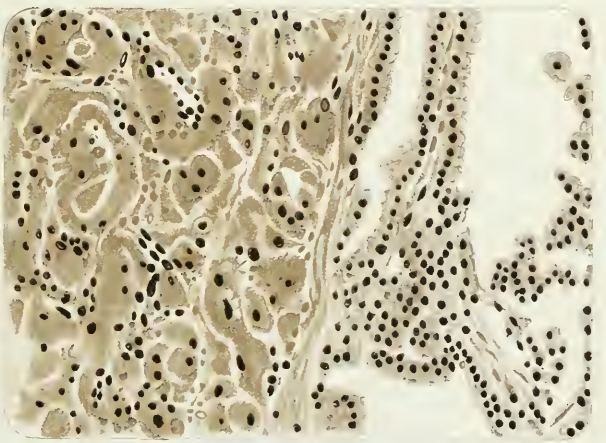


Fig 3.

DESCRIPTION OF PLATE XI,

Illustrating Mr. Walter Edmunds' Observations and Experiments on the Pathology of Graves's Disease. (Page 224.)

Fig. 1.—Section of the enlarged thyroid in a case of Graves's disease. It will be seen that there is a considerable area of secreting tissue, the cells of which are arranged so as to constitute tubes, and in which there are few vesicles containing colloid. In the periphery of the colloid in the vesicles are clear spaces; the nature of these "vacuoles" is discussed in the text. Below and to the right is seen part of an enlarged vesicle; its ramifying shape shows that the fluid in it could not have been under much tension. (× 220.)

Fig. 2.—Section from an adenoma of thyroid, removed by operation. The vesicles are enlarged, and the secreting cells lining them are multiplying and penetrating into the colloid, which has completely disappeared from the upper extension of the vesicle in the centre. The connective tissue between the vesicles is coarse in structure. (× 220.)

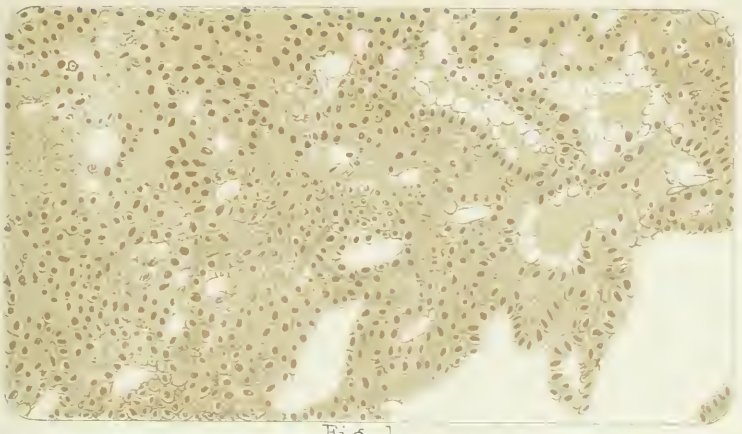
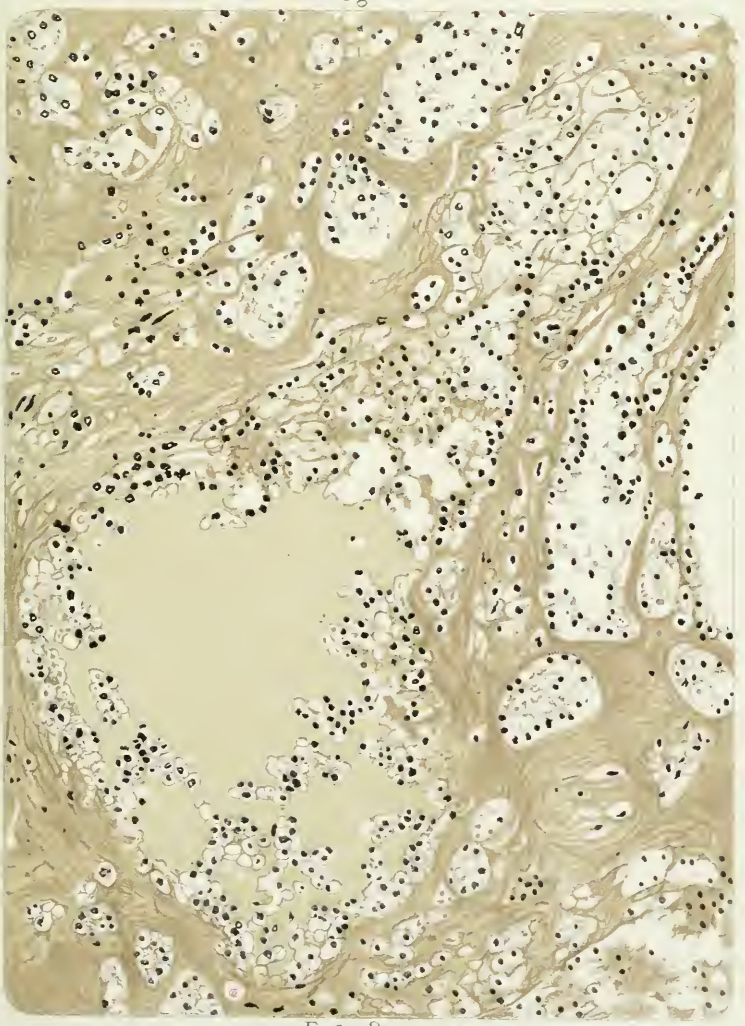


Fig. 1



M H Lapidge del.

Fig 2

Mintern Bros lith.

DESCRIPTION OF PLATE XII,

Illustrating Mr. Walter Edmunds' Observations and Experiments on the Pathology of Graves's Disease. (Page 224.)

Fig. 1.—Section of accessory thyroid of rabbit. 102 days previous to the rabbit being killed, and this specimen obtained, the whole of the thyroid proper of the rabbit had been removed, leaving only the two parathyroids. These after death were found not to be much, if at all, hypertrophied, nor was their microscopic structure materially altered; no vesicles and no colloid were seen. (× 380.)

Fig. 2.—The whole of one lobe, including the parathyroid and the greater part of the other lobe (excluding the parathyroid) of the thyroid of a dog was excised. No symptoms followed, and at the end of nine days the dog was killed. The figure represents, highly magnified, the lining (secreting) membranes of two adjacent vesicles back to back. It will be noticed that the membranes are greatly hypertrophied, and that this is effected by the enlargement of the cells rather than by their multiplication. Contrast with Fig. 4. Plate XIII, fig. 1, is from the same specimen as this figure. (× 500.)

Fig. 3.—Section of normal accessory thyroid of rabbit. It contains no vesicles and no colloid. The clear spaces are probably due to drops of secretion, but this does not stain in the same way that the colloid in the thyroid proper of the rabbit does. (× 380.)

Fig. 4.—Secretion of the thyroid of a cretin. It was obtained from the body of a girl aged ten, who was the subject of cretinism. The thyroid did not appear atrophied. The sections show little colloid in the vesicles, but there is a considerable multiplication of the secreting cells lining the vesicles. Contrast this with Fig. 2. It would seem that there is some antagonism between the multiplication of the cells and the performance of their secreting function. I am indebted to Mr. Bidwell for this specimen. (× 250.)

Fig. 5.—Section of small nodule from the surface or vicinity of the normal thyroid of man. (The patient died of phthisis.) It will be noticed that there are no vesicles and no colloid, and that the structure consists mainly of columns of cells, thus resembling the structure of the embryonic thyroid, and also of the parathyroid as seen in various mammals. (× 220.)

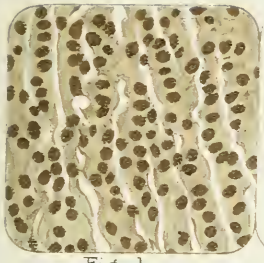


Fig. 1.

Fig. 2.

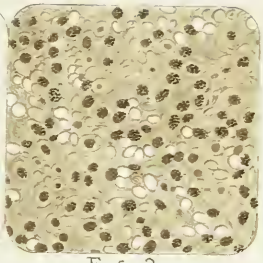


Fig. 3.

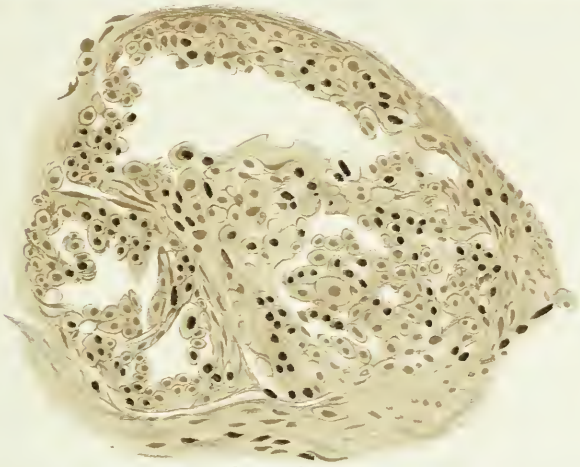


Fig. 4.

Fig. 5.

M H. Lapidge del.

Mintern Bros. lith.

DESCRIPTION OF PLATE XIII,

Illustrating Mr. Walter Edmunds' Observations and Experiments on the Pathology of Graves's Disease. (Page 224.)

FIG. 1.—From same specimen as shown in Plate XII, fig. 2. Section of small portion of thyroid left after the removal of the greater portion of the thyroid of the dog nine days previously. The thickening of the secreting linings of the vesicles and the absence of colloid from many of the vesicles is noticeable. (× 25.)

FIG. 2.—Transverse section of the normal parathyroid of the dog. It is seen half embedded in the thyroid proper, shown above and to the right. It contains no vesicles and no colloid, which latter in the thyroid proper is conspicuous by the dark colour which it has stained. (× 50.)

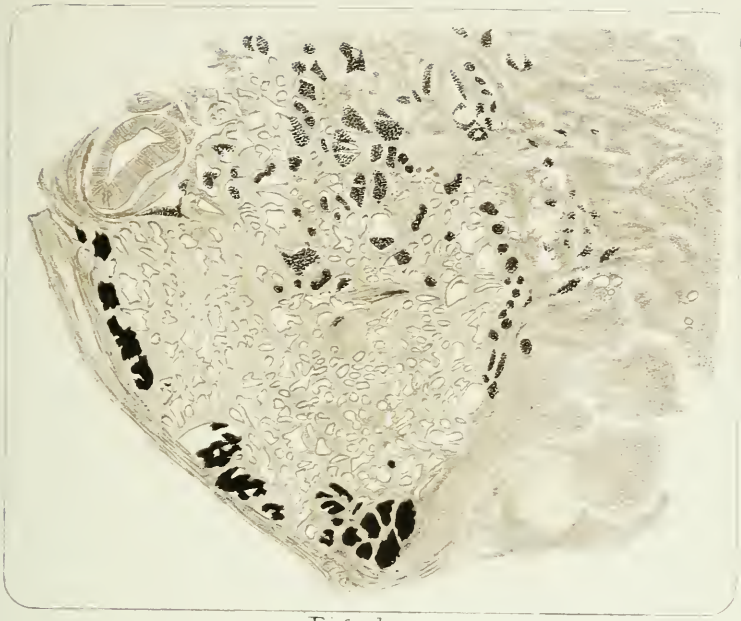


Fig. 1.

Fig 2.

were extracted from the spleens of dogs dead of athyroidea. Mr. White, Pharmaceutist to St. Thomas's Hospital, kindly did this for me. The principle of the method depends on the facts that alcohol precipitates in the spleen the albumoses, the albumins, and the globuloses. At the end of about three months the last two are insoluble in water, while the albumoses are still thus soluble. They are dissolved, and the bulk is concentrated by evaporation at a low temperature and barometric pressure, and precipitated again by alcohol, and this is repeated several times in order to obtain a pure product: the albumoses thus obtained were injected into guinea-pigs with an entirely negative result.

The experiments related above were made at the Brown Institution, and the writer has much pleasure in expressing his thanks to the Institution for the opportunities afforded him. *May* 21*st*, 1895.

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8. *Results following the experimental removal of portions of the kidney.*

By John Rose Bradford, M.D., F.R.S.[1]

In 1889 I began a series of experiments on dogs, with the object of investigating the effects produced on the circulation by the progressive removal of large quantities of the kidney substance. Very soon, however, owing to the unexpected results obtained in other directions, this part of the subject was not pursued. Attention was directed mainly to the character of the urine secreted under these abnormal conditions, and also to the disturbance of the general nutrition that was noticed to ensue in certain cases. A short summary of the results thus obtained was published in the 'Proceedings of the Royal Society' for 1892, and I purpose to publish shortly a full and detailed account of all the results hitherto obtained. On the present occasion, therefore, I propose to give a brief account of the main results, omitting the actual experimental details on which these results are founded.

Experiments of a similar nature have been carried out by several observers, but more especially by Tuffier, and he published his results in his work, 'La Chirurgie du Rein.' Tuffier, like most other observers, directed his attention mainly to the nature of the renal hypertrophy seen after experimental nephrectomy, and he does not seem to have had his attention drawn to the changes with which this paper is mainly concerned. This may be due to the fact that the plan of his experiments was different from that of mine. Tuffier removed one kidney, and subsequently, after intervals of varying length, he exposed the opposite and hypertrophied kidney, and excised from it pieces of varying size.

The procedure adopted in my experiments was different. I exposed one kidney, and removed a portion of it, and when the animal was quite re-established in health the opposite kidney was removed entire, thus leaving the animal with but a fraction of one kidney available for the discharge of the renal functions. For my purpose this was the preferable method, inasmuch as the removal of a

[1] These experiments were carried out whilst holding the post of Grocer Research Scholar.

portion of one kidney is a severe operation, and if this damaged kidney is the only one the animal possesses, results obtained directly after the operation would be liable to be vitiated by the fact that, for some hours at any rate, the animal is virtually without kidneys. On the other hand, inasmuch as the removal of a portion of one kidney is not followed by permanent serious effects, by allowing an interval of several weeks to elapse between the first operation and the subsequent removal of the opposite kidney, we give the damaged organ a chance to recover, and to approximate to a normal condition prior to observations being made on its functional activity.

This difference in the mode of conducting the observations may account for the fact that Tuffier's results and mine differ somewhat as regards the amount of hypertrophy obtained.

An animal of known weight was confined in a cage constructed in a manner suitable for the collection of the excreta. Daily determinations were made of the quantities of food and water consumed, and of the quantities of urine and fæces excreted. The amounts of nitrogen in the food, fæces, and urine were determined daily by Kjeldahl's method, and the daily excretion of urea was determined by the hypobromite method. These observations were usually carried out for a period of one week; the animal was then weighed, and, after being anæsthetised with chloroform and morphia, one kidney was exposed by a lumbar incision, and a wedge of varying size was removed, usually from the middle region of the organ. The apex of the wedge reached to the pelvis of the kidney, so that in all cases the pelvis was opened. The surfaces were brought in contact by sutures after arresting the very free hæmorrhage, and the wound was then closed in the usual manner. As soon as the abdominal wound was soundly healed the animal was again placed in the urine-collecting chamber, and the quantity and nature of the urine compared to that excreted previously by the normal animal. At a subsequent period the entire kidney of the opposite side was removed and the animal again placed in the collecting chamber, and the composition of the urine again determined. Finally a determination of the nitrogenous extractive matters in the blood and tissues was made, the animal being chloroformed and killed by bleeding.

The removal of a portion of one kidney in dogs is a severe operation,—in fact, far more severe than the removal of an entire kidney;

this is probably due to the hæmorrhage, which is always considerable, and to the shock of the prolonged operation.

There is some difficulty in estimating the ratio between the amount of kidney removed and the total kidney weight, since the kidney on which partial nephrectomy has been performed undergoes a varying amount of atrophy, and the opposite kidney hypertrophies. Hence the expression frequently used that two thirds or three quarters of the total kidney weight has been removed is only approximate. Control observations were made by determining in some fifty normal dogs the ratio between the weight of the two kidneys and the body weight.

I. *The results following the excision of a portion of one kidney.*— This operation is not followed by any notable or permanent ill effects as regards the general condition of the animal. There may be some emaciation immediately subsequent to the operation, but this is generally only of transitory duration, and it is only slight in amount. The body temperature remains at its normal height, and the animals have remained in good health for as long as six months after the operation. There is also no profound change in the composition of the urine, but the urinary water is frequently increased in amount; the increase is not as a rule considerable, but the daily quantity of urine has been doubled in some experiments; so great an increase is, however, decidedly exceptional. This increased excretion of water is seen as soon as the first week after the operation, and it has been observed as long as two months after. In one case it disappeared. With this increase in the amount of urine excreted the specific gravity falls until it is from 1020 to 1010. This increased excretion of urinary water is not necessarily accompanied by any increased excretion of urea, and when this latter effect is seen it is due to a more liberal nitrogenous diet. There is after this operation no increased excretion of urea associated with progressive emaciation.

The three main results of unilateral partial nephrectomy may be thus summarised:

Firstly. There is no progressive emaciation and failure of health.

Secondly. There is an increased excretion of urinary water.

Thirdly. When there is an increased excretion of urea due to a liberal nitrogenous diet, the quantity of urine is further increased; that is to say, the animal always excretes a more or less dilute urine,

whereas the normal dog excretes a very dense urine of high specific gravity even when excreting large quantities of urea.

Excision of a portion of one kidney is followed in a large proportion of cases by a variable amount of general atrophy of the kidney operated on, so that on *post-mortem* examination the wedge of kidney substance removed is obviously too big to fit the kidney from which it had previously been excised. In a few cases this atrophy was not obvious; sometimes it is extreme in amount. Usually the whole of the kidney fragment left is uniformly atrophied, but cases have been seen where the atrophy was more marked at one extremity of the organ than at the other. This atrophy occurs without the removal of the second kidney; it is a direct result of the excision of the wedge, and it is not affected in any way by the subsequent removal of the opposite sound kidney. This atrophy does not follow simple incision of the kidney even if the organ be split in two and then sutured, nor is it seen as a sequel of division of the renal plexus. Finally its amount is not altogether dependent upon the size of the wedge removed. Its mode of production is obscure, but it is not due to any interstitial nephritis or cirrhosis of the organ, as no general overgrowth of fibrous tissue occurs; the scar is quite a linear one. I am inclined to think that it is dependent upon interference with the vascular supply of the kidney fragment, partly by the ligatures necessary to arrest the hæmorrhage, and partly by the traction and torsion required in order to bring the cut kidney surfaces in contact.

It is interesting to observe that hypertrophy of the fragment is quite exceptional, and is, when present, slight in amount, provided the operation is performed on adult dogs. On the other hand, if this operation is performed on puppies, the damaged kidney does not atrophy, it grows considerably, but, as might be expected, it does not reach the size of its sound fellow.

Although excision of a wedge from one kidney leads usually to atrophy of this kidney, this operation is followed by hypertrophy of the opposite kidney. The amount of the hypertrophy is apparently not entirely dependent either on the amount of kidney removed at the first operation, or on the amount of consecutive atrophy that ensues.

II. *Results following complete removal of one kidney after previous excision of a portion of the other kidney.*—After the successful per-

formance of these operations the animal is left with only a portion of one kidney of varying size with which to discharge the renal functions.

The immediate effects of the second operation are but slight, there is but little shock, and the animal runs about apparently quite well within a few hours of the operation. Within the first few days, generally within the first twenty-four hours, of the operation, however, there is a great alteration in the composition of the urine, and in many cases a grave disturbance of nutrition ensues, leading to death in a few weeks after the second operation (*i. e.* the removal of the entire sound kidney).

The cases are divisible into two groups : in the first there is practically no great disturbance of nutrition, and the animal survives in fair health, the only departure from the normal being the greatly increased amount of urine that is excreted. In these cases, nine in number, approximately two thirds of the total kidney weight had been removed at the two operations, so that these animals had about one third of the original kidney weight available with which to discharge the renal functions. Some of these animals survived for as long as four months, and were then in fair health, so that doubtless they might have lived much longer ; there were no indications of approaching death at the time that they were killed. In the second group, consisting of fifteen animals, the results are very different. In addition to the greatly increased flow of urine there is great emaciation and weakness, and the animals only survived the operation for two or three weeks. In addition to the increased flow of urine there is in these cases an increased excretion of urea, and the amount of urine passed is greater than that seen in the first and non-fatal group. In this second group of cases, where death ensues, the quantity of kidney removed is greater, amounting approximately to some three quarters of the total kidney weight.

In none of the fatal cases did the quantity of kidney found *post mortem* amount to as much as one third of the initial total kidney weight, and in none of the non-fatal cases did it fall to as low as one quarter of the total kidney weight.

Observations on normal dogs showed that the ratio of kidney weight to body weight was approximately some 6·7 grammes of kidney per kilogramme of body weight. When the quantity of kidney found *post mortem* was reduced to some 2 grammes per

kilogramme the dangerous limit was reached, and if it fell below 2 grammes per kilogramme death supervened at varying periods, the average duration of life being from two to three weeks.

The prominent symptoms preceding death are thirst, weakness, emaciation, and a fall in the body temperature of some 5° to 6° F. The volume of the urine is increased to three or four times its normal amount, sometimes to as much as eight times its normal amount. The specific gravity is low, and there is, as mentioned above, a considerable increase in the daily output of urea, but there is no sugar nor albumen. The animals become rapidly weaker, and die apparently from failure of respiration. It is notable that vomiting, convulsions, and coma have not been observed. Diarrhœa, with offensive stools, is occasionally seen. The most striking phenomena are the emaciation and the muscular weakness. The emaciation is very rapid in its course and considerable in amount, the loss of weight being often as much as two fifths of the original body weight. The appetite sometimes fails; frequently, however, the animal will eat well, and notwithstanding this the emaciation is rapid. The substitution of a more palatable food, such as meat instead of dog biscuit (these animals will eat meat greedily when refusing biscuit), does not prevent the rapid emaciation, nor does it delay the advent of death, but it causes a still greater daily excretion of urea.

The increased excretion of urinary water begins within forty-eight hours of the operation, and once established it persists until shortly before death.

As regards the excretion of urea it may be said that in all cases where there was no failure in appetite the quantity was increased absolutely. In the cases where the appetite failed the urea excreted was relatively increased,—that is to say, the animal with a diminished diet, or in some cases with no food at all, excreted quantities of urea equal to those previously excreted on a liberal diet. The increased excretion of urea began usually some twenty-four hours later than the increased excretion of urinary water; the increase in the former was not so great as that of the latter. Thus the average increase of urea was about half as much as the normal; it was rarely double.

In the cases where, owing to the complete refusal of dog biscuit as food, there was no increase in the amount of urea excreted (the daily averages remaining the same as those seen in the normal dog on a liberal diet of dog biscuit) the substitution of meat for dog

biscuit was immediately followed by a large urea excretion. In other words, the fragments of kidney were quite able to excrete quantities of urea far larger than those they actually did excrete.

In only one experiment out of the total of twenty-four was the excretion of urea diminished after the second operation, and here at least eight ninths of the total kidney weight had been removed, and the animal refused all food after the operation.

It is clear from these experiments that, even when the kidney substance is reduced to one quarter or even less of its original amount, the mutilated fragment is quite capable of excreting the quantities of urea previously excreted by the two sound kidneys; and that, so far from there being any diminution in the amount of urea excreted, there is a considerable increase associated with rapid emaciation. This increased excretion of urea begins later than the increased excretion of urinary water, and it is usually well established by the fourth day after operation; so that in the cases where three fourths of the total kidney weight has been removed there is for some forty-eight hours a condition similar to that seen persistently in the non-fatal cases where some two thirds of the total kidney weight has been removed,—that is to say, a condition where, with a great increase in the excretion of water, there is no corresponding increase in the amount of urea excreted. When the animal survives the second operation for two or three weeks the maximum urea excretion is frequently seen in the second week,—that is to say, the increased urea excretion is progressive in its development. If there were any deficiency in the power of excreting urea it is not probable that the quantities excreted would progressively increase; one would rather expect a progressive diminution, and for the maximum urea excretion to occur very shortly after the operation. When the quantity of urea excreted is large the amount of urine is very large (as mentioned above, it may be eight times the normal), and hence these animals are quite unable to excrete a dense urine.

In the cases where the daily output of urea was decidedly above the normal, and where there was no great failure of appetite, the average amount of kidney substance found *post mortem* was 1·5 grammes per kilogramme of body weight, the normal being 6·7 grammes per kilogramme. On the other hand, in the series where there was only a relative increase in the urea, owing to the complete anorexia, the average amount of kidney was but 1·16 grammes per

kilogramme; hence in this latter series the amount of kidney found *post mortem* was decidedly less than in the former.

The fall in the temperature of the body becomes quite obvious when the increased excretion of urea is in full swing,—that is, at a time when the animal is emaciating rapidly. The rectal temperature falls to 97° F., or even to 95° F., but the animal is in a critical condition as soon as it falls to 98° F.,—that is, a fall of four or five degrees below the normal temperature of the dog.

Although the specific gravity of the urine is greatly lowered, the total solids and ash of the urine are increased, the lower percentage excreted being more than counterbalanced by the increased quantity of urine passed. Occasionally indican has been found in notable quantity, but this is exceptional.

The general blood-pressure remains high, even at the time when the animal is so marasmic as to be unable to stand; but the pressure is not greater than normal, and I have not been able as yet to detect cardiac hypertrophy on *post-mortem* examination. After double complete nephrectomy the blood-pressure falls.

These results may be summarised as follows:

Excision of approximately two thirds of the total kidney weight is followed by a condition of persistent excretion of a dilute urine, unaccompanied by any notable increase in urea excretion. The animal remains in fair health, and there is no great emaciation. After removal of three fourths of the total kidney weight, not only is the quantity of urine still further increased, but it is accompanied with an increase in urea excretion, a fall in the body temperature, emaciation, and death soon ensues.

The increased excretion of urea is a fact that requires a short discussion. The first question that presents itself is whether it is due simply to some severe mutilation, or whether it is actually dependent upon the amount of kidney tissue removed, and not upon the mutilation inflicted in removing it setting up some reflex or other disturbance. It is well known that after most severe operations transitory wasting is a marked feature, but in these cases it is associated with failure of appetite. In the kidney experiments, however, the appetite frequently remains good, and food is eaten in abundance; this, however, only increases the urea excretion, and does not check the emaciation or delay appreciably the fatal termination. Again, the phenomena do not ensue after the first and severe operation, but only after the removal of the second kidney.

This operation in animals, at any rate, is a comparatively trivial one from the mutilation point of view. There is, however, direct experimental evidence that the increased urea excretion is not due to what I have termed mutilation.

Firstly.—Removal of the two ends of one kidney is a more severe operation than the removal of a wedge from the middle of the organ, owing to the shape of the kidney and the difficulty of arresting hæmorrhage, and also the suturing of four cut surfaces instead of two. The amount of renal tissue that can be removed is, however, small. If after the successful performance of this operation the second kidney be removed, there is an increased excretion of urine, but no increase in urea. The phenomena are the same as in the cases where two thirds of the total kidney weight have been removed.

Secondly.—Division of the renal plexus, even when carried out as completely as possible, is not followed by any analogous disturbance.

Thirdly.—The most conclusive evidence is afforded by the results following excision of a wedge from each kidney. It is clear that if the increased excretion of urea were due to mutilation, and not to the quantity of kidney removed, under these circumstances, where comparatively little kidney is removed with the maximum mutilation, we should have the optimum condition, for its manifestation. Excision of a wedge from each kidney is followed by a condition precisely similar to that seen after excision of two thirds of the total kidney weight, the urine is greatly increased in quantity, there is no increased excretion of urea and no emaciation, and the animals have remained in good health for several months, *e. g.* two to four months. If, however, one of the mutilated kidneys be removed at a third operation, thus leaving the animal with but a fraction of one kidney, the typical disturbance of nutrition sets in, leading to rapid death, provided the fragment of kidney left is not more than one fourth of the original total kidney weight. On the other hand, if, notwithstanding the excision of a wedge from each kidney and the subsequent removal of one of the kidneys operated on, the remainder of the opposite kidney amounts to as much as one third of the original kidney weight, the increased excretion of urea and the marasmus do not occur, and the animal remains in fair health.

For these reasons I think there can be no doubt that the pheno-

mena depend upon the quantity of kidney removed, and not upon any reflex disturbance produced by the operative procedures.

Examination of the blood and tissues—*i. e.* muscles, liver, brain—of the animals where three fourths of the total kidney weight have been removed, shows the presence of a large excess of nitrogenous extractives. This excess is most marked in the case of the blood and the muscles, but it is also quite obvious in the case of the liver and brain. It can be readily detected at a time when the increased excretion of urea is in full swing, and hence it is not dependent upon any retention of urinary products. As much as fifteen times the normal amount of nitrogenous extractives has been found in the blood, and here the increase is confined to nitrogenous bodies soluble in absolute alcohol, and yielding practically all their nitrogen to the Dupré method,—that is to say, the yield of nitrogen by the Kjeldhal method was very slightly greater than that obtained by the Dupré, and hence, in all probability, this excess of nitrogenous extractives is probably mainly, if not entirely, urea. In the case of the muscles and other tissues the matter is not so simple, and I am not prepared to make any definite statement as to what nitrogenous extractive bodies are present, but simply to state that there is a very great excess. In the case of the muscles the amount may be greater than in the case of the blood. In the cases where two thirds of the total kidney weight has been excised, and where there has been no emaciation, there is no such increase in the amount of nitrogenous extractives. In a few cases, however, where removal of two thirds was followed by slight emaciation and some slight increase in the amount of urea excreted, the animals being in moderate health at the time when they were killed, there was a slight increase in the nitrogenous extractives of the blood; thus the amount soluble in absolute alcohol might be doubled. This is a point of some interest, both with regard to the question as to the cause of the increased excretion of water in the non-fatal cases, and also as showing that, to a certain extent, there is no hard and fast line between the two-thirds and three-quarter cases. It is a question of degree, and it would be interesting to know whether these two-thirds cases would be fatal after a lengthened interval.

Having thus attempted to show that the increased excretion of urea is a phenomenon associated with the quantity of kidney substance removed, or, to be more accurate; with the quantity of kidney found *post mortem*, its mode of production remains to be discussed.

Inasmuch as the increased amount of nitrogenous extractives in the blood and tissues is associated with an increased excretion of urea in the urine, it is clear that we have to deal with an increased production of urea in the tissues of the body, and not with any retention of urea from deficient excretory action of the kidney. The source of the increased urea production would be the rapid emaciation that occurs with or without failure of appetite, but not prevented by a liberal diet. This rapid emaciation and disintegration of the tissues might be dependent theoretically upon one of the following causes.

Firstly, the retention in the organism owing to inability on the part of the kidney fragment to perform its excretory functions properly, of some normal urinary constituent other than urea. This retained body might have a toxic action, and thus cause increased production of urea, &c. There are difficulties, however, which render this view untenable. Thus there is no difficulty on the part of the kidney fragment in excreting freely many of the constituents of the urine, *e. g.* urea, phosphates, sulphates, total solids, and ash. All these are increased; although the percentage amounts in the urine are diminished, the great increase in the amount of urine more than counterbalances this. Again, if the damaged kidney is unable to excrete, the typical phenomena ought to be seen after the excision of portions of both kidneys, but, as we have seen, this is not the case. It is difficult to see why, if the phenomena are due to retention, they should be so dependent upon the quantity of kidney removed when, as we have seen, the smaller fragments of kidney excrete larger quanties of urine and urea. Lastly, analysis of the blood shows that there is no accumulation of inorganic constituents, at any rate in the blood, since the ash of the serum is less in amount than normal.

The second possible explanation is that the kidney has, to use the nomenclature of Brown-Séquard, an internal secretion, and that in the absence or diminution of this the tissues, and more especially the muscles, undergo a rapid disintegration into urea and other products. The principal facts in favour of this view are, first, that the effect is so closely linked to the amount of renal tissue removed; and secondly, the negative fact so frequently insisted on above, that the fragment, small as it is, excretes urine and urea freely. Although I incline myself to this view, I feel that it cannot be considered as proved, unless by transplantation of pieces of kidney, or by injection of kidney extract, the emaciation can be diminished or

arrested. I have as yet failed in my attempts to graft portions of the kidney, and I have no observations on the effects, beneficial or otherwise, of the injection of kidney extract. In a few cases, after excision of a large wedge from one kidney, the ureter of the second kidney was ligatured instead of excising the organ. In these cases the fatal event was as rapid as if the kidney had been excised; but it is scarcely a fair experiment, since the disorganisation produced by ligature of the ureter is very great. Still, it is a result that militates to a certain extent against the internal secretion theory. I hope shortly to carry on some observations on the effects following the administration of kidney extract in these cases.

The third possible explanation is that the disturbance following the operation is dependent upon bacterial infection, a diminished resistance being produced as a result of the mutilation. This line of investigation also has not been worked out.

It seems to me that the main interest of the above experiments, from the pathological point of view, are—

Firstly, the quantity of kidney necessary for life to be maintained.

Secondly, that removal of a portion of one kidney only, or of a portion of one kidney together with the whole of the other, or of portions of both kidneys, is followed by an increased excretion of urine,—slight in the first case, considerable in the second, and very considerable in the third.

Thirdly, that removal of large quantities of kidney, *e. g.* three quarters of the total kidney weight, is followed by an increased production and excretion of urea.

In relation to renal diseases these observations, perhaps, throw some light on the increased excretion of urine seen in certain forms of renal disease. They also, perhaps, serve to show that we must widen our conception of uræmia from the retention of toxic products, to include also the formation of toxic products by increased tissue disintegration, as suggested long ago by Schöttin and Perls.

May 7th, 1895.

9. *A male fœtus showing reptilian characters in the sexual ducts.*

By Samuel G. Shattock.

[With Plate XIV.]

Before describing the condition of the sexual ducts it may be remarked that the abnormalities in question are associated with ectopia of the urinary bladder and epispadias, and that for this reason the ducts themselves, like the ureters, open on a free surface.

The ectopia of the bladder is associated, moreover, with prolapse of the intestine, which has taken place immediately above the extroverted bladder. There is thus a continuous free mucous surface, comprising the bladder and everted intestine.

Below and behind the convexity of the general protrusion is an empty scrotum and the rudiment of a penis, as in an ordinary case of epispadias. There is no intestine within the pelvis, and no anus.

Kidneys.—The kidney of the left side is normal; that of the right side so remarkably elongated that its lower end reaches far into the cavity of the pelvis. The contrast will appear from the following measurements:—the left from upper to lower extremity is 3·5 cm. in length; the right, 5·2 cm.; there is, nevertheless, no real excess in its volume.

The elongated kidney (which, like the left, is remarkably lobulated) has a single ureter, but the upper end of this is subdivided into three main branches, in correspondence with the abnormal figure of the organ. Each ureter opens on the free extroverted surface of the bladder at the upper angles of an area corresponding to the trigone.

Testicles.—On each side within the lower part of the abdomen there is a well-formed testicle, with epididymis and vas deferens.

The vas of the left side opens into the ureter about 1·4 cm. above the external orifice of the latter. On the right side the lower end of the vas is traceable by dissection slightly beyond the corresponding ureter, lying to its inner side without opening into it; its termination becomes lost in the tissues beneath the peritoneum.

DESCRIPTION OF PLATE XIV,

Illustrating Mr. S. G. Shattock's communication on "Fœtus with Reptilian Characters in the Sexual Ducts." (Page 248.)

The malformations described are complicated with ectopia of the bladder and imperforate rectum, the latter being everted and prolapsed at the umbilicus.

There are shown—

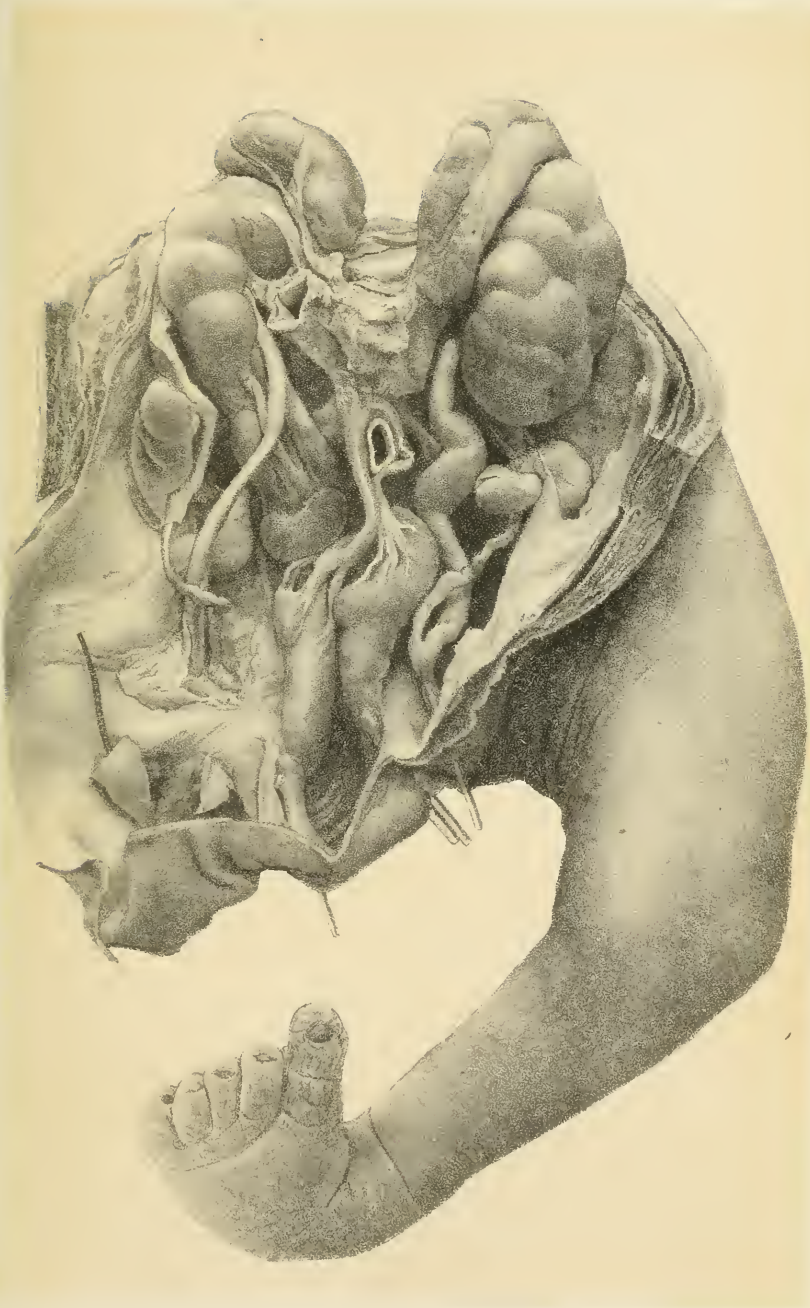
(1) The elongation of the right kidney.

(2) The persistence of both Müllerian ducts, which remain distinct throughout their course and open near the ureters on the exterior of the extroverted parts.

(3) The union of the ureter and vas deferens (on the left side) such as is met with in Lacertilia.

(4) The presence of two independent sacs, representing anal pouches; these lie in front of the lower ends of the Müllerian ducts.

The parts are shown of the natural size.



From Phot.

F Huth, Lith^r Edin^r

The *Müllerian ducts*, the persistence of which constitutes another of the valuable facts in the malformation, lie longitudinally, one on either side of the middle line. The upper end of each is bent sharply forwards and downwards upon itself for about 1·5 cm., and terminates in a blind rounded extremity. The upper end of the right is contiguous with the lower extremity of the kidney; between the upper end of the left and the corresponding kidney there intervenes a distance of 1·1 cm.

Each tube has an average diameter of 6 mm., except at the highest procurved part, where it is somewhat narrower, and from its upper point of duplicature to its lower opening the length of each is about 3 cm.

Inferiorly the ducts open on the exterior. Their openings lie to the inner side of and slightly behind the ureters; between the apertures of the persistent ducts themselves there is an interval of 1 cm.

A thick bundle of nerves extends from the hypogastric plexus to the tubes under consideration, the distribution of the nerves being chiefly to the upper part of each. Microscopic examination proves the fibres to be of the non-medullated kind.

A short way in front of the openings of the persistent Müllerian ducts are two others of lesser diameter, one on either side, which lead each into a narrow tube quite distinct from the first named. These lesser tubes lie longitudinally against the Müllerian ducts, are 1·7 cm. in length, and terminate in free blind upper extremities.

Remarks.—The prolapse of the intestine above the extroverted bladder obviously concerns the blind termination of an imperforate large intestine. The prolapse is not more than 3·2 cm. in length, but this represents all that is developed of the gut on the distal side of the umbilicus *i. e.* of the omphalo-meseraic duct. There is an aperture on the upper aspect of the root of the prolapsus which leads into the general small intestine.

In the forty-second volume of the Pathological Society's 'Transactions' Mr. William Anderson has reported the case of an infant (the specimen of which is in St. Thomas's Hospital Museum), in whom an umbilical fistula was associated with a similarly ill-developed condition of the large intestine; the latter terminated in a free blind extremity within the abdominal cavity, and did not exceed 18 cm. in length. This prolapse of the bowel in association with extroversion of the bladder is a well-recognised teratological

condition. I have seen it in another instance (lately added to the Hospital museum), where the eversion concerns chiefly the upper segment of intestine above the umbilicus, and is associated with an imperforate condition, but only slight prolapse, of the lower; both segments open freely about the upper part of the extroverted bladder. In this specimen the upper prolapse has an extent of 4 cm.; the blind distal segment, of 10 cm.; and within its umbilical opening lies the orifice of the appendix vermiformis. The

FIG. 23.

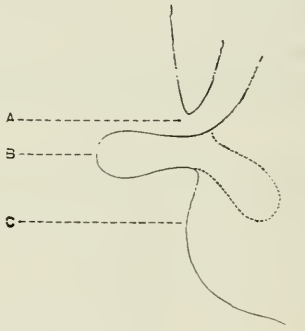


Diagram showing complete prolapse of the imperforate rectum at the umbilicus, described in the text. A. The superior opening into the upper part of the intestine. B. Completely everted, imperforate large intestine, the mucosa of which is continuous with that of C, the extroverted urinary bladder. The dotted line indicates the rectum in the unprolapsed condition.

exposed mucosa of the bladder is much thickened, and has in some parts a close-set papillary surface; whilst in others, though equally thick, it is smooth, as in a case of extroversion I have described in the forty-fifth volume of the Pathological Society's Transactions. The increase in the first instance is brought about by up-growth on the papillary type, in the second by down-growth on the glandular. The double prolapse has obviously taken place through the omphalo-meseraic duct, which seems to have been involved in the fissure affecting the urinary bladder.

Förster[1] gives figures, collected from various sources, of a similar condition (Tafel xxii); in some the upper segment is prolapsed, in

[1] 'Missbildungen des Menschen.'

others it is not. He classifies them all as examples of cloaca-formation associated with fissure of the bladder. This, however correct in a physiological sense, is misleading and erroneous in the more important morphological one.

Anatomically there is nothing homologous with a cloaca in this complication of ectopia: the large intestine is *imperforate* at its *distal* extremity; it opens, so to speak, at the wrong end, not into a cloaca, or on a cloacal surface, but about the umbilicus in the region of the omphalo-meseraic duct.

Ahlfeld[1] gives similar figures. Nevertheless what is morphologically a true cloaca may be present in cases of ectopia vesicæ, even where there is no proper anus,—if, for example, the normal developmental communication which exists between the front of the hind gut and the uro-genital sinus persist. Such a persistence is quite common in cases of imperforate rectum in the male (recto-urethral fistula), and occurring in conjunction with ectopia vesicæ would constitute a true cloaca.

The morphological test, in short, turns upon which end of the large intestine is open: if the distal end is absolutely closed there cannot be a cloaca; if this end opens on the mucous surface of the fissured uro-genital space or bladder, there is.

The remarkable elongation of the right kidney recalls the reptilian condition, such as is met with especially in the Crocodile, in Ophidia, and many Lacertilia; and it is of interest in conjunction with the corresponding reptilian disposition of the different sexual ducts to be immediately noticed. What is particularly remarkable, too, is that the elongation affects the *right* kidney, for in Ophidia the right kidney is much longer than the left. The elongated form of the kidney in reptiles is apparently related to that of the trunk; it is most pronounced in Ophidia, less so in Crocodilia and Lacertilia, whilst in Chelonia the organ is almost discoidal. So amongst Amphibia the kidneys of the frog are not strikingly long; in the newt they measure about a fourth of the entire body length, excluding the tail.

But to come to the ducts described, one on either side of the middle line. These cannot be regarded as other than persistent Müllerian ducts, which have retained throughout their primitive distinctness; there is nowhere any coalescence to form a uterus or vagina.

[1] 'Die Missbildungen des Menschen.'

As I have elsewere remarked,[1] it is a noteworthy circumstance that in cases of such persistence in the male, whether on one or both sides, the upper end of the duct is not found related to the testicle, but to the kidney, although, seeing that the hydatid of Morgagni is held to represent the upper end of the Müllerian duct, it would be natural to suppose that when persistent the duct would retain its relationship with the sexual gland during the descent of the latter into the scrotum.

In the present instance the duct of the right side is contiguous with the lower end of the kidney, but on neither side is it related to the epididymis or body of the testicle. Is there a hydatid on the testicle?

It is of paramount importance in this question to distinguish between true and false hydatids.

Let it be assumed, then, that *the* hydatid projects from between the globus major of the epididymis and the body of the testicle, and that such as project from the body of the testicle itself, or from the upper surface of the globus major, represent free ends of the Wolffian tubuli, what does the present specimen show?

In the paper last referred to I have pointed out that in one case the hydatid is stated to have been absent; in another it is recorded as having been present on the side corresponding with the persistent Müllerian duct, and absent on the opposite. There is a strong temptation to assume an erroneous transposition of "right" and "left" in this report, but so it stands, and so the specimen is figured.[2]

I may here state the results of a careful examination of a series (twelve) of fœtal testicles at different ages, which I made in order to observe the disposition of the hydatids. In one, and only one, was there a second hydatid; in this case *the* hydatid was a well-formed leaf-like appendage attached to the anterior edge of the globus major. The second, quite minute and spherical, was attached to the globus just above its anterior edge and to the inner side. In the other specimens the attachment of the hydatid lay in the fissure between the globus and the summit of the body of the testicle; sometimes it was to the under aspect of the globus, but usually to the bottom of the fissure. In the smallest specimen the body of the testicle measured 5 mm. in length; the hydatid (visible only through a lens) was fixed as last mentioned.

[1] "Parepididymal Cyst," 'Trans. Path. Soc.,' vol. xlii.

[2] Case by Chas. Rémy, 'Journ. de l'Anat. et Physiol.,' &c., Paris, 1879.

So far now as concerns the malformation under consideration, I may describe precisely the condition met with. On both sides there are hydatids. On the right side there is one hydatid attached to the summit of the body of the testicle; a second to the upper surface of the globus major, a short way from its extreme anterior margin; a third, more minute, to the line of junction between the body of the testicle and the globus major, there being no fissure between these parts as there usually is in the fœtus.

On the left side there are two minute hydatids attached to the anterior border of the globus major at the site of its adhesion with the body of the testicle, there being an absence of the usual fissure on this side as on the other. Whether *the* hydatid can be regarded as present I do not pretend to say; the result of the explanation is ambiguous and unsatisfying.

Had there been no extroversion of the bladder the persistent ducts would have opened into the uro-genital sinus, for their orifices lie slightly below, or, were the extroverted parts reduced, in front of, the ureters.

The complete independence and persistence of both ducts throughout their course must be regarded as a reversion to the reptilian type, where both oviducts open into a cloaca.

A similar persistence, of course, obtains in the Monotremata, Ornithorhynchus, and Echidna, but these characters are so essentially reptilian that they really relate the Monotremata to Reptilia; and the malformation under consideration is more correctly relegated to the last than to the lowest mammalian form. The justness of this will appear, also, in the disposition of the vas deferens to be presently noticed, which is one not found in Monotremata, but confined to Lacertilia.

As to the blind smaller tubes by the sides of the Müllerian ducts, these, it must be inferred by analogy, represent the structures so constant in certain groups of Reptilia, namely, the anal pouches which open into the cloaca.

The right pouch in the fœtus under consideration I examined by microscopic section. The wall presents a well-marked circular and longitudinal layer of unstriped muscle-fibre, and to the inner side of this a mucosa of lymphoid tissue, in which lie somewhat closely set, simple tubular glands or crypts, lined with a single layer of perfectly developed columnar epithelium.

There is finally another persistent embryonic feature, still more

interesting, and again explicable on the principle of atavism, or reversion to an ancestral type.

In the human subject the ureter is normally developed as a diverticulum from the Wolffian duct. On the left side this primitive relationship persists; the vas deferens opens on the surface in common with the ureter, or, to speak more accurately, the ureter still opens into the Wolffian duct, the original continuity of the two canals not having been lost by any subsequent dislocation in the course of development.

The arrest at this stage may be explained, then, as arising in a reversion to an antecedent reptilian type; in the same way that one so explains many of the anomalies affecting the cardiac cavities. Even what is usually regarded as a strictly pathological condition, namely, the extreme forms of hypospadias, may, it seems to me, be viewed in the same light; for among reptiles, the penis of Chelonia and Crocodilia, which is single and not paired as in Ophidia and Lacertilia, is not perforate, but merely grooved on the posterior or lower aspect, and attached to the anterior wall of the cloaca.

This commonness of the ureter and vas deferens is distinctly a reptilian condition. In the male of Monotremata the renal and seminal ducts open separately into the cloaca, as they do also in birds and most reptiles. But among Reptilia, lizards present precisely the condition shown in the specimen, *i. e.* the ureter and vas combine near their lower terminations, and open through a single aperture into the cloaca. I have ventured to figure this disposition from a particularly well-marked instance (Fig. 24).

Although the rule in Lacertilia, it is not, however, absolutely constant; Owen[1] describes the openings as distinct in *Lacerta ocellata*.

In the male of Amphibia the vasa efferentia are in communication with the kidney, through which the seminal products make their way—an arrangement considerably lower than that under consideration.

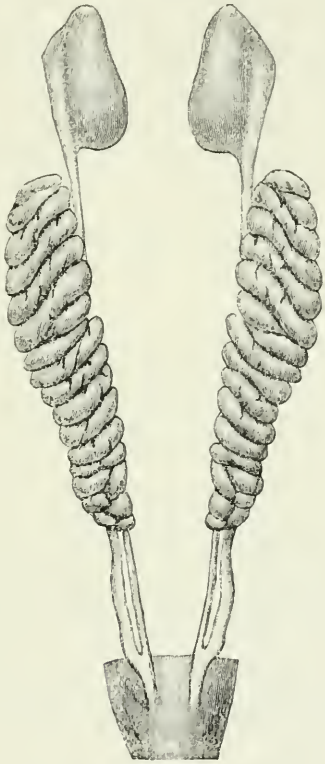
As to the unusual opening of the rectum above or in front of the apertures of the Müllerian or oviducts, such a position is met with in certain reptiles (Ophidia, Chelonia), but no true homology underlies the condition in the present case.

The intestinal aperture, as pointed out in the earlier part of this paper, does not correspond with such as would communicate with a

[1] 'Anatomy of Vertebrates,' pp. 5 and 6.

cloaca; the distal end of the large intestine is blind, and the external opening concerns not this but the proximal one, the bowel being prolapsed at the umbilicus in the neighbourhood of the omphalo-meseraic duct.

FIG. 24.

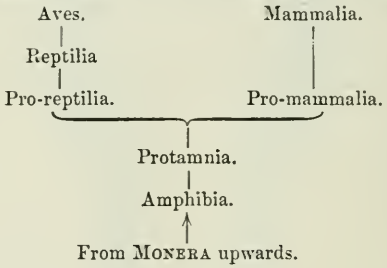


The genito-urinary organs of a lizard (*Varanus Salvator* ♂), Mus. Roy. Coll. Surg. The parts are viewed from the dorsal aspect. On either side are shown a testicle with the vas deferens, and below the testicle the much subdivided kidney. Below the kidney is the straight continuation of the vas, and, to its outer side, the ureter; these unite into a common duct before opening into the cloaca, the posterior surface of which is represented at the site of its perforation.

I have throughout referred the malformations in question to the reptilian type, because they are most conformed to this.

Haeckel,[1] in tracing the mammalian pedigree, after starting from the lowest invertebrate forms, at length reaches the Amphibia. From these he makes two diverging lines of descent,—to the one side Mammalia, to the other, Reptilia; and, beyond Reptilia, Aves. Not a few missing links there are in the pedigree, provisionally filled in. Thus above the Amphibia he places next in succession a hypothetical series of Protamnia, in which are included the primary forms of the three higher classes of Vertebrata, namely, mammals, reptiles, birds; and yet two further hypothetical groups before the proper Reptilia and Mammalia, Pro-reptilia and Pro-mammalia. The Protamnia Haeckel considers to have been most closely related to the existing Ornithorhynchus and Echidna.

Mammalian pedigree, constructed after Haeckel.



Assuming this scheme to be correct, all I can suggest is, that if the reversions in the present instance are not strictly reptilian, they are related to some of these missing groups; the reptilioid characters which they disclose might have pertained to the common ancestors of modern mammals and modern reptiles; they are lower than those of the lowest existing mammals (Monotremata), yet higher than those of existing Amphibia.

At the present time, however, there is a general agreement to relate Reptilia and Mammalia more closely, if not to regard the mammalian stem as terminating at Reptilia rather than Amphibia.

One of the more remarkable recent discoveries is the well-known fact that the ova of Ornithorhynchus are provided with a shell, and hatched, like those of reptiles, outside the body. Professor H. G. Seeley, in a paper on the nature and limits of reptilian characters in mammalian teeth,[2] remarks that if the tooth of the Ornithorhyn-

[1] 'History of Creation,' 1876.

[2] 'Proc. Royal Soc. London,' 1888, vol. xliv.

chus cannot be exactly paralleled in any other animal, it is at least evident that the teeth are as reptilian as the skeleton; that there are several features in which the teeth of reptiles and mammals resemble each other morphologically; and that the lower mammals emphatically approach towards reptiles in all essential characters of tooth form. Of teeth he gives six typical characters which are regarded as mammalian,—the presence of more than one root, &c.,—and proceeds with the statement that no one of these is constant in the class, and its loss is in every case an approach towards a reptilian type.

The same authority has, moreover, drawn attention to the skeletal affinities between reptiles and mammals, and after noticing that the most ancient mammals exhibit resemblances to monotremes, edentates, insectivores, and apparently carnivores, observes that it is among these orders that the closest correspondence is found, bone for bone, with reptiles. Seeley, nevertheless, is driven by the force of facts very close to Haeckel's scheme, as the following quotation will show. "The oldest known fossil representatives of both groups (*i. e.* reptiles and mammals) certainly approximate closer towards each other in all known parts of the skeleton, than do the orders which survive; so that it may be a legitimate induction that, in an earlier period of geological time, the characters of both groups were so blended that there existed neither the modern reptile, which has specialised by losing mammalian attributes, nor the modern mammal which has specialised by losing the skeletal characters which have come to be regarded as reptilian." In short, Haeckel's Protamnia are reptilian in type.

And this view of the mammalian pedigree is borne out by the remarkable facts disclosed in the malformation described, which in a certain sense confirm the conclusions not only of more recent zoology but those of palæontology. *February 19th*, 1895.

10. *Experimental observations on some cases of diphtheria, with a note on the mode of division of the bacillus.*

By Samuel G. Shattock.

During the month of May, 1895, three children of the same family were admitted into St. Thomas's Hospital.

Henry B—, aged eight months, admitted May 9th under Dr. Ord, having been ill three days; a very anæmic child, with discharge from the nostrils, slight retraction of the lower ribs and neck. Throat red and congested. There are two thin whitish patches on the lower part of the soft palate; the glands at the angle of the jaw on the right side are much swollen, those on the left side slightly so. There is a thick muco-purulent discharge from the nose. Breathing rapid, 33; slight stridor on inspiration with some retraction of the epigastric angle, the lower ribs, the supra-sternal region, and tissues of the neck generally. Lungs resonant throughout, but there are coarse crepitations and rhonchi to be heard generally; no tubular breathing. Heart-sounds healthy. Pulse 148, regular, somewhat weak. Temp. at midnight, 103·2°. General condition: child pale, feeble, but generally fairly well nourished; marked beading of ribs.[1]

Death May 10th, 11 a.m. The child received 7 c.c. of antitoxin at 1 a.m. May 9th, in the left flank.

The two brothers of the above patient were admitted suffering from mild attacks of the disease.

William B—, aged 2½ years, admitted May 12th under Dr. Ord. Noticed to be drowsy on May 10th, and had some cough; May 11th, difficulty in swallowing.

State on admission.—A healthy-looking child; throat somewhat red, and fauces generally very slightly swollen. On the right tonsil, at its lower part, there are two small round white spots, the tonsil presenting much the appearance of follicular tonsillitis; no patches on the pharynx, soft palate or uvula; the lymphatic glands at the angle of the jaw enlarged on both sides. No nasal discharge. Heart and lungs normal. Pulse 116, respiration 36; both regular. Temp. 102°.

May 12th, 2 p.m.—10 c.c. antitoxin injected into the right flank. Midnight: pulse 96; resp. 22; temp. normal.

[1] The clinical reports are throughout from the Hospital Case-books.

13th.—Considerable spreading of membrane; a large oval patch this morning on the left tonsil; coalescence of patches on the right tonsil; no affection of the soft palate, uvula, or pharynx. 10 c.c. antitoxin injected into the left flank.

14th.—Right tonsil clear; lower portion of patch on left persists; enlargement of the lymphatic glands at the angle of the jaw only slight.

15th.—No membrane on fauces.

26th.—Discharged.

Sydney B—, æt. $5\frac{1}{2}$ years, admitted under Dr. Acland May 10th, 1895. Complained of sore throat yesterday and coughed a good deal; had lost appetite, and was feverish. On admission was suffering from sore throat. Chest-wall moves well. Lungs resonant throughout; breath-sounds healthy. Resp. 24. Heart-sounds healthy; pulse 104. On the right tonsil there is a patch of greyish membrane; glands at the angle of the jaw enlarged. Temp. 99°. 10 c.c. of antitoxin were injected.

May 11th.—Patch of membrane can be seen on the right tonsil. 10 c.c. antitoxin.

13th.—No membrane visible; but the tonsils are much inflamed. Improvement was maintained, and patient was discharged on May 20th.

Cultivations were carried on from the two last cases. The medium used was pleuritic fluid sterilised in tubes on the slant at 100° C. in Koch's inspissator for $1\frac{1}{2}$ hours. I at first endeavoured to carry out Lorrain Smith's method of adding caustic soda in order to obtain a transparent alkali albumen, but the addition of the alkali completely destroyed the coagulability of the fluid; on almost neutralising, however, with tartaric acid solution, the original coagulability was restored.

From human blood serum Dr. Turney has obtained a beautifully transparent medium by coagulating after the addition of caustic soda. The medium used, however, was equally favourable for the growth of the bacillus.

The original culture from the case of S. B— showed only typical diphtheria bacilli. The culture was made May 11th and examined May 13th, after incubation.

The groupings and forms of the bacillus were quite regular; they exhibited the ordinary appearances of involution and transverse segmentation of protoplasm. Measured with a Zeiss's micrometer

eye-piece (compensating) the larger bacilli were 4 μ, the smaller 2 μ, though there were a certain number slightly smaller. Microscopic examination of the second subculture on serum showed a pure growth of typical bacilli.

In the case of William B— the microscopic characters of the original culture carried on May 12th and examined on May 14th were the same as in the other case, and the bacilli of corresponding dimensions; mingled with the bacilli were a few streptococci, none of which remained in the second subculture.

What I was now desirous of testing was the virulence of these cultures obtained from cases clinically mild. One child had died of the disease, and it is assuming nothing to hold that the three children in question were infected from one another, or from a common source. The interest turns upon this, that the bacillus in this trio of cases was presumably an equal quantity, and therefore that the cause of the difference in the ensuing result lay in some other factor.

Experiment 1.—May 29th, 1895. Sydney B—. For the injection I used a broth culture incubated at 35° C. for forty-eight hours, occasionally well shaken for aëration, and carried on from a second subculture on serum which was started on May 18th. The guinea-pig used weighed 560 grammes, and 10 minims of the broth culture were injected beneath the skin of the back, the operation being in all ways perfectly successful. The syringe had not before been used to inject any virulent culture of the diphtheria bacillus, and was sterilised with carbolic acid solution, &c., the cannula being boiled. The dose, calculated in minims, is that regularly adopted, viz. half a c.c. to every 500 grammes in weight of guinea-pig.

May 30th.—At 4 p.m. the animal was moribund; it lay on its side and breathing had nearly ceased; the seat of injection showed no trace of hyperæmia or anything abnormal to the naked eye. The animal was dead the next morning; on slitting up the skin there was slight œdema at the site of inoculation, and injection of the subcutaneous vessels.

It is clear from this result that the virus had not undergone attenuation.

Experiment 2.—June 10th, 1895.—William B—. I carried on a broth culture from the second serum subculture; incubated at 35° C., with occasional shaking.

June 12th, 5 p.m.—The properly calculated amount of the broth culture was injected beneath the skin, there being no hitch in the experiment.

13th.—The animal refuses food.

14th.—Dead this morning. No local lesion visible to the naked eye. On slitting up the skin there was a somewhat widespread subcutaneous œdema, and subcutaneous vascular injection, the œdema nowhere of great depth.

The observations above detailed show that the bacillus from the two milder of the three cases was not wanting in virulence, whence it is a legitimate deduction that in this set of cases the difference in result lay in the different resistance on the part of the individuals affected. That in other circumstances the difference in result is due to variations in the virulence of the bacillus is equally certain.

I may next recount two other cases of some interest, though the conclusion to be drawn is ambiguous, or perhaps none should be drawn.

Rose C—, aged 2 years and 3 months, admitted under Dr. Payne, March 19th, 1895. The patient was taken suddenly ill on March 19th. On admission the child was well nourished, and complained of difficulty in breathing; it breathed with marked stridor, and had a croupy cough. There was some retraction at the epigastrium on inspiration. The throat was red and inflamed; patches of membrane could be seen on the tonsils, the pharynx, and anterior pillars of the fauces. Lungs resonant throughout; no adventitious sounds. Heart-sounds normal. 10 c.c. antitoxin injected at 8.35 p.m., and tracheotomy performed at 10.50 p.m.; there was much hæmorrhage; a tube was inserted, and the child put back to bed; it was afterwards noticed that blood was trickling down the front of the thorax; the tube was removed, and there was some hæmorrhage; breathing ceased, and death ensued at 11.25 p.m.

Post-mortem examination.—Tonsils enlarged and congested; each presented small islets of membrane here and there. No follicular inflammation. The larynx was completely covered with a layer of membrane, the trachea and bronchi were free. No hæmorrhage into the air-passages. Heart in all respects healthy. Lungs: a little collapse here and there; no broncho-pneumonia.

When the mother came to the hospital for the death certificate, she brought with her an infant sister of the child just dead. This infant, Louisa C—, was 6 months old, and apparently quite well.

Mr. G. Gilbert Genge, at the time Dr. Payne's house-physician,

sagaciously examined the throat and saw a depression in the left tonsil, from which he inoculated a serum tube; the depression was not hyperæmic. About ten days later Mr. Genge was good enough, at my request, to visit Louisa C—, who did not enter the hospital, and for whom no treatment was adopted, as there was neither local nor general condition to treat.

The depression in the left tonsil presented just the same characters, without trace of redness or inflammation, from which it may be concluded that it had never been an ulcer.

The child was in perfect health, and had had no symptoms of disease. There had been no case of diphtheria in the Buildings where they lived, for twelve months, and both children (as well as another brother and sister both healthy) had been subject to the same conditions.

For two months before Rose's death they had been without water to flush the water-closet, which was next door to their living room. Their drinking water they fetched from a common pump downstairs during the time of the drought.

Observations on the Cultures.

Rose C—. The original culture showed typical diphtheria bacilli, with streptococci in certain numbers. From the original I carried on three subcultures at intervals of twenty-four hours, and obtained a pure culture, no liquefaction of the serum arising as happened in the original tube and the first subculture. Microscopic examination of the third subculture showed a pure growth of diphtheria bacillus typical as to groupings, involution forms, and segmentation of protoplasm; the range of sizes was from $2\,\mu$ to $4\,\mu$, though a certain number were smaller than 2 micro-millimetres.

Louisa C—. From the original culture I carried on three subcultures to serum at intervals of twenty-four hours. The macroscopic characters of the final subcultures on serum were identical with those of Rose C—; and so were streak cultures on gelatin made from the last subculture of each, the growth on gelatin quickly appearing and proceeding without any liquefaction.

Microscopic examination of the third serum subculture showed characteristic groupings of bacilli, many of the latter exhibiting typical clubbed and segmented forms. In size they had the same ranges as in the case of Rose.

If there were any differences, the segmentation of the bacilli in

Louisa was less marked a feature than in Rose, and the bacilli in general slightly less slender.

In order to again compare the micro-organisms, I carried on a fourth serum subculture from the third of Louisa, and a fourth serum subculture from the jelly culture of Rose, itself taken from a third serum subculture. I examined each tube after forty-eight hours' incubation.

Rose C—. Typical growth in small circular whitish colonies. Microscopical examination: groupings typical; bacilli short, none exceeding 4 μ; diplobacilli; involution forms; comparatively few segmented rods, these being longer than the others.

Louisa C—. Abundant growth. Microscopical examination: groupings typical; bacilli short—on an average 2 μ, but many are smaller and a few are longer, especially those which exhibit segmentation; scarcely any exceed 4 μ.

A certain number of involution forms; in many of the rods the protoplasm is intensely stained (Loeffler's methylene blue) at the end or ends of the bacilli, the colour tending to violet.

If there is any difference microscopically between the two cultures, it is that involution forms are more marked in Rose, and these being larger convey an idea that the bacilli generally are larger; but excluding this, any difference there is is so slight that it may fairly be ignored.

The macro- and microscopic characters in the two cases being identical, I determined to test broth cultures of both upon guinea-pigs.

April 27th.—Two broth tubes were inoculated from the third serum subculture of the cases, and incubated at 35° C. with occasional shaking.

29th.—Two large guinea-pigs were subjected to experiment. Two syringes and two different cannulas were used, all being carefully sterilised. The broth was shaken and poured out into sterilised capsules; the hair clipped in the middle line of the back, the surface washed with 1 to 20 carbolic acid solution and dried. (1) The first guinea-pig weighed 770 grammes. Thirteen minims from Louisa's case were injected beneath the skin. (2) The second guinea-pig weighed 957 grammes, and received 1 c.c. of broth culture from Rose's case.

May 1st.—The second guinea-pig died this morning; there was no lesion visible at the site of inoculation; on slitting up the skin the subcutaneous vessels were injected; there was very little œdema.

The first guinea-pig inoculated from the case of Louisa remained well and was kept for some weeks before being killed.

In order to be certain of the accuracy of this negative result, the experiment was repeated on another guinea-pig, a fresh broth culture of forty-eight hours being used after incubation and occasional shaking for aëration. The guinea-pig weighed 520 grammes, and received 10 minims from the same syringe as that used in the previous experiment from Louisa's case.

The injection was carried out without a flaw on May 17th. The animal remained free of all local or general trouble, and was killed several weeks later.

In this group of cases it will be seen, therefore, that a similar bacillus—similar in its cultural characters and microscopically—was obtained from a virulent case of diphtheria, and from the tonsil of the child's sister who presented no signs of any disease, either local or general.

The children lived together under the same conditions. The bacillus from the fatal case was highly virulent, as tested upon the guinea-pig; that from the other failed to produce any result whatever. The fact that the patients were sisters argues for infection having taken place from one to the other, or from some common source; but this is just the point on which strict evidence is not forthcoming.

It is here quite possible that the bacillus in Rose's case attained virulence, whilst in Louisa's it remained innocuous, or as a "pseudo-diphtheria" bacillus. This is the view my judgment would lead me to adopt in preference to the one that there was no common relation between the bacillus in the two cases, and that the presence of identical bacilli in the two children was merely a coincidence.

Observations on the Method of Division of the Diphtheria Bacillus.

One of the noteworthy points in the morphology of the bacillus is its parallel grouping. So remarkably parallel and regularly do the elements often lie that it is hard to suppose that the disposition is merely accidental. A careful study, especially of the preparations from the case of Louisa C—, has led me to interpret the grouping in question as due to a genetic relationship of the elements. What I could observe without difficulty was that between the transversely segmented bacilli and the groups of parallel elements all gradations were traceable.

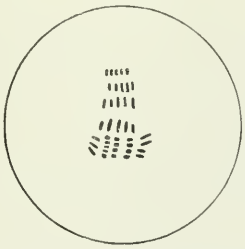
The segmentation of the protoplasm of a rod becomes more and

more pronounced until a group of separate elements results, at first not unlike the elements of a streptococcus which have undergone flattening from mutual pressure. In the next place the separate elements elongate at right angles to what was previously the long axis of the bacillus. One finds all stages between flattened coccus-like forms and a row of short parallel rods. The rods so resulting lengthen, and they may undergo a similar process of segmentation and eventually themselves give origin to another series of rods set at right angles to what was once their long axis.

That bacilli do not always divide at right angles to their long axis and then elongate in the direction of that axis is shown by an observation of Mr. Stanley Kent's, whose preparations I have had the opportunity of seeing. In the case of a particular bacillus which Mr. Kent has isolated from animals dying after removal of the thyroid gland, subdivision takes place in the direction of length, and there results a group of parallel rods ranged side by side, the middle elements being the longer, so that the whole might be circumscribed by a circle or ellipse.

The following figure will explain at a glance the view set forth.

FIG. 25.



The highest figure represents a diphtheria bacillus; below it is a parallel series of very short rods, such as would result from elongation of the segments of the bacillus at right angles to its long axis.

That the more ordinary mode of division occurs I do not deny; hardly any form is commoner in the diphtheria bacillus than a diplobacillus or two short rods conjoined; but the common method of subdivision would not account for the parallel disposition which is often so remarkable a feature in cover-glass preparations of the diphtheria bacillus, and the other method may, I think, be deduced from a study of the actual appearances themselves.

May 21*st*, 1895.

XI. SPECIAL COMMUNICATIONS.

A. Discussion on the Pathology of Diphtheria and the Antitoxic Treatment.

1. *The so-called Antitoxic Treatment of Infective Disease, illustrated by Diphtheria.*

By Bertram Hunt, M.B. (introduced by G. Newton Pitt, M.D.).

Introduction.—I must first thank the Society for the very great honour it has conferred upon me by inviting me to open this debate, and secondly publicly acknowledge my indebtedness to my friend and chief, Dr. Ruffer, for his great kindness in suggesting my name to you.

I feel myself very unworthy of my task; moreover the short notice given me—ten days—has increased my natural difficulties, and has prevented me from preparing my paper with the thoroughness which I should have desired.

In bringing this subject before you I must point out that the question of immunity invades all branches of science. Bacteriology finds itself planted firmly not only in pathology, but in physiology, biology, and chemistry, and it is, I think, creating a chemistry of its own which will form a new and advanced physiological chemistry. If, therefore, I trespass to-night into branches of science with which I am but little qualified to deal, I wish you to remember that I do so in all humility and as one seeking correction.

The subject will be taken in the following order:

1. A short glance at the history;

2. The bacteriology only so far as is necessary to a proper understanding of the production and nature of the toxin;

3. The result of introducing this toxin into animals, with the production and nature of antitoxin;

Finally, I intend to deal with the ordinary pathology so far as it affects the prognosis of the treatment.

My sketch of the history will not include all researches that are important to the subject, everything of importance being introduced where it gives most support to my argument; if, therefore, I seem to give insufficient information at first, I would ask you to remember that more will follow.

History.—The history divides itself into what may be called the pre-scientific and the scientific age.

Pliny[1] mentions that a certain king, fearing treachery, was in the habit of eating various poisons with a view of attaining to a condition of immunity to them, and that he kept a poison-eating duck, so that, if necessary, a supply of antitoxin might be at hand.

Urine has been used as a therapeutic agent, and not perhaps so foolishly as we should have considered a few years ago.

Direct inoculation against smallpox was introduced into this country from Turkey, and shortly afterwards Jenner, examining a local tradition, made that great scientific discovery of vaccination, namely, protection by naturally mitigated virus, which laid the foundations of the science of immunity.

The scientific period may be said to have originated with the genius of Pasteur, who discovered that protection could be conferred by artificial mitigation of virus, and the honour of it is fully shared also by Koch, who in the perfection of method founded a new branch of science, to the rapid progress of which our subject of debate to-night is sufficient testimony.

Then in 1887 there were three great discoveries, Salmon and Smith[2] proving that not only mitigated bacteria, but their products, were able to confer protection; Sewall[3] that immunity was possible to rattlesnake venom; and Fodor[4] that the blood was able to destroy bacilli.

Fodor's most important research was followed up by Nuttall,[5]

[1] 'Spät. Münch. med. Woch.,' 1894, p. 923. Pliny, 'Natur. Hist. Lib.,' xxv, s. iii.

[2] 'Proceedings Biol. Soc. Washington,' 1886, vol. iii.

[3] "Experiments on the Preventive Inoculation of Rattlesnake Venom," 'Journal of Physiology,' 1887, p. 203.

[4] "Die Fähigkeit des Blutes Bacterien zu Vernichten," 'Deutsche med. Woch.,' 1887, No. 34.

[5] 'Zeitschrift f. Hygiene,' 1888, Bd. iv, p. 353.

Nissen,[1] and Behring,[2] being finally perfected by Buchner,[3] it being found that the bactericidal quality of the blood passed into the serum, and was due to an active proteid, that is, a proteid destroyed by heat, which Buchner named alexin.

These investigations immediately and naturally led to an examination of the blood of immune animals, and in 1891 Behring[4] announced the discovery that if immunity to tetanus or diphtheria had been conferred upon animals, their blood or serum was found not only able to protect other animals against either the bacteria or their soluble specific poison, but even to cure them if injected subsequently to the virulent matter, and as a mixture of the serum with the toxin *in vitro* was found to be quite innocuous, he called the serum antitoxic, the unknown substance in the serum antitoxin, concluding that the curative agent and the toxin neutralised each other in the test-tube. The subject of debate to-night is, I take it, primarily an examination into the properties and nature of this so-called antitoxin.

In this same year, 1891, an equally important research was published, one that forms, or should form, what I will call our first reading book on this subject. I refer to Ehrlich's work on immunity to ricin and abrin.[5] Ehrlich, realising that toxins formed by bacteria were variable in strength and intangible in form, decided to investigate, on lines similar to those pursued by Behring, the two vegetable poisons ricin and abrin.

He was able to immunise animals by feeding, and the fatal dose being determinable with absolute exactness, could express the degree of the immunity by the number of fatal doses borne. He found the blood of such immune animals protective and curative to others, the amount of serum requisite to this purpose being proportionate to the degree of immunity attained, that is to say, the antiricin obtained equalled the ricin previously introduced.

[1] 'Zeitschrift f. Hygiene,' 1889, Bd. vi, p. 487.

[2] 'Centralblatt f. klin. Med.,' 1888, No. 38.

[3] 'Centralblatt f. Bakt.,' 1889, Bd. v, p. 25; Bd. vi, pp. 1 and 21. 'Archiv f. Hyg.,' 1890, p. 85.

[4] 'Deutsche med. Woch.,' 1890, Nos. 49 and 50. 'Brit. Med. Journal,' 1891, vol. ii, p. 406.

[5] "Experimentelle Untersuchungen ueber Immunibät," 'Deutsche Med. Woch.,' 1891, Nos. 32 and 44.

The present method is, on the other hand, to reckon the degree of immunity by the antitoxic value of the serum, and to express this as the ratio between the weight or amount of antitoxin necessary to protect and the weight of the animal protected.

There are, therefore, two ways known to us of protecting against infective disease.

1. The Pasteur method, *i. e.* the introduction of mitigated virus into an animal with consequent slight illness, recovery and protection against a virulent virus. This form of immunity is known as "active immunity," and is more or less permanent.

2. The Behring method, *i. e.* the introduction of mitigated bacteria or their products into one animal with consequent slight illness, recovery and protection against a virulent culture or toxin, and the transference of this immunity to another animal by the injection of blood or serum taken from the first. This transferred immunity is called "passive immunity," and is temporary only.

By the first method the animal is allowed to form its own antitoxin; by the second the antitoxin is previously formed in one animal, and transferred as a therapeutic agent to another. Antitoxic treatment is therefore natural treatment, seeing that in a case of diphtheria, should the child recover, it will if bled be found to have diphtheria antitoxin in its blood;[1] it recovers, that is to say, because it has been able to form antitoxin. It seems, therefore, most reasonable to manufacture this substance in some animal, and by introducing it into the human organism help it in a task which it is often unable to perform without assistance.

Production of the Toxin.—Roux and Yersin were the first to show that the diphtheria bacilli grown in bouillon formed a specific poison which, apart from the bacilli, could produce all the symptoms of experimental diphtheria, and they noticed that a certain supply of oxygen to the culture increased the virulence of the toxin. They observed that the culture fluid became acid at first, and then again alkaline after some weeks, the toxin only becoming virulent upon the appearance of this alkalinity.

Behring found that the older the cultures were the more virulent was the poison, and that they attained a maximum toxicity in about eleven weeks—a long time to wait.

[1] "Klemensiewicz u. Escherich," 'Centralbl. f. Bakt.,' 1893, p. 153. Abel, 'Deutsche med. Woch.,' 1894, Nos. 48 and 50.

Roux,[1] in his recent paper on the subject of diphtheria antitoxin, described his method of passing air over the culture, by which a strong poison is obtained in a few weeks; and with Dr. Ruffer's permission, I am showing this evening the flasks designed by him for the passage of air either over or through the culture.

Aronson[2] has lately described a way of obtaining very virulent toxin in a short time. He states that he inoculates the bacilli on the surface of the bouillon, but he mentions no method.

Now, seeing that the passage of air either over or through a culture gives a great deal of trouble, and has other disadvantages, I have endeavoured to devise some means of enabling the bacilli to grow on the surface of bouillon in an ordinary flask. Occasionally the bacilli do grow thickly on the surface, but their specific gravity being greater than that of the media, they sink as a rule to the bottom. When the surface growth does occur it seems to be due to the presence of some scum on the bouillon, probably caused by fatty matter either left in the bouillon when made or derived from the wool.

Schreider[3] has described the formation of a toxin of extreme virulence, when at Nenscki's suggestion he associated streptococci and diphtheria bacilli together in his liquid cultures; and working on the same lines I found that in this association—this mixed culture—a surface growth of the bacilli invariably occurred, and that the toxin produced was very powerful, the increase of toxicity being probably merely caused by the surface growth. It seemed, therefore, feasible to float something on the surface, to which the diphtheria bacilli might attach themselves, so as to secure this luxuriant growth. I have found that a little fatty substance, for instance even a little vaseline, will ensure this. Pounded or filed cork yields excellent results, and also little rafts made of cork wrapped round with wool and muslin, so as to form nutrient islands. In any of these ways a copious growth, an early alkalinity, *i. e.* a virulent toxin, is quickly attainable. Cork, however, has an unfortunate habit of sinking after prolonged boiling; but to my great surprise the bacilli seem to grow more luxuriantly than in ordinary bouillon, even when the cork is at the bottom or sticking to the

[1] 'Annales de l'institute Pasteur,' 1894, p. 609.

[2] 'Wiener med. Woch.,' 1894, No. 46.

[3] 'Centralbl. f. Bakt.,' 1892, Bd. xii, p. 9.

sides of the flask. Apparently they have an inveterate predilection to spread over a surface, and the addition of the cork, even if it sinks, naturally increases the area over which the bacilli can grow.

It seems best to mention this new method—this bouillon surface method—although the inquiry is incomplete.

Action of Oxygen on Diphtheria Culture.—This question of the action of oxygen on a pathogenic bacillus is extremely important and interesting. It has been a recognised tenet of bacteriologists that a pathogenic microbe was a facultative aërobe, that is, one able to take its oxygen either from the air or from the culture media, and that in the body a pathogenic microbe led an anaërobic existence, that is, lived without free oxygen.

Moreover, it has always been described how certain bacteria able to luxuriate in the animal organism grow but feebly on our nutrient media at first, but that as they become accustomed to the media and to the air, take on a saprophytic growth, luxuriate more and more, and with this increase of growing power are found to have lost their pathogenic quality—and Fraenkel's pneumococcus, the streptococci, and Loeffler's bacilli, were supposed to be typical examples of this. And yet a description has had to be given you of various methods devised apparently to bring about this saprophytic stage of the diphtheria bacilli, and the importance of them for the rapid production of toxin insisted upon.

To a proper understanding of this process it is necessary to consider the growth of the bacillus in two different ways. Let one culture be made in bouillon and incubated for three days; it will then be found of extreme virulence, at its maximum of virulence as regards the bacilli, but if filtered, if freed from the bacteria, a comparatively harmless and acid solution. Make the second culture in the subcutaneous tissue of a guinea-pig, and after twenty-four hours the animal dies, killed by the toxin produced by the bacilli. In this culture the bacilli have had no free oxygen, and yet have succeeded in elaborating a poison of a degree of virulence and with a rapidity unattainable by any bacteriological method. Why, then, is admission of oxygen apparently so essential in our flask cultures? A clue is afforded by the reaction. The virulent bacillus renders its culture media acid in twenty-four to forty-eight hours, and the toxin is only found in an alkaline culture—is, as I shall suggest later, only soluble in an alkali; and it must be noted that any acid formed is removed or neutralised in a child's throat or guinea-pig's tissue. Is the matter not explicable in this way, namely, that

the oxygen prevents the acidity altogether, and that although its free admission tends to encourage a merely saprophytic or non-pathogenic growth of bacilli, this disadvantage is more than counterbalanced by the maintenance of an alkaline reaction?

Dr. Ruffer has found that cultures exposed freely to a supply of air do remain alkaline.

If therefore the bacillus is forced to derive its oxygen from the nutrient media, an organic acid is formed by the reduction of some constituent in it, and accumulates.

Pasteur's classical experiments with yeast cells form an interesting comparison. He found that in order to obtain a vigorous yeast it was necessary to make surface cultures freely exposed to the air, and observed the fact that, although there was in such cultures a remarkable proliferation of yeast cells, little or no fermentative action occurred—the latter, on the contrary, only taking place when some of this aërobic culture was afterwards cultivated anaërobically. By analogy, therefore, the cultivation of Loeffler's bacilli with a free supply of oxygen should lead to a rapid growth of cells and to a lessened fermentative action.

What is found is that the proliferation of the microbes is astonishing, and that as far as the formation of the acid is an index, its absence is a sign that the ordinary fermentative processes are in abeyance.

There is no evidence, however, that this exuberant aërated growth of bacilli has acquired any accession of virulence. On the contrary, in my paper[1] on methylene blue and Loeffler's bacilli I showed that the bacilli, by the continuous reduction of the blue in their struggle against the stain, were quickly attenuated and eventually killed, and that the fact that the reduction of the blue was accelerated by a temperature 44° C., namely, what I described as the mitigation temperature, was an additional proof of this attenuation by oxidation.

By adding a little methylene blue, in a proportion of 1—50,000, to a three days' culture in a flask, the culture being one inch in depth, and allowing permanent reduction, I have found that the bacteria produce no acid, but that the culture perishes in about nine days; in other words, a constant supply of oxygen is soon fatal to them.

Although aëration of a culture leads to a rapid formation of

[1] 'The Lancet,' 1894, vol. ii, p. 733.

toxin, I have reason also to believe that its continuous supply rapidly mitigates the poison, and that apparently after fourteen days the toxicity declines.

Filtered toxin left about even in yellow bottles rapidly loses its virulence, and I have, in some experiments I have made as to the effect of oxidation and reduction on the poison, discovered that whereas oxidation, however effected, mitigates it, reduction distinctly increases its virulence.

A free admittance of oxygen to the culture promotes therefore the growth of the bacilli, and leads to an early formation of the toxin, suggesting that the specific poison is some constituent of the bacterial protoplasm.

Nature of the Toxin.—Bacterial specific poisons were at first supposed to be ptomaines, and although bacteria do many of them produce alkaloidal and other poisons, they are of no importance to the subject this evening, nor indeed in any problem of immunity, in that they are not specific.

Brieger and Fraenkel[1] described a bacterial poison as toxalbumen or proteid poison—an excellent name, for it implied a specific nature,—and placed bacterial toxins in a class with such bodies as ricin abrin, and cobra poison, to which they so evidently belong, viz. poisons against the action of which a rapid and specific immunity and not a mere tolerance is attainable; and in this country Hankin[2] and Dr. Sidney Martin described the formation of albumose in the culture media. Roux and Yersin, in their paper on diphtheria, came to the conclusion that the toxin was an enzyme similar to diastase, it being precipitated by entanglement.

The choice of the word albumose is unfortunate, for it is necessary to distinguish carefully between the vital chemical processes of the bacteria and of the action of these on their environment,—between the bacterial metabolism and any fermentative action it may exert; and I have found that an old bouillon culture of the bacilli can be entirely freed from toxin by Roux's method of precipitation by calcium phosphate, viz. by entanglement. The filtrate from such a precipitate was neither toxic nor protective; in other words, the products, if any, of fermentative action were harmless and innocent.

[1] 'Berlin klin. Woch.,' 1890, Nos. 11 and 49.

[2] 'British Med. Journal,' 1889, vol. ii, p. 810.

Hankin's[1] experiments with his protective albumoses militate against this view, seeing that he took the precaution of removing by a precipitate of calcium phosphate any active proteid present in the solution.

Buchner,[2] however, has succeeded in growing tetanus bacilli in a solution of asparagin, and in obtaining by precipitation with sodium-magnesium sulphate a most virulent toxin.

Guinochet[3] has grown diphtheria bacilli in urine with similar results.

These two experiments show that toxin is elaborated not in the media, but in the protoplasm of the bacteria,—a proteid poison being formed in a solution containing no albumen,—and that the production of bacterial poison is due to synthetic and not fermentative action. The effect of aëration of the diphtheria bacillus cultures, the rapid growth, the suggestive absence of fermentative action along with a rapid production of toxin, all agree with these two conclusive experiments.

I will define, then, the diphtheria toxin as a specific proteid poison. But it must be clearly understood that it is not necessarily the proteid which is the poison, but what may perhaps be described as its disposition, its active and specific quality. Such active proteids have been called living proteids; if this were adopted, then the toxic quality must be defined as the life in the proteid. The proteid having adherent to it this toxic quality is probably the myco-nucleo-albumen described by Gamaleia,[4] a substance soluble only in alkaline media, and possibly only on the death of the bacilli.

The analogy between well-known proteid poisons, such as ricin and abrin, and diphtheria toxin makes the word proteid seem better than protein, and myco-proteid more suitable than Nenscki's myco-protein. These proteids are, however, apparently albuminoid in character.

The production of antitoxin.—The toxin, the vital chemical quality of bacterial protoplasm, is concerned in the metabolism of the bacteria, but it must be considered to have a more important function, and one of special interest to us. It constitutes the

[1] 'British Med. Journal,' 1889, vol. ii, p. 810.

[2] 'München med. Woch.,' 1893, Nos. 24 and 25.

[3] 'Archiv. de med. Experiment.,' t. iv, 1892.

[4] 'Compt. rend. de la Soc. de Biol.,' 1892, p. 153.

offensive and defensive weapon of the microbe in its struggle for existence. I would say that in all living cells the protoplasm possesses this vital quality, and I maintain that all pathogenic bacteria have this specific and active quality in their protoplasm, but that it is not necessarily toxic apart from the bacteria, although it enables them to grow and produce other poisons in the animal organism.

It is necessary therefore, I think, to regard the animal organism as a collection of pure cultures of cells of various types, living together in harmony and in a state of complete chemical compatibility; as the forms of life fittest to survive in that particular environment, the animal body; as resenting the intrusion of foreign substances, whether alive or dead, and with offensive and defensive weapons to maintain their existence, these weapons being chemical ones: in short, to apply Darwinism to this question of immunity, and consider the strife between the cells and the bacteria as a struggle for existence fought out between the synthetic vital processes arrayed on both sides. And as the cells may be said to acquire an accession of virulence in endeavouring to defeat the bacilli, as their chemical quality becomes more toxic to the bacteria, so, as Pasteur showed, bacteria may be made more virulent by passage through a refractory animal, that is, when the struggle is imposed on them.

In animals, then, which have a natural immunity to any infective disease it is obvious that the specific proteid elaborated by the bacteria causing that disease must be either inoffensive or easily destroyed by the cells, and that it would occasion no struggle, no additional chemical activity in the animal cells, *i. e.* no constitutional or local disturbance. We ought not to expect, therefore, that such a body would be modified in any way, but merely excreted or quietly and quickly destroyed.

Kitasato found that fowls were naturally immune to tetanus; he was able to inject them with very large doses of the specific poison without causing any symptoms, nor did he find any protective substance in their blood.

I have investigated the fate of diphtheria toxin in white rats and mice. Mice were injected with doses sufficiently great to kill thirty guinea-pigs in forty-eight hours, their urine was collected, and they were killed after four, eight, twelve, and sixteen hours, an extract being made of the whole mouse, the stomach, intestines,

&c., being removed. The urine was found toxic at first, but after about eight hours practically harmless; the extracts were found to follow a similar rule.

Behring has succeeded in making mice ill with large doses, but as he used old bouillon cultures, there were probably besides the specific poison other deleterious substances present. I used toxin precipitated with alcohol, and so free from this objection. The point however, of importance is that the urine and the extracts were found first toxic, then harmless, but never protective, *i. e.* no curative agent, no antitoxin was formed. Moreover there was no evidence of any struggle, not even a local reaction following these large doses.

In susceptible animals, on the other hand, it is a struggle, for a foreign proteid is introduced offensive and harmful to the animal organism. And this struggle particularly concerns us this evening, for if the animal organism gains the upper hand it is able to yield us a substance of the highest therapeutic value.

The effects of injecting virulent diphtheria bacilli or their filtered toxin into susceptible animals are a local reaction at the place of injection, accompanied by a slight rise of temperature, a laboured breathing with eventual cyanosis, and then six hours before death collapse and diarrhœa, the temperature falling perhaps to 32° Centigrade.

If, however, the animal has been previously treated with mitigated toxin, the injection of the virulent matter is followed by a considerable rise of temperature, local reaction, and general symptoms of illness with marked loss of weight, then improvement and recovery. As soon as the health is completely restored, and the weight has attained its former level, it may be again injected, and this time with a larger dose. Such a process carefully repeated with ever-increasing doses of toxin is found to confer a high degree of immunity on the animal, and a corresponding antitoxic value on its blood.

Certain laws must be obeyed in this process of immunisation, which we owe chiefly to Behring's observations. (Behring deserves the credit of these, although one or two were actually formulated by others.)

1. That it is absolutely necessary to wait until the animal is completely restored to health before a fresh injection is given.[1]

[1] Behring, 'Deutsche med. Woch.,' 1890, Nos. 49 and 50.

2. That the antitoxic value of the blood reaches a maximum coincident with this return to perfect health, and then falls somewhat to a more or less constant level.[1]

3. That any fresh injection of toxin is best made when the antitoxic value is at its highest.[2]

4. That the more susceptible the animal—in other words, *the harder the struggle is*—the greater the degree of immunity finally attainable, and the more antitoxic the blood.[3]

5. That the immunisation can be pushed too far and a condition allied to natural immunity brought about,—a condition to be avoided, seeing that, as I have shown, animals naturally immune produce no antitoxin.[4]

As regards the choice of animal.—Behring mentions the horse, but preferred the more susceptible sheep and cows, &c. The process of immunisation, however, of these animals is a very tedious one, and many of them die.

Aronson and Roux with Nocard chose the horse. This animal was not found to be very susceptible, but could be raised to a sufficiently high degree of immunity in a short time with but little trouble or anxiety, and although probably never able to yield so much antitoxin as a more susceptible animal, yet proved the most convenient to the purpose.

Nature of Protective Action of Antitoxin.

1. *Is it antitoxic?*

It is better to repeat that Behring, finding a mixture of toxin and antitoxin in proper proportions in a test-tube harmless to guinea-pigs, concluded that the two substances had neutralised each other *in vitro*. If he has yielded now from this conclusion it has been with reluctance,[5] and it has seemed best to show that direct antitoxic, antidotal action takes place neither *in vitro* nor in an animal organism.

[1] Brieger u. Ehrlich, 'Zeitschrift f. Hyg.,' 1893, Bd. xiii, p. 336.
[2] Behring u. Knorr, 'Zeitschrift f. Hyg.,' 1893, Bd. xiii, p. 414.
[3] Behring, 'Zeitschrift f. Hyg.,' 1892, Bd. xii, p. 56.
[4] Behring u. Knorr, 'Zeitschrift f. Hyg.,' 1893, Bd. xiii, p. 414.
[5] 'Deutsche med. Woch.,' 1894, No. 8.

Buchner[1] may be said to have settled this question once for all time by his very clever experiment with tetanus antitoxin.

He injected ten mice and ten guinea-pigs each with one tenth milligramme of his tetanus toxin. The ten mice all died, the guinea-pigs recovered. It is easier, therefore, to kill the mice than the guinea-pigs.

He then took twenty-three mice and twenty-three guinea-pigs, and injected each animal with fourteen milligrammes of tetanus toxin mixed some time previously with 1·35 milligrammes of his tetanus antitoxin, *i. e.* time was allowed for any neutralisation in a tube. Each mouse, therefore, received 140 fatal doses. Of the twenty-three mice only three died, eleven exhibited passing tetanic symptoms, and nine showed no symptoms at all.

If this had been due to any neutralisation in the mixture, then a still better result should have obtained in the case of the guinea-pigs. But of the twenty-three guinea-pigs eight died, twelve had somewhat severe tetanic spasms, and only three showed no symptoms at all.

There could, therefore, have been no direct antitoxic action. Buchner explains it admirably as being due to the fact that the tetanus antitoxin is less efficacious as a stimulus to the cells of guinea-pigs than it is in the case of the white mice.

Roux[2] has proved in a different way the same fact in regard to the diphtheria antitoxin.

He made such a proportional mixture of diphtheria antitoxin and diphtheria toxin as he found harmless when injected into healthy guinea-pigs, and then with the same mixture treated some pigs whose vitality he had lowered by an infection of a different kind. The latter succumbed to the mixture.

The two substances, therefore, antitoxin and toxin, exist side by side, and no neutralisation occurs either *in vitro* or in the animal organism. The antitoxin, moreover, acts merely as a stimulus to the chemical processes of the cells; and if these cells be enfeebled in any way and their vitality lowered, the stimulus fails to rouse them and the antitoxin is of no avail.

Now to gain a correct view of the protective action of antitoxin, and to properly appreciate how untenable the idea of any direct antitoxic action is, it is necessary to briefly consider some of the other infective diseases, particularly those in which the bacilli would seem to produce no specific poison.

I must remind you that it was maintained that all pathogenic bacteria must have within them a specific chemical quality able to cope with the protective power of the animal cells, and that I defined the substance possessing this quality as a specific mycoproteid, and pointed out that it was not necessarily poisonous

[1] 'München med. Woch.,' 1893, Nos. 24 and 25.

[2] "Congress Budapest 1894," 'Annales de l'Institut Pasteur,' 1894, p. 722.

apart from the bacilli, the symptoms being caused chiefly by non-specific poisons elaborated by such bacteria, non-proteid or proteid.[1]

If this reasoning was correct, it follows that just as in animals immune to diphtheria a curative substance is found in the blood, so a similar curative substance must be obtainable in the case of all disease caused by the invasion of the animal organism by any kind of cell foreign to it.

Now, in animals or humans immune to any infective disease in which the microbe causing that disease has been isolated and grown by bacteriologists, this curative quality of the serum has been demonstrated.

This curative quality of serum in immunity to disease has been designated as antitoxic only in tetanus and diphtheria, and not in the others, because the bacteria concerned in their production do not produce any definite specific poison for the serum to have been erroneously supposed to be able to neutralise.

It has not been called antibiotic because it was far easier to show that such serum possessed no antibiotic power, than that so-called antitoxin has no antitoxic power; for it was but necessary to cultivate the bacteria in the curative serum to determine that point. For instance, the serum of animals immune to cholera is not antibiotic to cholera bacilli *in vitro*, but is none the less curative.

Hence there have been no false tenets upheld, and the name antibiotin has not been invented for such curative agents; for while a milligramme of serum could be supposed by some to

[1] *Explanation of difficulty.*—For instance, with regard to this quality of the bacterial protoplasm being the offensive weapon of the microbe, and yet not necessarily the poison.

Bacteria.	Poisons Formed.	
	A	B
1. *Bacillus diphtheriæ.*	Offensive quality.	Nil.
2. *Bacterium x.*	Offensive quality.	Proteid or non-proteid poison.

In the first case immunity to bacilli and toxin is identical.

In the second case immunity to bacilli does not necessarily imply immunity to toxin. Treatment with filtered culture might confer immunity to bacilli but not to toxin, and similarly serum from a protected animal would only protect against bacilli and not against toxin.

neutralise a cubic centimetre of toxin either in the test-tube or in the body, no one has ventured to assert that so small a quantity could destroy the virulent bacilli contained in 1 c.c. of a bouillon culture, either *in vitro* or after introduction into an animal.

It must not be supposed, however, that any possible increase of the natural germicidal power in the blood of the immune animal is denied, but it is only maintained that the substance here designated antibiotin has no antibiotic quality in itself; and, as Buchner has pointed out, the serum of an animal may be deprived of its antibiotic, its bactericidal quality by heat, and yet retain its specific curative quality. Increase in this germicidal quality of serum will be referred to later.

2. *Antitoxic treatment an immunisation.*

In order to prove that antitoxic treatment is in reality a rapid process of immunisation it is only necessary to compare the action of one of these "antibiotins" with diphtheria antitoxin.

Pfeiffer,[1] in his recent investigations into the curative action of the blood of animals immune to cholera, has described an extraordinary rapidity of protection.

He introduced virulent cholera bacilli into the peritoneal cavities of guinea-pigs, along with a small dose of protective serum, and removed from time to time some of the peritoneal contents for microscopical examination.

It was found that the bacilli lost their motile power almost at once, and were in one case killed in a quarter of a hour. Seeing that the protective serum was found to exert no bactericidal action on the bacilli *in vitro*, it is sufficiently obvious that it must have acted as a stimulus to the cells whose environment was contaminated, must have instantly conferred upon them the chemical ability to cope with the invading microbes.

This treatment of guinea-pigs with curative serum in experimental cholera infection may be defined, therefore, as being merely a rapid immunisation method, so rapid as to be practically instantaneous; and there is no reason to doubt but that the action of antitoxin in diphtheria is precisely similar. The best way, therefore, to express the method and meaning of this process of protection is by calling these protective and curative qualities of the blood of immune animals specific immunising or curative agents.

It follows from this that diphtheria antitoxin, *i. e.* the specific immunising agent in diphtheria, is also antibiotic; that is to say,

[1] 'Zeitschrift f. Hyg.,' 1894, Bd. xviii, p. 1.

by its presence it enables the animal cells to cope with the specific quality inherent in the protoplasm of the Loeffler bacilli, this quality being not only the poison, but probably the vital chemical factor in that microbe's existence. In other words, antitoxin confers both antitoxic and antibiotic power on the cells.

The argument followed leads inevitably to this conclusion, and it is hardly necessary to remind you that antitoxin protects against both toxin and bacilli in experimental diphtheria.

3. *The rapidity of this immunisation.*

Attention may now be drawn to the rapidity of the immunisation in diphtheria.

In an ordinary poisoned wound, say of the finger, we are able to trace the absorption of the poison by the lymphatic system. There is evidence in the swollen lymphatic glands of some struggle. In simultaneous injection of diphtheria toxin and antitoxin as ordinarily practised, the mixed solution must pass through the lymphatic glands, and in the presence of the antitoxin the cells are able to deprive the toxin of its injurious character, and therefore no illness results, but—and is it not amazing—there may be no local reaction; in other words, a condition of immediate immunity would seem to be conferred on the tissues in which the injection is made, *a condition having more analogy with the natural immunity described in white mice* than with any protected condition hitherto known to us, where local reaction has been welcomed as proof of increased resistance. Pfeiffer's experiment, however, ought to lead us to expect this rapid local immunisation.

From this absence of local reaction it must be concluded *that the power of dealing with specific proteids or bacteria cannot be limited to any one type of cell, but that all can take their share in the work;* and, further, it becomes clear why more antitoxin is requisite when it is injected separate from the toxin, for it is only in the presence of the antitoxin that the cells are able to deal with the toxin, and damage is done before the two are brought together. By that time the cells are in a damaged condition, and, as Roux's experiment showed, unable to answer to the protective stimulus unless the stimulus be increased, *i. e.* a larger dose of antitoxin be given.

Nature of Antitoxin.

Before, however, discussing the way in which antitoxin confers this immunity it is necessary to consider its nature.

Attention has already been drawn to the fact that mitigated toxin is able to confer immunity, but only after an illness and the lapse of time; moreover that the immunity produced was more or less permanent.

Antitoxin is, however, very different in its action from that of any modification of toxin *as yet known* to us. For it is therapeutic, whereas toxin mitigated by any of the ordinary methods, if injected simultaneously with virulent toxin, is found by me to accelerate the fatal termination. Antitoxin is, moreover, perfectly harmless; it produces no symptoms, and the immunity which it confers is immediate and temporary. There is therefore apparently no similarity between the two methods of conferring protection.

Buchner would seem at one time to have thought that antitoxin might be obtained directly from the bacterial protoplasm, but it must, I think, be considered to be either a direct or an indirect product of the animal cells; in other words, either as a secretion or as excreted foreign matter.

Is antitoxin a direct product of the cells?—Buchner[1] has given a very valuable comparison between the bactericidal substance present in serum—namely, alexin, which is a direct product of the animal cells—and the so-called antitoxin. He points out—

1. That alexin is able to destroy bacilli and even the leucocytes of the blood of a different species of animal.

2. That it is very unstable, being destroyed at a temperature of 55° C., and by sunlight, and that it loses its activity rapidly *in vitro*.

3. That, moreover, it varies with the species of animal; in one species it is able to kill one bacteria, in another species another.

That antitoxin, on the other hand, has very different physical properties.

1. It has no bactericidal action.

2. That tetanus antitoxin will withstand a temperature of 70° to 80° C. without losing its antitoxic power, and is, moreover, unaffected by sunlight or even by putrefaction. Diphtheria antitoxin, as Wernicke showed, is not destroyed by peptic digestion.

[1] 'München med. Woch.,' 1894, Nos. 24 and 25.

3. That antitoxin never varies with the species of animal, but always with the species of bacteria through whose agency it was formed.

Buchner insists—and rightly, I think—upon this specific quality of antitoxin—that tetanus antitoxin cures tetanus but not diphtheria, that diphtheria antitoxin cures diphtheria but not tetanus—as being strong proof that these specific curative agents, found in the blood of immune animals, cannot be direct products of the cells.

A short illustration is necessary to emphasise this specific character. Pfeiffer's cholera experiment has already been described, namely, how cholera bacilli introduced along with the curative serum into the peritoneal cavity were at once destroyed.

To prove the specific character of this immunisation process, Pfeiffer sowed in the guinea-pig's peritoneum a mixture of two kinds of bacteria, cholera bacilli and the Nordhafen vibrio, injecting simultaneously the serum protective against cholera; and he found that the cholera bacilli were destroyed, the other bacteria left uninjured. He perfected this brilliant experiment by reversing it, namely, by introducing the same mixture of bacilli, but on this second occasion a serum protective against the Nordhafen vibrio, and found that this time the cholera bacilli escaped destruction while the Nordhafen vibrio succumbed to the cellular secretion.

It might be argued that this experiment is, on the contrary, a proof that the cells are able to secrete a specific agent, a substance able to pick out and destroy a particular species of microbe; but this specific secretion will, I think, be found to be similar in its physical properties to alexin rather than to antitoxin, for, according to Pfeiffer's experiment, it was very unstable.

I consider the specific nature of these curative agents to militate strongly against the assumption that antitoxin is a direct product of the cells.

Buchner has also a further and weighty argument in support of this contention with reference to the transference of immunity.

Natural immunity is not transferable; it is impossible to bestow bactericidal power on the blood of one animal by the introduction of an efficacious alexin from that of another. A well-recognised direct secretion of cells is, therefore, not transferable.

It is hardly necessary to state that the antitoxic treatment of diphtheria is the successful transference of some curative agent, and this distinction between alexin and antitoxin suggests that antitoxin is some foreign matter circulating in the blood of the immune animal.

Antitoxin is modified toxin.—I now proceed to show the very strong reason there is for regarding antitoxin as an excretion of the cells, and I will define antitoxin and the specific curative agents found in the blood of animals immune to infective diseases as being the specific proteids of the bacteria to which immunity has been attained, conquered, modified, and digested by the cells; and that whatever their chemical nature is, they must be considered as derivatives from such myco-proteids, still possessing some degree of their specific nature, but *with a wholly beneficent character*. To regard specific curative agents as being of this nature is to find an explanation of many otherwise most puzzling facts.

First in support of my argument let me remind you that the antitoxic value of any serum depends directly upon the degree of immunity existing in the animal yielding such serum, and that the degree of immunity varies directly with the amount of virulent matter previously introduced. Ehrlich's classical experiments with ricin and abrin are proof of this.

It has been shown that in the naturally immune animal the specific toxins are excreted and destroyed, that no beneficent modification occurs,—that is to say, no curative serum is obtainable. If now the conclusions arrived at be correct, it would follow, that if a series of animals were taken of all degrees of susceptibility, from one possessing a natural immunity up to an animal of the most extreme susceptibility, the further removed the animal was from the condition of natural immunity, the more antitoxic the serum should prove; for in the very susceptible animal no destruction, but only the requisite beneficent mitigation of the poison would take place. Now this is one of Behring's laws.

One observation militating strongly against this conception of antitoxin has been reserved until now, because the answer to it affords a clue as to the way in which it is formed.

Roux[1] made the really remarkable discovery that if a horse

[1] "Congress Budapest, 1894," 'Annales de l'Institut Pasteur,' 1894, p. 722.

highly immunised to diphtheria toxin is bled, and then subsequently bled, without any intermediate injection of toxin, the second bleeding yields serum with an antitoxic value equal to that yielded by the first bleeding. In other words, fresh antitoxin was obtained without any fresh introduction of toxin. Roux concludes, therefore, that antitoxin is a direct product of the cells.

Curiously enough, the solution of this point is, in my opinion, to be found in the same number of the 'Pasteur Annales' in a paper by Metschnikoff.

I must remind you of something very familiar to all; I refer to cumulative poisoning. Strychnine, for instance, is given in small doses three times a day for a considerable time. At first all goes well, but one day, after taking the usual minute dose, symptoms of strychnine poisoning manifest themselves. This has been explained as partly due to the lessened secretion of urine, and partly perhaps as due to the retention in certain cells of the drug.

Metschnikoff in his paper described some most interesting experiments lately carried out at Dorpat by Kobert and others,[1] in which a soluble salt of iron (Ferrum Oxid. Sacch.) was injected into animals. These animals were eventually killed, and the tissues and cells subjected to a micro-chemical test by treatment with ferrocyanide of potassium. The iron was discovered to have been retained by cells in the liver, spleen, marrow, and also in the leucocytes and endothelial cells of the liver; and it seems reasonable to suppose that diphtheria toxin may be cumulative. As soon as the cells of the horse are by previous treatment accustomed to the toxin, they begin to take it up, and to slowly change it into the form at present known as antitoxin; but this process is a constant one, the whole is not modified at once, but much toxin is kept stored up in the cells, so that even if no fresh introduction of toxin is made, the blood might yield antitoxin for a considerable time.

To show the reasonableness of this explanation, it is, I think, only necessary to consider another very difficult question, one that has been a great puzzle. Behring found that if an animal immune and yielding serum of high antitoxic value, *i. e.* an animal able to protect, able to cure another,—if this immune animal was

[1] Lipski, 'Arbeiten des Pharmakol. Institutes zu Dorpat,' 1893, Bd. ix.

given a second dose of toxin before the reaction caused by the last had quite passed away, it appeared to be more susceptible than an unprotected animal; in other words, that an antitoxic animal might be in a state of extreme susceptibility. This difficult matter seems explicable by this idea of cumulation. One can picture the cells, each with its load of toxin, each struggling to modify it, and succeeding in slowly excreting it in its harmless state, the blood containing the excreted matter, the antitoxin; but in the height of this struggle for mastery a fresh supply is brought to them, the opposing toxic forces are reinforced, and before this fresh recruited force the cells retreat, yield up the toxin already taken captive, the system is flooded with poison, and the animal organism succumbs to an overwhelming dose.

Finally, that antitoxin has certain physical similarities to the toxin which produced it is shown by two points.

Tizzoni[1] draws attention to the fact that as tetanus toxin, when introduced into an animal, produces no symptoms at first, but only after such an interval of time as enables it to cause certain changes in the nerves, so the tetanus antitoxin appears also to act slowly, and a definite delay occurs before it seems to rouse the cells to action.

I mentioned that diphtheria toxin could be precipitated by entanglement, and Aronson[2] has lately used this method for the separation of the antitoxin from the serum, choosing the formation in it of aluminium hydroxide for this purpose; and it is additionally noteworthy that just as the diphtheria toxin appears soluble only in alkali, so Aronson has found that the antitoxin can be extracted from the precipitate only by the use of a weakly alkaline solution. This is, at any rate, a most striking coincidence, if not a strong argument in favour of the conclusions brought before you.

That Ehrlich discovered that antitoxin was excreted in milk is no argument against my hypothesis, seeing that many drugs are so excreted.

[1] 'Berlin. klin. Woch.,' 1893, Nos. 49—52.

[2] Ibid., 1894, No. 19.

Manner of Action of Antitoxin.

If, then, it be true that antitoxin is merely toxin altered and excreted by the cells with a new and altogether beneficent quality, how can we explain its action as an excito-cellular stimulus?

Buchner shows that the injection of any proteid matter foreign and strange to an animal organism increases the antibiotic power of the blood, and thus the general resistance of the animal. He injected a vegetable proteid into the pleura of a rabbit, and, on withdrawing the exudation formed, found it to possess far greater bactericidal power than the serum of the animal. He draws attention also on this point to the fact that Rumpf[1] succeeded in obtaining distinct therapeutic results in typhoid by the injection of the dead bacilli of blue pus, and that Klein[2] found many dead bacteria protective against cholera. I have myself found that the injection of nuclein simultaneously with diphtheria bacilli or shortly afterwards, provided both injections are made in the same part, is able to prolong the lives of guinea-pigs by some forty to fifty hours. In a former part also of this paper it was pointed out that the cells resent the intrusion of foreign proteid matter or living protoplasm, and are able in health to keep their environment, the body, free from them. That this function of destroying or modifying substances strange and injurious to them may be strengthened by practice is generally acknowledged and more or less recognised as explaining protection by mitigated virus or toxin. If it be true, as has been to-night maintained, that antitoxin, or indeed the curative agent found in the blood of an animal immune to any infective disease, is merely the specific toxin or protein digested by the cells, and possessing a new and beneficent character, the question of how it acts as an excito-cellular stimulus may be explained in two ways.

Firstly, that there is only one law, one method of protection known to us, the law accidentally discovered by Jenner, and enunciated by Pasteur—namely, protection by mitigated virus,—but that we have attained a rapidity of immunisation hitherto undreamed of. Although the analogy is false as an illustration,

[1] 'Deutsche med. Woch.,' 1893, No. 41.

[2] 'Centralbl. f. Bakt.,' Bd. xiii, p. 13.

the stimulus afforded by antitoxin to the cells might be likened to the jam in which Gregory's powders can be successfully administered to the reluctant child, or to the effect of eating cucumber peelings after an exceptionally heavy meal.

But I beg to suggest a more subtle explanation to you. The specific myco-proteids were described as active proteids, with a quality or disposition hostile and injurious to animal cells. This quality may consist of some particular molecular arrangement or vibration. If the cell succeeded in conquering, in digesting this proteid poison, they would effect this by causing an alteration of such molecular arrangement ; this altered arrangement being the result of a cellular effort of a particular kind, and possibly bearing the mark of that effort stamped upon it.

It might, I suggest, be easily conceived that whenever this altered substance was brought into contact with cells similar to those which had bestowed the fresh molecular arrangement upon it, a cellular effort identical with that originally excited might be instantly induced.

This explanation of its action would make clear the passive and temporary character of the immunisation produced by such substances, *a condition of immunity approximating to a temporary refractory state*, and perhaps best described as *induced resistance*.

Both, however, involve an absolute recognition of the law of "Specifität," as the Germans express it, a word awkwardly rendered in our language by the word specificity.

I have spoken, however, of methods of increasing natural resistance, and a vista of wonderful possibilities is opened up to us, for some day a substance may be found able to confer a natural resistance sufficiently great to protect perhaps against most infective disease; and in childhood not only would the arms and legs be developed by healthy exercise, but the cells be put through a regular course of digestive training.

Some such prospect as this I believe to be considered by Buchner as within the range of possibilities.

Pathology as Bearing on Prognosis.

As regards mixed infection, it is only necessary to point out that the association of streptococci with Loeffler bacilli distinctly increases

their virulence. There is ample proof of this, and I could, if I had time, lay more before you.

This increase of virulence, however, does not affect antitoxic treatment; it merely tends to render useless local applications calculated to mitigate the bacilli.

But anything which can depress the vitality of the animal cells may render the antitoxic stimulus of no avail, and mixed infections may in this way be fatal to the treatment.

The essential factor in prognosis is the amount of damage already done before treatment is commenced.

Dr. Sidney Martin,[1] in his valuable lectures on diphtheria, pointed out the early degenerative change in muscles and nerve; and struck by the laboured breathing and cyanosis in guinea-pigs infected with the bacteria, I examined into the cause, and found an extremely early fatty degeneration of muscle structure, and in particular of the muscles having most work to do, namely, the heart and muscles of respiration, and, as the difficult breathing led me to expect, both in the case of the ordinary and extraordinary respiratory muscles.

Professor Ribbert kindly allowed me to examine some fifteen children who had died of diphtheria, and in twelve of these I discovered, as I had expected, that in such muscles as I have described an advanced fatty degeneration was present. As controls, muscles at rest, such as those of the leg, were also examined, but only on two occasions was any fatty degeneration discovered, and the heart only fatty on two occasions. With mechanical impediment to respiration, therefore, and with respiratory muscles in an enfeebled condition, the patient has but little chance of recovery.

But the early appearance of this degeneration in experimental diphtheria, namely, often in forty-eight hours, is very important to the prognosis of antitoxic treatment, particularly if the view of the nature of antitoxin which I have put forward to-night be the correct one, and we can understand fully how it is that the best results are obtainable by its early exhibition, and how a larger dose may be necessary if given later to effect the requisite excito-cellular stimulus.

I will define the action of the toxin elaborated in the life processes of the Loeffler bacilli in this way.

Where the poison is concentrated, namely, locally, it is able to

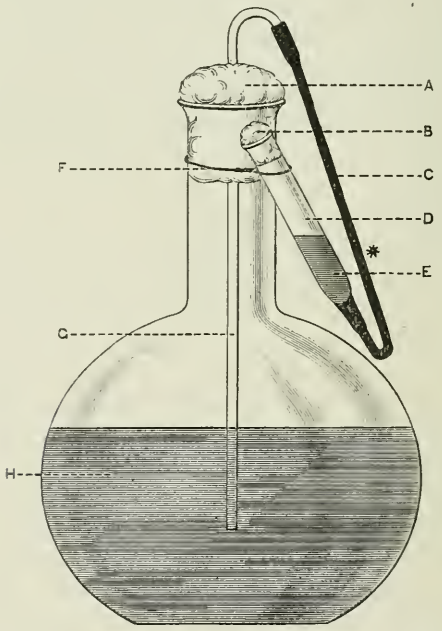
[1] 'Brit. Med. Journ.,' 1892, vol. i, p. 697.

occasion such an injury to the tissues as to produce first inflammation, and then necrosis; but that diluted, namely, after absorption into the general system, it occasions not inflammation, but progressive degenerative change. *March 5th*, 1895.

Method for the inoculation of large quantities of fluid media.—A large flask, holding two to four litres, is filled with bouillon and the neck plugged with cotton wool or a rubber bung, according as admission of air is advantageous or not.

Through the centre of the plug (wool or bung) a glass tube is passed, which reaches well below the surface of the bouillon, and

FIG. 26.



A. Cotton-wool plug in flask, B that in test-tube D. C. India-rubber tubing. * At this point there is a clip. E. Culture fluid in test-tube. F. Wire fixing up tube to neck of flask. G. Tube passing into culture medium H.

its upper end, where it projects above the plug, is bent downwards. A glass tube is now required, shaped like a test-tube in its upper four inches, but drawn out at the bottom into a thin pipette tube, on to which rubber tubing is fitted and connected at the other end

with the bent tube passing through the plug. A spring clip is fixed on the rubber tubing, and the small tube is fastened with copper wire to the neck of the flask in an upright position. Some bouillon is put into this tube, and it is plugged with wool.

After sterilisation the small tube is inoculated, and after twenty-four hours some of its contents are run into the large flask by opening the spring clip and raising the tube, and a culture is then made from the remainder. If this culture is found to be pure, the whole may be incubated; should, however, accidental contamination have taken place, the small tube can be washed out, filled with fresh bouillon, and the whole apparatus re-sterilised.

From time to time, by opening the spring clip and applying suction to the small tube, some of the contents of the flask may be removed, and the degree of the toxicity of the culture estimated.

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2. *The cultivation of the diphtheria bacillus on hydrocele fluid, with remarks on an examination of thirty cases.*

By J. A. Hayward, M.D.

The bacteriological examination of thirty cases of diphtheria in which hydrocele fluid has been chiefly employed as a nutrient medium for cultivating the bacillus, forms the subject of my communication to the Society.

I first employed hydrocele fluid in December, 1893. Previously I had found that it was no easy matter to separate the bacillus from the other micro-organisms present in membranes or exudation, when cultivations were made on nutrient agar and incubated at a temperature of 37·6° C.

Under these conditions there was nothing characteristic in the growth of the colonies within twenty-four hours, and the abundant growth of streptococci, staphylococci, and diplococci, rendered the examination of individual colonies exceedingly tedious, and the separation of pure sub-cultures a matter of difficulty. Using ox serum the diagnosis could be made earlier, often within twenty-four hours; but in my experience good serum tubes are not easy to obtain; the diffused hæmoglobin often renders the medium opaque

and discoloured, and there are many difficulties connected with the collection and removal of blood from slaughterhouses which involve a waste of time and energy in the absence of skilled assistants, and when only small quantities are required from time to time.

In preparing the hydrocele fluid it was drawn off with aseptic precautions into a sterile flask, decanted into sterilised tubes, and subjected to a temperature of 55° C. for three or four hours at a time on three successive days; in the intervals the tubes were kept at a temperature of 37° C.

This method of fractional sterilisation was found quite satisfactory. Finally the tubes were placed on the slant in the hot air incubator and kept at a temperature of 68° C.; in a short time the fluid coagulated, forming a pale greenish-yellow, semi-transparent, and sufficiently firm medium. At a higher temperature the albumen is thrown down in whitish flaky masses.

The diphtheria bacillus grows readily on this solid medium; small white colonies appear within twenty-four hours; maximum growth is attained in about four days; sub-cultures made on different media grow readily, and the bacilli retain their characteristic microscopical appearance and virulence.

The colonies do not when isolated grow as large or as quickly as on ox serum.

The special advantage of hydrocele fluid lies in the fact that it forms a very unsuitable nutrient medium for the majority of the other micro-organisms found in membrane from the fauces or elsewhere. *Staphylococcus aureus* and *albus* are put out of court altogether in my experience. Streptococci grow, but not readily, and the colonies are easily distinguishable from those of the diphtheria bacillus.

Hence it is not difficult to recognise and obtain pure sub-cultures within a very short time.

To illustrate the relative growth of the bacillus, *Streptococcus pyogenes*, and *Staphylococcus albus* on hydrocele fluid, ox serum, and nutrient agar, the following experiment was performed. A mixture of the organisms in sterile salt solution was made. Cultivations were made from this solution on the three media. In twenty-four hours the colonies on the agar were so numerous that a separation would have been a matter of great difficulty, and the coccus colonies were largely in excess.

On ox serum the surface was also overcrowded with all three organisms.

On hydrocele fluid there were numerous exceedingly minute colonies of streptococcus hardly visible to the naked eye; many whitish larger colonies of *Bacillus diphtheriæ;* no staphylococcus had grown, nor did any colonies appear subsequently. I have since repeated this experiment, and with the same result.

In making cultivations direct from diphtheritic membrane on hydrocele fluid, there have been on several occasions no other colonies except those of the bacillus visible within twenty-four hours.

It would appear then, that hydrocele fluid is obnoxious to the growth of many of the micro-organisms found in diphtheritic membrane, and especially to the so-called suppuration varieties. This is confirmed to a certain extent by the clinical fact that suppuration after tapping for hydrocele is a rare event; and this, too, was the case in the days of septic surgery.

To sum up, then, the merits of hydrocele fluid as a cultivating medium for the diphtheria bacillus:

(1) It is easy to obtain and prepare, and forms a clear firm, solid nutrient medium.

(2) The *Bacillus diphtheriæ* grows readily upon it, and can be recognised within twenty-four hours.

(3) It is inimical to the growth of the majority of the organisms found in diphtheritic membrane.

Through the kindness of Dr. Klein, who has lately provided me with some of the antitoxic serum obtained from one of the horses at the Brown Institute, I have been able to make a few experiments, using the serum as a cultivating medium.

The serum was solidified by mixture with 2 per cent. agar-agar. Other tubes were prepared by solidification after Lorraine Smith's method at a high temperature in the autoclave.

Cultivations made, showed that on the antitoxic serum and agar the bacillus grew but feebly. After two days' incubation a streak culture showed no visible colonies. A cover-slip specimen showed a few well-formed bacilli, and many irregular forms; but sub-cultures made on other media grew readily, showing that the bacilli had retained their vitality. Similar results were obtained when fluid antitoxic serum was used. On the serum solidified at a high temperature the bacillus grows readily and as well as on ordinary ox serum.

The following experiment was performed:

Guinea-pig (*a*) was injected with ten minims of a cultivation of the bacillus of forty-eight hours' growth at a temperature of 37° C. in alkaline beef broth.

Guinea-pig (*b*) was injected in the same way with a cultivation of the bacillus in fluid antitoxic serum, forty-eight hours' growth.

Guinea-pig (*c*) was injected in the right thigh with ten minims of the broth cultivation, and in the left thigh with ten minims of the fluid antitoxin cultivation.

Guinea-pig (a) died within forty-eight hours; guinea-pigs (b) and (c) remained perfectly well to all appearance.

Thus it must be inferred that in guinea-pig (c) the injection of the fluid antitoxin cultivation neutralised the effects of the virulent broth cultivation, and therefore the bacilli, though remaining active in the serum as proved by sub-cultures, had not interfered with its antitoxic properties during the two days' incubation.

Now the injection of antitoxin in diphtheria appears to have a very distinct local effect on the membrane, and probably on the vitality of the bacillus; and granting this, the result must be brought about not by any direct action of the remedy on the membrane or bacillus *in situ*, but either by a direct neutralisation of the harmful chemical products formed, or by acting as a stimulus to the natural antagonistic forces at work, rendering as it were the best of all charitable aid in helping the tissues to help themselves.

In the thirty cases examined the bacillus was detected in two instances in membrane occurring on the conjunctiva; in one case on the skin of the upper eyelid, and in another case in membrane found after death in the stomach.

In most cases examination of the cultures showed that long and short varieties of the bacillus occurred together, and I certainly was not able to come to any conclusion as to whether the preponderance of one form over another had any clinical significance.

Indeed, from cultivations it is remarkable what an influence the temperature, duration of incubation, the medium employed, and the isolation or confluence of the colonies have on the shape of the bacillus, and any statements as regards varieties of the organism must, I think, be made from direct examination from the membrane itself, and not after artificial cultivations.

In all the cases examined the bacilli were associated either

with streptococci, staphylococci, or diplococci, and no difference was observed in regard to the association of either of these organisms with severe or mild cases of the disease.

In three cases the fauces were examined bacteriologically ten days after the disappearance of membrane in which the bacillus had been readily detected. In neither of these cases was the bacillus detected at the second examination; but of course negative evidence from one examination is practically of no value.

As regards the duration of time during which the bacillus can be detected, the following case is of interest.

A child aged seventeen months was admitted on May 14th, 1894, for urgent dyspnœa. Tracheotomy was performed at once, and abundant membrane was expelled through the tube; membrane was also present on the fauces. No membrane was coughed up after the 16th, and the tube was removed on the 18th. The wound had healed and the child was apparently quite well on June 4th. On June 6th there was recurrence of croupy cough, and on the 10th the wound had to be re-opened and a tube re-inserted for urgent dyspnœa. On the 11th a measles rash appeared. On the 15th a piece of membrane was coughed through the tube, and again on the 23rd. The child died on the 25th with pneumonia and diarrhœa.

Post-mortem.—The larynx and trachea were coated with thick membrane, which extended far down into the bronchi.

In this case it must be supposed that the formation of membrane ceased after the first tracheotomy, and that a renewed activity of the bacillus resulted coincidently with the catarrhal condition of the air-passages preceding the measles rash, a fresh formation of membrane taking place twenty-eight days after its last appearance. It seems more reasonable to suppose that the bacilli were latent during this period than that a second infection took place so soon after the first attack. Virulent bacilli were obtained from the membrane in the trachea after death. *March 5th*, 1895.

3. *The cultivation of* Bacillus diphtheriæ *on hydrocele fluid.*

By Charles Powell White.

In October, 1894, I undertook the bacterioscopic diagnosis of the cases of diphtheria admitted to St. Bartholomew's Hospital.

Hearing from Dr. Hayward of the use of hydrocele fluid as a culture medium for the *Bacillus diphtheriæ*, I, at Dr. Kanthack's suggestion, applied to it the method introduced by Dr. Lorraine Smith for solidifying blood-serum, and published by him in the 'British Medical Journal' for June 2nd, 1894.

This method consists in adding to the medium a certain quantity (for ox serum it is ·1—·15 per cent.) of caustic soda, and afterwards heating the tubes in a sloping position in the autoclave to a temperature of 120° C. for twenty minutes.

After several trials I found that the amount of caustic soda to be added to the hydrocele fluid was about ·07 (·06—·09) per cent. The exact amount must be found out for each specimen of hydrocele fluid by trial tubes containing 10 c.c. each.

The caustic soda is used in the form of a 10 per cent. solution. The resulting medium is as clear as nutrient gelatine.

On this medium the *Bacillus diphtheriæ* grows better than any of the organisms usually associated with it. I have obtained a distinct growth after seven hours' incubation.

Streptococci grow on it, but are not usually visible as a growth till twenty-four hours after inoculation.

Staphylococcus aureus grows very slowly, and does not produce its yellow pigment (at any rate during the first few days). (Specimens shown.)

In order to separate the bacilli I inoculate one of these tubes directly from the false membrane.

Examination eighteen hours after will show the presence of the diphtheria bacillus, often without any associated organisms.

The advantages of this hydrocele fluid medium are—

1. It is (in hospital practice) easy to obtain.

2. It is perfectly transparent and free from suspended matter and blood-pigment.

3. It appears to be especially suited for the separation of the

Bacillus diphtheriæ, as the associated organisms grow less rapidly on it. *March 5th*, 1895.

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4. *The immunisation of horses for the preparation of diphtheria antitoxine.*

By W. Robertson, M.R.C.V.S. (introduced by G. Newton Pitt, M.D.)

Mr. President and Gentlemen,—It is my intention to-night to describe to the best of my ability the method employed in the immunisation of horses for the preparation of diphtheria antitoxine, and also to describe the process of bleeding these animals when immune. I find suitable horses of the heavy draught class can be purchased for a price varying from £3 10*s.* to £7. On purchasing a horse the animal is placed in an isolation box, where it is tested with mallein (generally twice), then with tuberculin, and if the test is negative it is placed amongst the other horses.

The seat of inoculation which I find most convenient is just in front of the shoulder; this part is easily accessible in the horse, and standing there one is not liable to be kicked by the animal. Previous to inoculation the syringe, &c., are boiled for fifteen minutes and the part washed with ether, and then with a solution of carbolic acid, 1 in 20. The syringe, with needle affixed and charged with toxine, is held in the right hand, a fold of the cleansed skin is pinched up with the left, the needle inserted, and the piston gently pushed home. As a rule the horse stands quietly enough, and seldom exhibits any symptoms of pain or uneasiness during the inoculation.

In commencing the immunisation of an animal very small quantities of the toxine are used at first, the initial dose being as a rule 1 c.c. In the case of the first horse experimented on, I used toxine mixed with Gram's solution of iodine; this method was soon discontinued, as it was found the solution of iodine acting as an irritant caused local swellings, slow of absorption. The local lesion following the first inoculation is as a rule well marked, and

appears in the form of a diffuse soft swelling, slightly painful on pressure. This swelling reaches its greatest height in from six to seven hours after inoculation, generally persists for two or three days, and then disappears. Co-existent with the local lesion we get a rise in temperature; this rise reaches its maximum in from six to seven hours after inoculation—that is to say, at the same time at which the local swelling is greatest,—and generally falls to normal within thirty-six hours. When the local lesion has disappeared and the temperature has fallen to normal the dose of toxine is repeated, and if this produces very little local or general effect the amount is increased by degrees. Thus, in one case, the primary dose was 1 c.c., at the end of a week again 1 c.c., followed weekly by 5 c.c., 10 c.c., again 10 c.c., and then 25 c.c. When the dose has reached 50 c.c. we give the horse this quantity three times a week for a fortnight, and if this amount does not produce any reaction the dose is raised to 100 c.c. three times a week for the same length of time, and finally to 200 c.c. at the same intervals.

The period of time allowed to elapse between each inoculation varies with different animals, and we take as a guide the local swelling and the temperature; until both have subsided we do not continue the inoculations. This is an outline of the method of immunising horses, but I have noticed a few facts in conjunction with the above method which are of some interest, although of rather a disjointed nature.

No two horses are alike in their power of resistance to the action of diphtheria toxine. I have an animal at present under my charge which received 10 c.c. toxine, and the day after received 100 c.c., and this without producing any very marked effect; while in another horse the initial dose of 1 c.c. produced a violent local and general reaction, and after an interval of a fortnight a second dose of 2 c.c. caused paralysis of the hind quarters, and the animal had to be destroyed. I may add the same toxine was used in both cases. Again, the local lesion in the neck disappears twice as fast in some animals as in others.

The rise in temperature following inoculation is also very variable. I have a record of a horse, the temperature of which during the whole process of immunisation never exceeded 103° F., and I have a record of another horse, also made immune, which after each inoculation had a rise in temperature, in one case exceeding 105° F.

Amongst all the horses I have inoculated, even when the temperature was very high, I have never known one refuse its food. But I have noticed that following on a large dose of toxine *some* animals have a fit of shivering, and exhibit distinct rigors.

In a very few cases out of many hundred inoculations I have seen necrosis of the skin and subcutaneous tissues follow inoculation, and the skin over the swelling become brown and hard, and on falling off leave a glazed red surface; this, however, soon heals up under a boracic acid dressing. When the horse is considered to be sufficiently immune it is allowed to rest for a clear week after the last inoculation before it is bled.

The vein from which we bleed, is the jugular vein, found on the side of the animal's neck, lying in what is termed the jugular furrow, and separated from the skin by the panniculus carnosus, that sheet of muscular tissue which stretches subcutaneously over the upper part of the horse's body. The skin over the vein is shaved, and washed thoroughly with ether and then with a 1 in 20 carbolic solution. The vein is raised by pressure with the fingers, and with a scalpel a small incision about half an inch in length is made through the skin and panniculus carnosus.

At first the cannula was inserted directly into the vein through the skin, but afterwards it was found better to first make an incision over the vein, holding the edges of the wound open with forceps. Connect the cannula to a Kitasato's flask by a piece of quarter-inch rubber tubing, then take it in the right hand, raising the vessel with the left, and insert the tube, taking care you do not get merely into the sheath of the vein. The blood should flow freely, and when the flask is sufficiently full you can replace it by an empty one as follows :—Pinch the rubber tube with the left hand and withdraw the full flask, which should be handed to an assistant to plug. Take an empty flask in the right hand, insert its long glass tube in the end of the rubber piping which, when released from the pressure of the fingers, will allow the blood to flow.

The amount of blood which can be removed from an animal with impunity varies with its size. The amount I generally take is 10 litres, but I have removed as much as 16 litres without any injurious effects to the horse. This is not to be wondered at, seeing that one sixteenth part of the animal's body-weight is blood.

The reason why, as a rule, not more than 10 litres are drawn

off at a time is, because it is found that if more is taken, the latter portion does not clot properly, and the serum which separates is of a pink colour.

As soon as the blood is firmly clotted, it is advisable to twist the flask in the hand so as to separate the clot from the vessel wall.

When sufficient blood has been drawn, press on the vein anterior to the cannula and withdraw the tube. Sponge gently with 1 in 20 carbolic, and fasten the edges of the wound with two catgut sutures. Dust with iodoform, and seal with a piece of sterilised wool dipped in collodion.

I have never had any difficulty in stopping the bleeding, and the wounds have always gone on satisfactorily. The veins are in no case obliterated or obstructed, and in one horse which has been bled fourteen times the vessel is just as pervious as in any other animal.

It is hardly necessary for me to state that all instruments, &c., are boiled for half an hour previous to an operation.

As regards methods of restraint in this operation, those, of course, depend upon the animal, but I have usually found horses stand quiet enough when being bled.

I should like to say a few words about the flasks in which the blood is collected, and the method of decanting the serum.

The flasks are ordinary two-litre and four-litre filtering flasks, each fitted with a rubber cork and two pieces of glass tubing, one of wide calibre to allow air to escape; the other of narrower dimensions, over the orifice of which is slipped the rubber tubing connected to the cannula. The two tubes and the branch tube are plugged with cotton wool, and the flasks are sterilised in the steamer, for three hours, on three separate occasions. When the flasks are full and have been twisted after the blood has clotted, they are placed in a cool cellar, and in twenty-four hours a large amount of serum will have separated. The branch tube of the flask is flamed in a spirit lamp, the wool plug removed, and the serum poured off into sterilised Winchesters. The branch tube is now repeatedly wiped free from serum by pellets of sterile wool, and finally replugged. As a rule a two-litre flask of blood yields one litre of serum. This varies, the blood of some horses not yielding anything like that quantity. *March 19th*, 1895.

5. *Three specimens illustrating the pseudo-diphtheria bacillus, otherwise the attenuated or non-toxic bacillus.*

By Lennox Browne.

The first of these microscopic specimens was obtained from a diphtherial membrane afforded from the laboratory of Dr. Roux. The preparation represents a pure culture, but the original contained a few staphylococci. If one compares it with others of admitted virulence, it is impossible to detect any real difference either in form or arrangement. The likeness consists not only in the appearance of the bacilli separately, but in that fantastic alphabet arrangement as of the open V Y, or in obtuse angles like circumflex accents and letters of cuneiform character, which constitutes a recognised characteristic in the identification of the true organism. In fact, looking at the specimen, no bacteriologist would hesitate to give an opinion as to the true diphtherial character of the case from which it was taken.

From the culture on blood-serum typical diphtherial colonies were exhibited in eighteen hours. The rest of the colony was mixed with sterilised bouillon and injected into a guinea-pig with entirely negative results, both locally and generally. It was therefore declared to be a "pseudo-bacillus."

(2) The second case was that of a male patient aged 25 years. He was first seen by me on November 11th, 1894. Temp. 101·8° F. The whole of the fauces were of a deep red colour; the uvula clinging to the *right tonsil*, which was greatly enlarged, and with similar inflammatory thickening of the anterior pillar projected as a somewhat flattened ridge-like tumour far beyond the middle line. On the surface of the tonsil were several widely open and deep lacunæ, some covered with the ordinary caseated secretion which characterises acute lacunar tonsillitis. In addition there were several patches, on spaces between the lacunæ, of pellucid exudation, not difficult to remove, nor when removed leaving a bleeding surface. The left tonsil was less swollen and less inflamed, and with but one blocked crypt.

November 13th.—Both tonsils were much more enlarged, and with the fauces were of a purple livid colour, covered in patches with

tough, dirty yellow exudation, and altogether more characteristic of diphtheria, but not inconsistent with the first diagnosis of acute lacunar tonsillitis.

A culture was made on November 11th, and in due course showed numerous small discrete colonies of milky white growth.

The *microscope* demonstrated an almost pure cultivation of the Klebs-Loeffler bacillus of the long variety, and with a decided tendency to chaining. The patient made a good recovery without paralytic sequelæ.

(3) This specimen refers to the same patient as No. 2, a male aged 25.

On February 28th, 1895, the patient came to me for the purpose of removal of his hypertrophied tonsils.

March 2nd.—On examining the throat there were seen on the lower and inner edge of the wounded surface, where the *right tonsil* had been, two separate patches of pearly-grey exudation, more elevated than is usual in diphtheria, as if the surface were fungating, and not unlike a condyloma. These were removed by forceps with the result of free bleeding. On the *left side* there was a single pellicle of very soft whitish exudation. This was removed without the least force, but the removal was *also* followed by some bleeding.

Two cultures were made, one from membrane taken off by the forceps, the other from membrane adhering to the swab. These cultures obtained were both of the same character—large, isolated, greyish-white colonies, about twenty on the swab culture, and about twelve in number on the other.

On *microscopic examination* bacilli of the same character were observed in each. They were short segmented bacilli, the ends club-shaped, and showing the characteristics of the short variety of the *Bacillus diphtheriæ;* they were shorter than specimens of the Klebs-Loeffler organism usually obtained, and may be best described as typical examples of the "pseudo-bacillus" of Roux.

Two *sub-cultures* were made on blood-serum. Rapid growth occurred, and on microscopic examination the growth was observed to contain bacilli similar to the Klebs-Loeffler, but somewhat longer than those originally present. They were fewer in number, the colonies consisting mainly of cocci of various descriptions.

Two further cultures were made from these sub-cultures. The growths again occurred rapidly, but on microscopic examination

no bacilli resembling those of diphtheria were observed, the whole consisting of cocci.

The patient's throat recovered quickly under the use of an antiseptic gargle, but on March 11th there was still some cloudiness, and another culture was made, with the result that it yielded almost pure cultivations of *Staphylococcus pyogenes-aureus.* A few days later the throat was quite healed.

Remarks.—We know that the virulence of the true bacillus decreases at the end of a few weeks or months, and in process of time entirely disappears.

Introduction of fresh bacilli into an attenuated culture will bring about a recrudescence of its toxic properties. If this can be effected in the laboratory we may understand the position which the so-called pseudo-bacillus holds in the estimation of various observers, one set believing it to be capable of regaining its toxic power, and the other that, once innocuous, it is incapable of ever again inflicting injury.

The term "pseudo-bacillus" is indeed a most unfortunate one, for the specimens being typical of what is usually found in similar circumstances proves that they are true bacilli, undergoing a process of attenuation in development and virulence.

As a corollary of Dr. Thorne-Thorne's theory of progressive development of infectiveness in the waxing of an epidemic, not only of diphtheria, but of other infectious diseases, it is within experience that there is a decrease in virulence as it wanes. It is suggested that it is in this aspect that the non-virulent bacillus is to be regarded, and it would be desirable, before confusion has become more widely disseminated, that it should be rechristened by some term which would definitely express its attenuated properties.

Unless some such broad view as is here suggested be taken of this question, it would not be difficult to convert the "pseudo-bacillus" into a very Frankenstein, which would speedily destroy acceptance of the bacillary origin of diphtheria as at present recognised.

I also take this opportunity to protest against the importance that has been attached to a coccus described by Louis Martin, a colleague of Roux, and called by him, as must be admitted somewhat unscientifically, "*Brisou*," after the name of the child in whom it was first discovered. Martin describes it as forming

colonies which have resemblance to those of diphtheria, and he states that, in the case of the child in whom he first witnessed it, clinical features so singularly confused the diagnosis that the little patient was taken seven times to the diphtheria ward for a diphtheria which he had not.

This organism is frequently found in the secretions of the oral and respiratory passages quite irrespectively of diphtheria, and is according to my experience without either diagnostic or prognostic significance. *March 19th*, 1895.

Discussion.

Dr. A. A. Kanthack exhibited microscopic sections showing diphtheria bacilli in the diphtheritic membrane in the smallest bronchioles of the lung, as well as specimens showing phagocytosis in guinea-pigs killed by injections of diphtheria bacilli into the muscle of the thigh; although death ensued, most of the leucocytes at the seat of inoculation contained bacilli. The part played by phagocytosis, therefore, was not to be unduly exaggerated in the phenomena of immunity. The chief point he insisted upon was that because serum will immunise against an organism, it does not prove that the organism is the cause of the disease. Again, although it was generally true that from animals naturally immune to a disease a curative serum could not be obtained, it had been lately shown that if fowls were given large doses of tetanus cultures the serum acquired an immunising property. In some diseases (vibrio Metschnikovi) it was not so easy to immunise against the toxin as against the micro-organism; the toxin would still kill after the other immunisation had been brought about. In the case of cobra poison it was, the author had found, very difficult to immunise, though animals might be made to stand increasing doses. As to the nature of the toxalbumins, it was not clear that albumins were essential parts; they were probably only the vehicles in which the poisons were carried down. The terms albuminoid bodies, or simply toxins, were therefore perhaps the best. Even Brieger had admitted that in the case of tetanus the presence of the albumen was an accident only.

Dr. J. W. Washbourn remarked that Dr. Hunt's paper had raised many points of the greatest interest. He had given us many interesting facts with reference to the production of toxins by the diphtheria bacillus. His observations confirmed those of

Roux that free access of oxygen favoured the formation of toxin, and the experiments of making little rafts of corks in order to keep the bacilli near the surface were very ingenious. The production of toxins only occurred when the reaction of the cultivation changes from acid to alkaline. Dr. Hunt considered the alkalinity of the cultivation to be the essential factor in the production of toxin, and considered the action of oxygen to be due to its influence in preventing the formation of acid. Although this was a possible explanation, yet the speaker could not think that very conclusive evidence had been brought forward in its support. In fact, the experiments Dr. Hunt quoted with calcium carbonate yielded negative results. Direct experiments could easily be made by the continuous addition of alkali to the cultivations. He was particularly interested in the question about the diminution in the virulence of the toxins when the cultivations were freely exposed to oxygen for some days. Dr. Hunt had said that after fourteen days the toxicity declined rapidly. This was an important practical point, and he would ask Dr. Hunt to give further details of experiments in this connection. It was also suggested that free access of oxygen rapidly destroyed the bacilli; in experiments made with methylene blue the cultivation died out in nine days. He would ask whether this was the case with cultivations through which oxygen was passed. It was certainly not what one would expect. Possibly the methylene blue acted deleteriously upon the cultivations in other ways than by simply carrying oxygen. Another question of importance in this connection was the relation between virulence and the production of toxin. Roux had stated that the original virulence of the cultivation was no index to the amount of toxin it would produce. Dr. Hunt went still further, and said that a cultivation which had produced a powerful toxin did not necessarily contain bacilli of great virulence. Now, as some of his theoretical conclusions were based upon this statement, the speaker would like to hear further details of his experiments. With regard to the nature of the toxin there was still much to be learnt. Dr. Hunt had told us that the toxin was a specific proteid poison, but that we must clearly understand that it was not necessarily the proteid which was the poison, but only its disposition and its active and specific quality. He could not help feeling that the author was passing beyond the boundaries of pathology, and trespassing upon the realms of metaphysics.

Surely a body could only act by virtue of the properties it possessed. He hoped that Dr. Hunt would pardon him if he offered the criticism that his paper was rather too speculative, and that he had formulated theories upon facts that were too scanty. How dangerous this was could be shown by the reliance Dr. Hunt had placed upon the supposed non-formation of tetanus antitoxin in fowls. Fowls were not affected by the injection of large doses of tetanus toxin, and Kitasato stated that after treatment with toxin no antitoxin was found in the blood. Now, as Dr. Kanthack had already pointed out, this statement had been refuted by M. Vaillard, and experiments shown to Kitasato in Paris convinced him that he was wrong in his first conclusions. The contradiction was probably due to the time at which the blood was removed after the last injection. The eighteenth to the twentieth day was the most suitable time. If the blood was renewed too early, instead of being antitoxic it was toxic. In a paper upon the pneumococcus, which the speaker read recently before this Society, he insisted upon this, and stated that one of the important factors in obtaining a pneumonic antitoxin was the withdrawal of blood at the right period after the last inoculation. It seemed to him that Dr. Hunt's failure to obtain a diphtheria antitoxin from mice after injection of toxin was due to an error of this nature. He observed that the antitoxic property of the blood was not tested later than sixteen hours after the injection of the toxin. With regard to the question whether antitoxin was simply toxin converted by the cells, or a secretion from the cells under the stimulation of the toxin, he would not at present like to give an opinion. The evidence was not yet sufficient. According to Roux and Vaillard, there is no correspondence between the amount of toxin injected and the antitoxin formed. The same quantity of tetanus toxin was injected into two rabbits in the course of two months, the one receiving thirty-three small doses and the other nine large doses. The antitoxic properties of the blood were then tested and found to be much more potent in the case of the rabbit which received the toxin in small, frequently repeated doses. From this they concluded that the antitoxin was secreted by the cells. These results might be due to an elimination of the toxin by the urinary tract when given in large doses, and this would account for the scanty formation of antitoxin. The chief argument against the actual conversion of the toxin into antitoxin was the experi-

ment that the antitoxic power of the blood was not sensibly diminished after removal of a quantity of blood equal to that of the whole body. Dr. Hunt explained this by supposing that a store of toxin was still present and locked up in the various organs. He would ask him if there was any direct evidence in support of this view. The next point was with regard to the specific nature of antitoxin. Dr. Hunt looked upon this as quite settled. The speaker would remind him that Dunschman had shown that the serum of animals immunised to symptomatic charbon protected against the septicæmia bacillus, and that M. Calmette had shown that the tetanus antitoxin protected against snake poison, and that the same was true of the serum of animals protected against hydrophobia. Another interesting question was that with reference to the difference between the infection with living bacilli and with their toxins. It had been shown in several cases, such as hog cholera, that the serum of immunised animals would protect against living bacteria, but not against their products. Was this perhaps after all only a question of degree? He could not feel that the experiments made in this respect were quite satisfactory. There was one point which appeared to him of importance, and that was, what was exactly meant by saying that an animal was immune? The mere fact that an animal survived after an inoculation was not a sufficient proof that it was immune. He thought that the only proof of immunity should be that the animal suffered no local or constitutional effects after inoculation. Surely we did not consider a patient to be immune to any infectious disease because he had recovered after being infected. With the pneumococcus he had frequently rendered rabbits so immune that inoculation with a virulent cultivation produced no local reaction and no fever. The question of natural immunity was assumed by Dr. Hunt to be due to the bactericidal property of the blood. The speaker did not think that this was by any means definitively settled; but that opened up the whole question of immunity, and he thought that this could hardly be entered upon at the present time. One of the most interesting questions in regard to the pathology of diphtheria in the human subject was the presence of living diphtheria bacilli in the throat long after the symptoms had subsided. Were the bacilli under these circumstances continually secreting poison, and was the effect of the poison annulled as soon as it was absorbed? The same remark applied to those

instances where virulent bacilli had been found for long periods in the throats of healthy individuals without producing symptoms. It would be very interesting to know if the blood-serum of such persons possessed antitoxic properties. The association of other bacteria with the diphtheria bacillus was another question of great interest. There were two ways in which such an association had been considered harmful; the one was by the association of putrefactive bacteria producing a septic intoxication, and the other was the association with streptococci, causing a mixed infection. When the exudation was examined microscopically many kinds of bacteria could be found. The majority of these did not grow upon blood-serum, and it was probable that many of these produced putrefactive changes. In a series of cases examined by Drs. Goodall, Card, and himself, they were unable to find that the preponderance of any particular kind of bacterium in the exudation had any influence upon the severity of the case. With regard to the association with streptococci there was no doubt that secondary complications, as broncho-pneumonia or septicæmia, might arise from such an association. The majority of so-called "septic" cases of diphtheria were, however, not due to a mixed infection with streptococci, but to direct poisoning with the diphtheria toxin. In diphtheria it was rare to get suppurating glands or metastatic suppuration. This contrasted with what occurred in scarlet fever, where a secondary streptococcal invasion was frequent. He certainly thought that the influence of the association with streptococci had been exaggerated, and felt sure that a simple bacteriological examination of the throat did not point to any association of other bacteria being of serious import. As a matter of fact, we found that the more diphtheria colonies that developed in the tubes the more severe the case. The last point was with reference to the varieties of the diphtheria bacillus. Three varieties had been described—the long (or usual) variety, the medium, and the short. These varieties were virulent in the order named. He must say that with the short he had rarely produced a fatal effect in guinea-pigs. He looked upon the short variety as the most usual form of the pseudo-diphtheria bacillus. He did not know whether these varieties can be converted into one another. Mr. Peters had been making investigations upon this subject at Guy's Hospital, and, though these were not yet completed, he had found that the varieties kept their characters through several generations.

Were mallein and tuberculin reliable as diagnostic agents when used to test the health of horses before inoculation with diphtheria toxin? Mallein he believed was, but tuberculin not absolutely so in the case of animals. Dr. White and Dr. Hayward had recommended hydrocele fluid in place of blood-serum, but there was no difficulty in preparing the latter if it were allowed to stand, and well clot, before being removed from the slaughterhouse.

Dr. Woodhead said he had been struck by the great differences in the quantity or activity of the toxins produced in different broth cultures, even when seeded with diphtheria bacilli from the same source, and when apparently identical conditions were maintained. In order to determine some of the conditions under which the most virulent toxins were produced he had tried various methods of growing the bacilli. He first tried Roux's method, using bacilli taken almost directly from the membranes from a case of virulent diphtheria. These bacilli were of the long form. Fairly active poison was obtained. He then with the same bacillus seeded flasks containing a considerable quantity of Roux's fluid, bubbled the air through it, and kept the fluid constantly agitated. In this case it was found that although the activity of the growth was not interfered with, the bacilli remaining alive at the end of a month, the amount of toxin produced or remaining was comparatively small. When, however, much thinner layers of fluid were used and the surface was left undisturbed there was not only a luxuriant growth of the organisms, but there was a considerably larger amount of toxin formed.

From these experiments he gathered that two distinct sets of conditions had to be taken into consideration: (*a*) supply of oxygen to the bacilli; (*b*) supply of oxygen to the chemical products of the bacilli. The one appeared to be absolutely necessary for the active growth of the bacilli, but the other seemed to involve a diminution in the activity of their toxic products by bringing about more or less oxidation. The problem to be solved, therefore, appeared to be how to encourage the action of the oxygen on the bacilli, and to prevent its action on the toxins. For this purpose a surface growth of the bacilli was always to be aimed at. He pointed out that the poison-forming power of the bacilli might be quite distinct from their virulence; and it certainly did not follow that because a bacillus did not flourish in the tissues, it would not therefore form large quantities of poison. Micro-organisms,

though only saprophytes—as in the case of the saprophytic form of the *Bacillus anthracis*,—might nevertheless produce toxins; and there seemed to be a probability that a somewhat similar state of matters might hold good in the case of modified forms of the diphtheria bacillus. Next as to the question of the growth and toxin-forming power of bacilli in an alkaline medium. Mere alkalinity, though important, was not of such moment as a free supply of oxygen, as a culture kept alkaline with soda did not yield such an abundant supply of toxin as did a similar culture when kept supplied with a quiet and regular supply of oxygen. He thought, therefore, that the result of oxygenation could not be wholly explained by the alkalinity it induced. There was evidently something special in the process. He found, moreover, that by keeping the solution alkaline he was not able to increase the capacity of the organism for producing toxins, although they appeared very rapidly after the normal alkaline period had set in. The difference in the resistances to the effect of the toxins offered by different horses, on which Mr. Robertson had insisted, he had also observed as a fact of very great importance. This was the universal experience as regards the action of other toxins on different species of animals. It was his experience that the animal which withstood the largest amount of toxin must take a longer time to give antitoxin. He could not, therefore, wholly endorse Dr. Hunt's statement that animals naturally immune did not yield antitoxin. He recalled the experiments with tetanus toxin, showing that if the relative immunity of a given animal (fowl or dog) were overcome by large doses of toxin, a more powerful antitoxic sérum was obtained than from a comparatively susceptible animal—a fact which he maintained held good as to the immunisation of the horse with diphtheria toxin. This was a much more complicated process than we had yet appreciated. Roux and Vaillard, although maintaining that the action of the toxin in producing antitoxin was essentially through its effect on the body-cells, found that this action was exceedingly rapid, for it was found that blood withdrawn from the lateral vein of the ear of a rabbit, immediately (thirty to thirty-five minutes) after the introduction of toxin, contained an appreciable amount of antitoxin. Either the action must be spread over a large number of the cells of the body, or there must be a direct action on the plasma of the blood. He agreed that it was better to give smaller quantities of toxin at shorter

intervals after the first few inoculations, but as yet it would be safer, he thought, to adopt a medium course. Like Dr. Kanthack, he had found the diphtheria bacillus in the lung in a certain number of fatal cases of diphtheria; but, so far as he could make out from his notes of about fifty *post-mortem* examinations, in only five instances had he been able to find the bacillus in this position. Micrococci in the pneumonic patches, so far as his experience went, were most frequently associated with tracheotomy, but he should like to make this statement with due reservations. It must be admitted, he said, that it was almost impossible, from the examination of a single tube, often of a very mixed culture, to say what organisms were present in a given case of diphtheria, and especially to say that the Klebs-Loeffler bacillus was absent. In perhaps five per cent. of the cases he had examined the bacillus could not be found in the first culture, though present in abundance in the second; whilst in some cases it might be identified in the first culture, absent in the second, and present again in the third. There was, in short, always a certain risk that it might be overlooked. He believed, however, that by-and-by, when physicians compared the clinical features of their cases with the bacteriological reports, given, for the most part, in ignorance of the nature of the case, much valuable information would be forthcoming.

In answer to Dr. Washbourn's question as to the reliability of the mallein test in cases of glanders, he might give his own experience. He obtained the mallein used from Professor McFadyean of the Royal Veterinary College, to whom he was greatly indebted for several hints as to the method to be adopted in the use of this reagent, and the special points on which an accurate diagnosis can be based. He found that if the resulting swelling continued to increase after sixteen or at most twenty-four hours from the time of the injection, and this was accompanied by a marked and continuous rise of temperature of 3° or 4° F., glanders was certainly present. It was this *progressive* swelling, not a mere swelling after the injection, that was the real diagnostic feature in glanders.

Post-mortem examination had in his cases invariably confirmed the mallein diagnosis. Of course, these were all cases in which none of the ordinary clinical signs existed during life, and when the animals had been passed as free from glanders after a thorough veterinary examination. In these cases the typical lesions were found

in the lung. Tuberculin as a diagnostic agent might not be quite so reliable as mallein, but if properly used it was certainly a most valuable weapon in the diagnostic armamentarium. It must be remembered, of course, that tuberculosis, though much commoner in the horse than was at one time supposed, was still a much rarer disease than glanders. In conclusion, he pointed out that the diphtheria bacillus was a far more protean organism than was usually recognised. He had come across numerous varieties—long, short, wedge-shaped, pointed, club-shaped, and irregular—of this bacillus; and sometimes it was necessary to make a number of sub-cultures, and even a series of injection experiments, in order to be able to determine the identity of the organism. In his experience the short form was most commonly met with in certain patients during the period of convalescence.

Mr. Bokenham described a modification in the apparatus mentioned by Mr. Robertson. The serum was drawn off from below the clot; this was effected by pushing the tube of outlet far into the filter, so that the clot was prevented from lying against the bottom. His observations had shown him that antitoxins in general were not antibiotic. Dr. Klein's diphtheria antitoxin, however, destroyed both the bacillus and the antitoxin.

Dr. Bertram Hunt in replying said:—Although I have come armed with facts and illustrations in support of my paper, the hour is so late that it does not seem advisable to make any lengthy reply, and, as to meet the argument brought against much of what I have advanced would occupy much time, to only touch on one or two points. Both Dr. Kanthack and Dr. Washbourn have objected to my definition of toxin as a specific mycoproteid; Dr. Kanthack pointing out that Brieger claims to have shown that tetanus toxin is non-proteid, and Dr. Washbourn contending that the expressions "quality" and "character" of a substance such as I have used are metaphysical rather than scientific. Now I have maintained that the toxin is the vital activity inherent in the bacterial protoplasm, and adherent to it; and whatever its chemical nature may be, the expression specific mycoproteid seems to me to be the most fitting, since it implies the definition I have given. Should this activity of protoplasm be found by chemists to be a separable substance, non-proteid in character, it will, I take it, be a great advance in physiological chemistry; but, as has been pointed out, toxin is precipitated by entanglement, and the objection might

be raised that Brieger had merely succeeded in detaching this "activity" from the proteid, and in transferring it to some non-proteid substance; in other words, that he has replaced a natural combination with an artificial one. I myself doubt whether this quality of active proteids will ever be isolated. Then as regards refractory animals, Dr. Kanthack has drawn attention to the fact that Vaillard, repeating Kitasato's experiment, found that fowls could be made to yield tetanus antitoxin; and both Dr. Kanthack and Dr. Washbourn have used this fact as an argument against my conclusion. As a matter of fact, Vaillard's experiment, if carefully examined and criticised, rather tends to support my generalisation, that the more susceptible the animal the more antitoxin yielded by it. It might, in the first place, be urged that fowls are not so immune to tetanus as was at first imagined, and that Vaillard's experiments merely prove this. But accepting for the moment that a fowl is absolutely and naturally immune to tetanus, let us consider Vaillard's facts. He injected a fowl with 50 c.c. of tetanus toxin, and as a result of this treatment found that he could protect a mouse with 5 c.c. of the fowl's serum; *i. e.*, since a mouse weighs 20 grammes, the 50 c.c. of toxin had conferred an antitoxic value of 1—40 on the fowl. Now a large fowl weighs 4 lbs., and a big horse 2000 lbs.; an equivalent dose of toxin for the horse would be therefore 25 litres. A horse which had received such an enormous dose of tetanus toxin would possess an antitoxic value of about 1—4,000,000. Vaillard's experiment, therefore, shows that the difference in antitoxic value between the refractory and the susceptible animal is 100,000. I could repeat my contention in these words, then: of every 100,000 parts of toxin injected into a refractory animal 99,000 are destroyed, and only one part altered into antitoxin; whereas of 100,000 parts of toxin injected into a susceptible animal 100,000 parts antitoxin are obtained. As to the association of streptococci with Loeffler's bacilli, there is no doubt but that an increased virulence of the latter is brought about, both in the disease and *in vitro*. The part played by the streptococci also in the causation of diphtheria requires consideration. The experiments performed by Barbier are important. He found that it was impossible to inoculate Loeffler's bacilli on a healthy mucous membrane, but that if streptococci were also applied a mixed local injection resulted. I have tried the effect of putting pure toxin and the toxin pro-

duced in the mixed culture into the eyes of animals, and have once or twice obtained a conjunctivitis with the mixed product, but never with the pure. As regards the *Staphylococcus aureus*, the association of this micro-organism in both the disease and in experimental diphtheria would seem to mitigate the morbid process, and it may perhaps be explained as being due to increased natural resistance. It only remains for me, Mr. President and gentlemen, to thank you most warmly for the patience with which you listened to my very long and tedious paper, and for the courtesy and kindness shown me by the Society in the course of the debate.

Mr. W. Robertson, in his reply, stated that although mallein was in general reliable, it at times failed as a means of diagnosing glanders, as proved on *post-mortem* examination.

B. Experiments with the Pneumococcus with Especial Reference to Immunity.

By J. W. Washbourn, M.D.

In opening this discussion I propose to touch lightly upon all those points which I have not studied, especially, myself; but I shall treat in detail that part of the subject in which I have had the greatest experience.

I hope that by giving a brief outline of the whole matter I shall facilitate the discussion which will follow this paper.

History.—With regard to the history of the subject I shall not detain you longer than to point out the confusion that arose at the time when the pathology of the disease was first studied. Friedländer described diplococci as occurring constantly in the exudation from pneumonic lungs. These diplococci were characterised by possessing a capsule; and on making cultivations on gelatine, a diplococcus grew, and was considered by Friedländer to be the cause of the disease. For some time Friedländer's pneumococcus was accepted as the cause of pneumonia. Further investigations, especially those of Fränkel, Talamon, and Weichselbaum, showed that the diplococcus cultivated by Friedländer was only present in a few cases of pneumonia; and that, in fact, it was only of accidental occurrence. It differed also in morphology from the diplococcus found microscopically in pneumonic lungs, being more elongated, and resembling a bacillus rather than a coccus. Talamon and Fränkel, however, were enabled to cultivate the true pneumococcus in broth and on agar, and they found that it differed entirely from Friedländer's pneumococcus both in virulence and in its mode of growth. It is with this pneumococcus that we have to deal.

The pneumococcus as the cause of disease in the human subject.—There is a vast mass of evidence to show that the pneumococcus is the cause of acute lobar or croupous pneumonia. It is also responsible for some cases of lobular pneumonia, but the majority of the cases of this latter disease are caused by other bacteria, notably the streptococci.

But the pathogenic *rôle* of the pneumococcus in the human body

is not limited to the production of pneumonia. It is the cause of many cases of pleurisy and empyema, meningitis, and otitis, occurring quite independently of pneumonia; and is also the cause of ulcerative endocarditis, and of various suppurative affections of the joints and other tissues following upon an attack of pneumonia.

Last year, in a paper read before the Royal Medical and Chirurgical Society, I brought forward evidence to show that the constitutional symptoms of pleurisy and empyema, when caused by the pneumococcus, are exactly similar to those of pneumonia; and I have no doubt that they are due to the same cause, *i. e.* the absorption of the toxins produced by the pneumococcus. In other cases, such as meningitis, the general symptoms are masked by the local effects of the inflammation. This is quite in accord with what occurs in other microbial diseases, such as influenza and malaria.

With regard to the *distribution of the cocci* in cases of lobar pneumonia, I have had but little experience. They, however, are found most abundantly in the affected lung, and are generally absent from the viscera; but a number of cases have been recorded in which the cocci have been found in small numbers in the spleen, kidneys, and blood.

The occurrence of the pneumococcus in the secretions from healthy individuals.—The pneumococcus has frequently been found in the secretions from the mouth, nose, and bronchi of healthy individuals without producing any symptoms. Indeed, it was first discovered by Sternberg by inoculating rabbits with the saliva of healthy individuals.

Now this is no argument against the pathogenic *rôle* of the pneumococcus. The same applies to the diphtheria bacillus, which has frequently been found in the throats of healthy individuals without producing any injurious effects. In a note by Dr. Hopwood and myself, in a recent number of the 'British Medical Journal,' we mentioned a case where virulent diphtheria bacilli were constantly present in the throat of a healthy individual for so long a period as six weeks.

Cultivations of the pneumococcus.—The pneumococcus is a difficult micro-organism to work with, on account of the variability in its virulence, and of a number of peculiarities in the manner of its growth.

In the course of my investigations I have inoculated some 200

animals (some of these experiments have been made abroad), and have made innumerable cultivations upon different media, so that I can claim to have some acquaintance with its life history.

To obtain cultivations from the human subject the best method is to inoculate mice or rabbits with material containing the cocci. The animal dies after a variable time, and from its blood cultivations can be obtained.

Conditions of growth of the pneumococcus.—The growth depends upon the temperature, and upon the nature of the medium in which the cultivation is made. As a rule, no growth occurs at temperatures much below that of the human body, although varieties have been described which grow at a temperature of 20° C.

As to the medium, I consider the reaction to be the most important factor; unless the medium is distinctly alkaline no growth takes place, but here again varieties have been described which will grow in an acid medium.

The extreme rapidity with which cultivations die out has been noted by all those who have worked with the pneumococcus. Agar cultivations generally die within a week, and broth cultivations within two or three days. I have often found broth cultivations dead at the end of two days. Many investigators have, from time to time, recorded exceptional instances where the cultivations have retained their vitality for a long period.

In one instance I injected 1 c.c. of a broth cultivation twenty-three days old into the peritoneal cavity of a rabbit. Death ensued in four days, and the blood was found to be crowded with pneumococci. In another instance I examined a cultivation upon the surface of agar, and found it alive sixty-four days after it had been planted.

Emmerich, who has made some interesting observations upon this question, has come to the conclusion that the pneumococcus forms spores. He made the following observations :—A cultivation was made in half a litre of broth, and after incubation for two days was placed in the dark, at the room temperature, for two months. The whole of the sediment from the cultivation was then transferred to a tube of broth and placed in the incubator. A growth of pneumococci occurred in the tube. It is necessary to take the whole of the sediment, because only a few spores are formed, and a small quantity of the sediment may not contain any.

Arkharow mentions that in old cultivations, among a large

number of dead cocci, a few are sometimes met with which stain well. I have frequently made the same observations, and I think it probable that these cocci which stain well represent the spore forms.

The short life of the pneumococcus under ordinary circumstances renders investigation difficult; for, unless fresh inoculations are constantly made, the cultivations die out, and fresh cultivation must be obtained from the human subject.

Foà and Arkharow have got over this difficulty by preserving the blood of infected rabbits in sealed tubes in the dark.

I have adopted this method, and have been able to keep the cocci alive and virulent for as long a period as three weeks; but after this time they usually die.

The method is not altogether satisfactory; for, owing to clotting, there may be a difficulty in filling and emptying the tubes. I consequently searched for a better method of preserving the vitality of the cultivation. This I have attained by cultivating upon the surface of agar covered with a thin layer of blood, according to the method of Pfeiffer for the influenza bacillus.

I adopted this method because I had observed that cultivations on agar made from the blood of infected animals retained their vitality longer when a large quantity of the blood was transferred to the tubes. The tubes are easily prepared by spreading, under aseptic precautions, the blood from an animal recently killed. They are placed in the incubator for twenty-four hours to see that they are sterile, and are then ready for use.

On this medium the pneumococcus grows well, and retains its vitality and virulence for as long a time as fifty days. I have been using this method during the whole of last year, and have found it very satisfactory.

For the purpose of inoculation I make a cultivation in broth, and use this for injection.

I will quote an example to show how long the virulence is preserved. A broth cultivation was made from a blood-agar tube forty days old. One c.c. of this was injected into the peritoneal cavity of a rabbit. The animal died in fourteen hours from pneumococcal septicæmia.

By this procedure experiments with the pneumococcus are much facilitated, for there is no danger of the cultivation dying out at inconvenient times.

I find that E. Fränkel and Reiche, in the 'Zeitschrift für klinische Med.' for 1894, have quite independently made the same observations, and were led to use this method of cultivation by the same course of reasoning.

Defibrinated rabbit's blood is also a good medium for the growth of the pneumococcus. I have been using this medium for the preparation of toxins, and find that the pneumococcus retains its vitality as long as fifty-six days.

Morphology of the pneumococcus.—The morphology of the pneumococcus varies according to different conditions of growth. The usual form is that of a diplococcus. The prevailing shape of the individual cocci is lanceolate; but they are sometimes rounded, or oval, or even rod-shaped. In size they vary very much. Straight chains of three or four cocci are common, and long twisted chains containing forty or fifty cocci are met with.

In the blood of animals diplococci are almost exclusively found, and they are generally provided with a capsule. The capsules vary in size and distinctness, and in some cases I have failed to discover any at all.

In cultivations on artificial media the capsule is usually absent.

In peritoneal exudations the individual cocci are often elongated so as to look almost like bacilli.

In broth cultivations short chains are common, and in cultivations made in broth from blood-agar tubes the chains are often long, and no diplococci are to be found.

I have met with the longest chains in cultivations in the blood-serum of immune rabbits.

I have always found these streptococci forms to be converted into diplococci in the blood of inoculated rabbits.

While discussing the morphology, I may mention that there is a bacillus producing septicæmia in rabbits which, under certain conditions of growth, bears a resemblance to the pneumococcus.

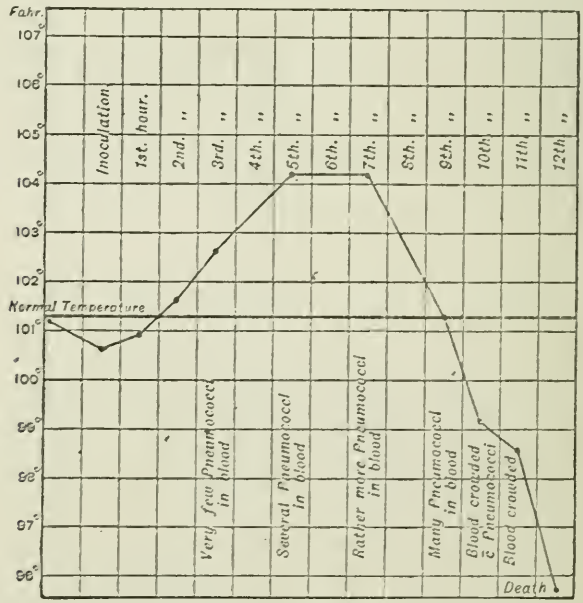
At one time, after inoculating rabbits with the pneumococcus, I found, in the blood, bacteria differing from the pneumococcus in character.

I thought at first that I had introduced some impurity, but was at a loss to discover how. The matter was soon cleared up by the death of several rabbits in the stock cage from a form of septicæmia. The blood contained bacteria belonging to the group of *septicæmia hæmorrhagica*, which often appear under the form of diplococci.

I have no doubt that the peculiar bodies described by Arkharow as occurring in the blood after inoculating immune rabbits with the pneumococcus, and considered by him to be modified pneumococci, were due to an epidemic of septicæmia hæmorrhagica. Metschnikoff, in a foot-note to Issaef's paper, makes a similar remark about Arkharow's work.

Pathogenic effects in animals.—Many animals are susceptible to inoculation with the pneumococcus; others enjoy immunity. The most susceptible animals are mice and rabbits. *Guinea-pigs* are much less susceptible, but die when inoculated with virulent cultures in the peritoneal cavity. In the inoculations I have made the animals died in from one to seven days. At the *post-mortem* there was extensive peritonitis, with many cocci in the exudation; the blood in the cases dying early was crowded with cocci, but in the prolonged cases only a few were present. *Mice* die in two or three days after subcutaneous inoculation, and the blood is crowded with cocci.

FIG. 27.



Dogs are said to be more susceptible to subcutaneous than to intra-venous or intra-peritoneal inoculation.

Pigeons and *fowls* appear to be immune. I have made several attempts to infect these birds, but have always failed.

Rabbits are very susceptible, and as my experiments have chiefly been conducted on these animals, I shall quote my observations in detail.

Effects on rabbits—intra-peritoneal injection.—The most satisfactory method of inoculation is to inject either the blood of an infected animal or a broth cultivation (one day old) into the peritoneal cavity. I usually inject 1 c.c. of a broth cultivation or ·5 c.c. of blood. The advantage of this method is that the animal almost always either dies within two days or recovers. In only one case, among some hundreds of inoculations with cultures of different virulence, has death occurred as late as three days, and in one case as late as four days. This rule also holds good for immunised or partially immunised animals. If protective serum is injected with the cultivation into the peritoneal cavity, then death may be prolonged as late as nineteen days.

With the cultivations I am now using death occurs in twelve to sixteen hours.

The most marked symptoms produced by a cultivation of this virulence are fever and dyspnœa.

The *course of the fever* is shown in the above chart. (The temperature is always taken in the rectum, and this is an important point, for, as Dr. Hale White and I have shown, the temperature of the groin of a rabbit is always higher than that of the rectum.)

Immediately after the inoculation the temperature begins to rise, and reaches its maximum of 104° F. in about five hours. The temperature remains at the maximum for two or three hours, and then begins quickly to fall. For two or three hours before death it is subnormal.

Respirations.—The respirations increase in rapidity with the temperature, and by the time the latter is at its maximum they begin to be laboured. As the temperature falls the dyspnœa becomes more marked, the head moving with each respiration.

General condition.—The animal refuses food, but does not suffer any pain, and it is not until the temperature begins to fall that it appears at all ill. It then becomes quiet and crouches up in a corner of the cage, and remains in this condition until it dies. Death is often preceded by convulsions.

The invasion of the blood by cocci.—I have made a number of observations upon the presence of the cocci in the blood at different times after inoculation. Either the animals were killed at different stages, or a drop of blood from the ear was examined during life.

At the end of three hours a few cocci are found in the general circulation, and the number increases as the temperature rises. It is only, however, when the temperature begins to fall that any large numbers are found. During the last two or three hours of life the blood is crowded with cocci. I cannot, therefore, agree with those who consider that the large number of cocci found in the blood at the autopsy is due to a multiplication occurring after death.

Subcutaneous inoculation.—The result of subcutaneous inoculation depends upon the virulence of the cultivation and the quantity injected. If the cultivation is very virulent, and as much as ·5 c.c. of blood or 1 c.c. of broth is injected, death occurs within twelve to sixteen hours without any local lesion, and with the same symptoms as occur after intra-peritoneal inoculation.

If a smaller quantity is injected, or if the cultivation is less virulent, death occurs at a later period, generally in from three to six days, sometimes later; and in one of my experiments as late as thirty-six days after inoculation.

When death occurs at a late period the most marked symptom is emaciation, the weight in one case falling from 3000 to 1780 grammes. In two cases where death occurred with marked emaciation, after a long period, changes were found in the kidneys, and no cocci could be found in the organs or blood. Cases of death from marasmus, some time after inoculation, have been recorded by other observers.

Local reaction.—The extent and nature of the local reaction depend upon the duration of life. If death occurs within twelve to sixteen hours there is usually œdema at the seat of inoculation; but in some cases I have found no local reaction whatever.

When death occurs in two or three days there is extensive œdema; in one case an enormous œdema of the head and face followed upon inoculation at the base of the ear.

When death occurs between the fourth and tenth days a hard swelling forms at the point of inoculation. The swelling consists of a fibrinous, or of a mixed fibrinous and serous exudation.

When death occurs late, or if the animal is partially immunised and recovers, an abscess forms. The skin over the abscess generally sloughs, and gives exit to a thick creamy pus.

These lesions are of interest as showing that the same micro-organism may give rise to various forms of inflammation—serous, fibrinous, or purulent; and we can thus understand how the pneumococcus may produce in the human subject such conditions as fibrinous pneumonia, acute œdema of the lung, fibrinous pleurisy, empyema, otitis, &c.

Post-mortem appearances.—Peritonitis is usually present after intra-peritoneal inoculation, but with very virulent cultivations the peritoneum may appear quite healthy. It is not uncommon to find peritonitis after inoculation in the subcutaneous tissue of the abdomen.

The peritoneum may be covered with a fairly thick layer of fibrin, or there may be only a few shreds of fibrin between the coils of the intestines.

In most cases no fluid is found in the peritoneal cavity, but sometimes a clear or turbid fluid is found.

The *intestines*, when there is peritonitis, are congested; and now and then hæmorrhages are to be seen in the mesentery or sub-peritoneal tissue.

The *lungs* are often congested, but frequently appear quite healthy.

Changes are not usually seen in the *liver* or *kidneys*.

The *spleen* is either quite normal in size and consistency or is enlarged, and then may be abnormally soft or hard.

The *local lesions* at the seat of inoculation have already been described.

Œdema in the anterior mediastinum is not uncommon.

The *blood* is usually clotted if the *post-mortem* examination is made a few hours after death, and in any case has always readily clotted on removal from the heart. It is almost always distinctly alkaline. Although I have often made inoculations with a pneumococcus quite as virulent as the one used by Issaef, I cannot confirm his observations with regard to the acidity of the blood and the loss of power of clotting.

The *number of cocci* in the blood depends upon the duration of the disease and the local lesion. When death is the result of intra-peritoneal inoculation the blood is almost invariably crowded with cocci. The same is the case when death occurs in three to four

days after subcutaneous inoculation, and there is only œdema at the spot of inoculation.

If death occurs at a late period there is a fibrinous exudation or an abscess at the spot of inoculation, and then the blood contains but few cocci, or none at all. A large number of cocci are usually found in the local lesion.

As *unusual lesions* I may mention *pneumonia* and *pleurisy.*

In two cases I found *pneumonia.* Both occurred after intra-peritoneal inoculation, followed by death in two days. In one case the whole of the upper lobe of one lung was solid, and there were several patches of lobular pneumonia in the lower lobe. Microscopical examination showed that the alveoli were filled with cells. There was thick fibrin over the pleura. In the other case there was a patch of lobular pneumonia and pleurisy.

Pleurisy without pneumonia was observed in three cases.

In one of these cases the animal lived for eleven days after subcutaneous inoculation, and there was thick fibrin in the peritoneum, as well as on both pleuræ. In all the cases, when there was pneumonia or pleurisy, the heart blood only contained a few pneumococci. Several investigators have quoted cases where they have produced typical fibrinous pneumonia by inhalation experiments, or by intra-tracheal injections in dogs and rabbits.

Nephritis.—In two instances there was a parenchymatous nephritis. In both cases death occurred at a late period, in one case after thirty-six days with much emaciation. The kidneys were speckled with yellow and white spots on the cortex, and microscopically fatty changes were found in the epithelium. No pneumococci were found in the blood or organs.

The observations of Fränkel and Reiche are interesting in connection with nephritis. In a number of cases of pneumonia in the human subject they found changes in the epithelium of the kidneys, and from the juice of these organs they were able to obtain cultivations of the pneumococcus.

Virulence of the pneumococcus.—The virulence of the pneumococcus varies, and is dependent upon a number of circumstances. In making comparative experiments the quantity injected and the age of the cultivation must be taken into account. The method of inoculation, whether intra-peritoneal or subcutaneous, and the weight and age of the animal are important factors.

The direct injection of material from the human subject is no test

of the original virulence of the cocci, because we cannot say how many living cocci are present in the material injected.

Kruse and Pansini have made extensive observations with pneumococci derived from different sources, and describe a large number of varieties differing from one another in virulence and morphology. They do not, however, consider these varieties to represent constant types. I am convinced that the virulence cannot be foretold from the morphological appearance. I have frequently found cultivations, consisting entirely of streptococci, virulent enough to kill rabbits in twelve hours when injected in doses of 1 c.c. into the peritoneal cavity.

Varieties of pneumococcus.—There is, however, evidence to show that distinct varieties of the pneumococcus exist.

Fowitzky has separated a variety which produces a brick-red pigment, and which constantly produces pneumonia in rabbits on inhalation.

Foà describes two distinct varieties, both occurring in pneumonic sputum.

The one variety he calls the pneumococcus, and the other the meningococcus, because it is frequently met with in meningitis.

The *meningococcus* or septic variety, after subcutaneous inoculation, causes death in rabbits in three days without local reaction. The spleen is hard and firm, and the blood full of cocci.

The *pneumococcus* or toxic variety, after subcutaneous inoculation, causes death in twenty-four hours. There is much œdema at the seat of inoculation, the spleen is soft, and the blood contains but few cocci.

I have made experiments with pneumococci from various sources, but have never succeeded in obtaining distinct varieties existing as constant types.

As far as the spleen is concerned, I have found it both hard and soft, and the inoculation with the blood of a rabbit dying with a hard spleen has frequently produced a soft spleen in another rabbit, and *vice versâ*. In one case the spleen was four or five times its normal size, and remarkably hard, yet another rabbit inoculated with the blood of this one died with a soft spleen.

The nearest approach to the "toxic variety" I have met with was the following:

A rabbit was inoculated in the subcutaneous tissue, and died in twenty-four hours. There was enormous œdema at the seat of inoculation, and the spleen was soft; and the blood, though con-

taining many cocci, was not crowded with them, as is so often the case.

Now the cultivation from this rabbit produced various types of the disease in other rabbits; and again, the cultivation from which this rabbit had been inoculated had also produced different types of the disease, according to the quantity introduced and the mode of inoculation. As far as my own experience goes, the varieties of the pneumococcus have only differed in virulence, and can be converted into one another by repeated passages. In order to obtain *a type of constant virulence* I have adopted the method of Issaef of frequent passages through the peritoneal cavity of rabbits, and in my later experiments I have used a type which appears to be constant; 1 c.c. of a broth cultivation, or 0·25 c.c. blood, injected into the peritoneal cavity of a rabbit causes death in twelve hours, while 0·5 c.c. of the blood injected subcutaneously kills in about fourteen hours.

I have found too, like Issaef, that sometimes, after repeated passages through rabbits, the virulence has become lessened, but that it has been regained by the passage through the body of a guinea-pig.

Toxins,—With regard to the toxins produced by the pneumococcus, I propose to leave what I have to say upon the subject to a subsequent occasion.

Production of immunity.—Various methods have been adopted for obtaining immunity to the pneumococcus. All are based upon general principles, and consist in inoculating with attenuated cultivations or in injecting with chemical products treated in various ways. The method recommended by G. and F. Klemperer is the following:—Recent broth cultivations are heated to 60° C. for one or two hours, and are used for injection. According to these authors, immunity is conferred at the end of fourteen days after subcutaneous injection of 24 c.c., and in three to four days after intra-venous injection of 8—12 c.c. I have injected into the circulation of fourteen rabbits cultivations treated in this manner, in doses of 12—15 c.c., and subsequently the rabbits were inoculated with virulent cultivations at different periods after the injection, in order to see when immunity occurred and how long it lasted.

The result showed that immunity was not conferred until after the twentieth day; that it was present between the twenty-fourth and fifty-first day, and then disappeared.

The rabbits inoculated on the fifth, ninth, sixteenth, and twentieth days died; those inoculated on the twenty-fourth, twenty-fifth, thirty-second, forty-third, and fifty-first lived, and those inoculated on the sixty-fourth, eighty-second, and eighty-fifth days died. Two of the rabbits died after the injection with the heated cultivation, one on the seventh and the other on the tenth day. They were both much emaciated, but the organs appeared healthy, and no bacteria were found in the blood or organs.

Emmerich produces immunity by injecting into the veins very diluted cultivations, and Foà uses a glycerine extract of the blood of infected animals.

I have had no experience with these methods.

Several investigators have produced immunity by inoculation with *attenuated cultivations*. This method is unsatisfactory, because so many animals die during the process.

In the course of other experiments, I have in a few cases produced immunity in this way. For instance, a rabbit was inoculated subcutaneously with a small quantity of an agar cultivation four days old. An abscess formed at the spot of inoculation, from which the animal recovered. At the end of seventy-six days it was inoculated with a virulent cultivation, and was not affected.

I have also produced immunity by the inoculation of *filtered cultivations*. For instance, 20 c.c. of a filtered cultivation in defibrinated blood was injected into the subcutaneous tissue of a rabbit; twenty-one days later the rabbit was inoculated with a virulent cultivation without being affected.

In testing the immunity it is always necessary to make control experiments, so as to be sure that the cultivations are virulent.

After inoculation with a virulent cultivation, immunity, when established, will last for a long time. I have frequently found it present fifty or sixty days after inoculation. In one of the experiments I have already quoted it was present on the seventy-sixth day.

As a rule, when an animal has withstood inoculation with a virulent cultivation, I find it will withstand repeated inoculations, provided they are not made too quickly after one another.

The blood-serum of immune animals.—G. and F. Klemperer, Emmerich and Fowitzky, Foà and Carbone, were the first to show that the blood-serum of immunised rabbits would protect other rabbits when injected, either at the same time or subsequently to inoculation with the pneumococcus.

Arkharow and Issaef have obtained similar results. I have made a number of experiments in this connection, injecting the serum at the same time, or shortly after inoculation, with a virulent cultivation. As a result of these experiments I find that the blood-serum of immunised rabbits sometimes protects perfectly, sometimes partially, and sometimes not at all. I have endeavoured to ascertain the conditions which give rise to the formation of a protective serum in the blood of the immunised animals.

In most of the cases both the serum and the cultivation have been injected into the peritoneal cavity. As examples of perfect protection I will quote the following :

1. A rabbit weighing 1840 grms. was injected with 6 c.c. of serum and ·25 c.c. virulent blood directly into the peritoneal cavity. At the same time a control rabbit weighing 2135 grms. was injected with ·25 c.c. of the same virulent blood. The control died in thirty-one hours of a general infection, while the protected animal was not affected, and was quite well three months later, having steadily gained in weight during this time.

2. A rabbit weighing 2030 grammes was injected with 10 c.c. of serum, and at the same time with ·25 c.c. virulent blood, both into the peritoneal cavity. A control rabbit weighing 2525 grammes was inoculated with ·25 c.c. of the same virulent blood. The control died in thirteen hours of general infection. An abscess developed in the abdominal wall of the protected rabbit, but this healed, and the animal was quite well four months afterwards, having in the meanwhile gained in weight.

3. A rabbit weighing 2480 grammes was injected with 12 c.c. of serum, and at the same time with ·5 c.c. virulent blood, into the peritoneal cavity. A control rabbit was injected with ·5 c.c. of the same blood. The control died in forty hours of general infection. The protected rabbit was alive and well two months afterwards.

4. A rabbit was injected with 10 c.c. protective serum and 1 c.c. virulent broth cultivation, both into the peritoneal cavity. A control rabbit of about the same weight was injected with 1 c.c. of the same virulent broth. The control died in twenty-six hours of a general infection, while the protected animal was alive and well a month later.

5. A rabbit weighing 2100 grammes was injected with 15 c.c. of protective serum, and at the same time with ·25 c.c. of virulent blood. A control was injected with ·25 c.c. of the same virulent

blood. The control died in seventy hours of a general infection. The protected animal was alive and well seven weeks later.

As examples of partial protection I will quote the following:

1. A rabbit was injected with 10 c.c. serum and 1 c.c. virulent broth, both into the peritoneal cavity. A control was injected with 1 c.c. of the same virulent broth. The control died in twelve hours of a general infection. The protected animal appeared unaffected at first, but died nineteen days later with peritonitis.

2. A rabbit was injected with 10 c.c. protective serum into the peritoneal cavity, and at the same time ·5 c.c. virulent blood was injected subcutaneously. A control was injected with ·5 c.c. of the same blood into the subcutaneous tissue. The control died in eighteen hours, of general infection. The protected animal developed a swelling at the seat of inoculation, became emaciated, and died in seventeen days. On *post-mortem* examination there was a fibrinous exudation at the spot of inoculation, and peritonitis. The lymph on the peritoneum contained an abundance of pneumococci, but the heart blood only a few.

In these cases the serum only prolonged life.

I will quote the following cases to show that the blood-serum of an immune rabbit sometimes possesses no protective power.

1. A rabbit was injected with 12 c.c. serum and ·25 c.c. virulent blood into the peritoneal cavity. A control was injected with 25 c.c. of the same virulent blood. Both rabbits died in sixteen hours.

2. A rabbit was injected with 10 c.c. serum into the peritoneal cavity, and with ·5 c.c. of virulent blood into the subcutaneous tissue. A control received ·5 c.c. of virulent blood subcutaneously. The first rabbit died in eighteen, and the control in twenty-eight hours.

3. A rabbit was injected with 10 c.c. serum and with ·37 c.c. of virulent blood, both into the peritoneal cavity. A control received ·37 c.c. of virulent blood. Both rabbits died in twenty-six hours.

The protective power of the serum of immunised rabbits is of a specific character, and does not exist in the blood of normal rabbits.

I will quote experiments to show that the blood-serum of a normal rabbit presents no protective properties.

1. A rabbit was injected with 10 c.c. of normal serum and ·12 c.c. of virulent blood, both into the peritoneal cavity. A control rabbit received the same quantity of virulent blood but no serum. Both animals died in fifteen hours of general infection.

2. A rabbit was injected with 9 c.c. of normal serum and 1 c.c. of virulent broth cultivation, both into the peritoneal cavity. A control received 1 c.c. of the same broth cultivation. The first rabbit died in sixteen hours, and the control a few hours later.

I thought it possible that immediately after an inoculation with a virulent cultivation the first effort of the body to resist infection would be the formation of a protective serum in the blood. The following experiment gives no support to this view:

A rabbit was inoculated in the peritoneal cavity with a virulent cultivation. Five hours after inoculation the rabbit was bled. 12 c.c. of the serum (which contained no cocci) was injected into the peritoneal cavity of another rabbit, together with a virulent cultivation. A control rabbit was inoculated with the same quantity of the same cultivation. Both rabbits died in twelve hours.

Now what are the conditions which determine the protective power of the serum of immune rabbits?

In the first place, it is essential that the rabbit should be quite immune.

I believe that some of the cases where I failed to obtain a protective serum was due to the fact that the animals were not perfectly immune, although they had resisted previous inoculation.

The next point is the period at which the serum is removed after the last injection. I have generally found eight or nine days after the last inoculation to be the best time for removing the serum. I have not removed serum earlier than seven days. As a rule, if serum is removed as late as eighteen days it has no protective power, but I have known the serum to be protective after nineteen days, and in one case as long as sixty-two days after the last inoculation.

In this latter case the test was not a very severe one, as the control rabbit did not die until seventy hours after intra-peritoneal injection.

An important question arises with regard to the relationship between immunity and the protective power of the serum.

Is the former directly dependent upon the latter?

I do not feel that I am in a position to give a definite answer to this question at present.

An interesting point in this connection I have found is that the removal of protective serum from an immune animal renders the animal susceptible for a time. If it is inoculated within two days

after removal of the serum it dies; but if the inoculation is postponed for four or five days it is not affected.

It would appear that new protective serum requires to be re-formed before immunity is again established.

The action of the protective serum upon the growth of the pneumococcus.—Various statements have been made about the growth of the pneumococcus in the serum of immunised rabbits. Some, such as G. and F. Klemperer, simply state that the serum is a good medium for the growth of the pneumococcus, and that the cultivations remain virulent. Others consider that the protective serum actually destroys the pneumococcus. Others again, such as Arkharow, Issaef, and Mosny, state that the pneumococci grow in the serum in a special manner, while the virulence is not diminished.

I have made a number of experiments in this direction, and I find that the method of growth depends upon the protective power of the serum. In fact, the mode of growth in the serum appears to me to give a good indication of its protective power. If the serum presents marked protective properties the mode of growth is quite characteristic, and presents a marked contrast to the growth in normal serum.

When normal serum is inoculated with the pneumococcus it becomes quite turbid at the end of twenty-four hours. The turbidity is shown in microscopical examination to be due to an abundant growth of diplococci. After a few days the turbidity increases, and the serum becomes milky. When protective serum is inoculated it appears perfectly clear at the end of twenty-four hours, but at the bottom a sediment is seen. The sediment consists of pneumococci staining well and grouped in masses. In addition to diplococci, streptococci, often in exceedingly long chains, are seen. Sometimes only streptococci are found. If the pneumococci are transplanted to broth, an abundant growth occurs. Inoculation of rabbits with this broth shows that the virulence has not been affected.

For instance, I sowed a tube of normal serum and one of protective serum with pneumococci, and at the end of twenty-four hours broth tubes were inoculated from the serum tubes. After incubating for twenty-four hours, two rabbits were injected with 1 c.c. into the subcutaneous tissue. The rabbit inoculated with the culture from the normal serum died in four days, and the rabbit

inoculated with the culture from the protective serum in three days. The blood of both contained many cocci.

Issaef has made extensive experiments with regard to the virulence of cultures in protective serum, and considers that it is not at all affected.

In making these observations it is important to test the protective power of the serum. It is not enough to rely upon the fact that the animal from which the serum is taken is immune.

On two occasions I found that the serum of immune rabbits when inoculated became turbid; but when the serum was tested it was found not to possess protective properties. On another occasion the serum became slightly turbid, and on testing it, it was found to possess only partial protective power.

Serum of patients sufferiny from pneumonia.—Klemperer states that the serum taken from patients during convalescence from pneumonia possesses protective properties. Others deny this. I have only made a few experiments, on account of the difficulty of obtaining serum. In two or three cases, however, I have been able to obtain serum from blisters which have been applied during convalescence for some reason or other. As a rule the quantity has been too small for any result to be obtained.

In one case 8 c.c. of fluid was obtained from a patient seventeen days convalescent from pneumonia. This was injected into the peritoneal cavity, together with 0·5 c.c. of pneumonic blood. The rabbit died in eighty-seven hours, and the control in thirteen. The serum in this case possessed some protective power.

The serum during the pyrexial stage of pneumonia.—I have had no difficulty in obtaining serum from blisters applied during the acute stage of pneumonia.

In seven cases this fluid was injected into the peritoneal cavity of rabbits, either simultaneously or some days previously to inoculation. In one case both animals died in seventeen hours, but in all the others the animal which had received the serum died earlier, sometimes much earlier than the control.

In one case 0·5 c.c. of serum was injected into the peritoneal cavity of a rabbit seven days previous to the subcutaneous inoculation of an attenuated cultivation; the animal died of pneumonic infection in five days, while the control was not in any way infected.

It would thus appear that the serum increases the virulence of the pneumococcus.

Control experiments made with blister fluid from healthy individuals showed no modification of the disease.

In concluding this paper I feel I have added but little that is new to our knowledge. It is only because the subject has received such slight attention in this country that I have ventured to bring the results of my investigations before you to-night.[1]

February 5th, 1895.

[1] In these investigations I have been assisted by a Government grant from the Royal Society.

XII. DISEASES, ETC., OF THE LOWER ANIMALS.

1. *On the possible relation of swine fever to general or simple ulcerative colitis.*

By Leopold Hudson.

The subject of swine fever has long engaged the attention of veterinary practitioners and comparative pathologists in this country, and its possible relation to typhoid fever in the human subject has also been discussed. Indeed, so long ago as 1865, Dr. Budd, in a lecture before the Royal Agricultural Society, endeavoured to prove that swine fever was the exact counterpart of human typhoid fever. He rested this statement chiefly on the fact that the intestinal appearances in the two seemed to him to be identical; but Dr. Murchison, in his treatise on continued fevers, denied that there was any similarity between the two maladies; the cutaneous and intestinal affections in the respective diseases being, according to him, quite different.

Recent experience of these maladies lends weight to the conclusion of Dr. Murchison; for on the one hand the clinical course of the affection in the pig bears little resemblance to human typhoid fever, and on the other hand the small intestine of the pig in swine fever is free from ulceration. But is there any other malady in the human being which can be regarded as in any sense identical with swine fever?

I exhibit a series of recent specimens of the large intestine of pigs which are affected with swine fever. They were obtained from different parts of England and Scotland, and were sent to the Board of Agriculture for the inspection of the Scientific Committee on Swine Fever at present sitting. This committee has been appointed to review the experience gained since the Swine Fever Act of 1893 came into force, respecting the ætiology, pathology, and morbid anatomy of the diseases classed as swine fever, and to supplement that experience by a series of experiments as to the bacteriology and life history of these diseases, and as to their

communicability either directly or indirectly from animal to animal.

I wish to point out the similarity in distribution between these lesions in swine fever and the condition in the human being which has been described as simple or general ulcerative colitis, and further to raise the question whether this disease is communicable from swine to mankind.

In the specimens shown the ulceration is seen to be confined to the cæcal aspect of the ileo-cæcal valve and to the large intestine, and every stage can be seen from the small more or less circular simple ulcer to the large confluent areas of destroyed mucous membrane with adherent masses of necrotic tissue. The whole of the specimens shown are from pigs which have been suffering from the chronic form of the disease, but in the acute variety the sloughing is less marked, and the lesions then resemble very closely indeed specimens of ulcerative colitis in the human subject which have been shown at this Society.

Many such cases of human ulcerative colitis have been brought before the Society during the last few years, and the impression is gaining ground that this affection is much commoner than has been supposed.

The ulceration in the human being is, as in the pig, limited to the large intestine, the mucous membrane of which is often extensively destroyed. But the likeness between the two diseases does not end with the morbid anatomy. With regard to clinical symptoms in the pig, the disease assumes either an acute or a chronic form; the acute form having apparently a short incubation period, lasting but three or four days, being accompanied by high fever, and producing a rapidly fatal result.

In the chronic form the pig shows but few signs of illness, and, indeed, in many cases is regarded as well until at slaughter the characteristic lesions are revealed. In this variety the temperature often remains subnormal, while later chronic diarrhœa and marasmus usually occur. In the human being ulcerative colitis likewise presents either an acute or a chronic form. It may be well here to attempt a definition of what is referred to as ulcerative colitis. By this term is meant an affection characterised by ulceration of the large intestine, which is not due to tubercle, syphilis, typhoid, lardaceous disease, or malignant deposit; nor is it associated with fæcal impaction, nor with dysentery. Examples of the acute form

of ulcerative colitis have been recorded in the 'Transactions' of this Society by Dr. Allchin,[1] Dr. Sharkey,[2] and others, the disease being accompanied by fever of an irregular type, and by the passage of blood and occasionally of sloughs by the bowel. In the chronic form, on the other hand, the temperature is often subnormal, and the main symptoms are the progressive emaciation and diarrhœa.

With regard to bacteriology, there is already in the case of swine fever an extensive literature. In America two distinct diseases are recognised, namely, hog cholera and swine plague. In hog cholera the first effect of the disease is believed to be upon the intestines, with secondary invasion of the lungs, In swine plague the first effect is believed to be upon the lungs, and the invasion of the intestines a subsequent process. Salmon[3] states that the hog cholera organisms are slightly larger and more elongated than those of swine plague; they are provided with flagella which enable them to move rapidly in liquids, while the swine plague microbes have no such organs and are non-motile. But Silberschmidt[4] shows that the diseases of swine which have been described as swine plague and hog cholera by Salmon, and that known in France as pneumo-entérite infectieuse are caused by one and the same virus. Although different in some morphological characters, the three microbes are shown to be analogous from the point of view of the microbic products, the pathogenic properties, the morbid symptoms, and the lesions produced in animals experimented on.

With regard to the bacteriology of human ulcerative colitis but little has as yet been accomplished, though the *Bacillus coli communis* has been accused of being the causative agent.

It is remarkable that in Dr. Allchin's case the patient herself attributed her illness to the eating of pork,[5] and in the first of the two cases contributed by Dr. Tooth[6] the clinical clerk learnt from the patient that in a situation where she was she had to eat pork daily, and she thought that this disagreed with her, and may have caused abdominal trouble. These details were not published in the history of the case, but were kindly gleaned for me from the notes by Dr. Ormerod.

[1] 'Trans. Path. Soc.,' 1885, p. 199.
[2] Ibid., 1891, p. 112.
[3] 'Hog Cholera and Swine Plague,' Washington, 1894.
[4] 'Ann. de l'Institut Pasteur,' February, 1895.
[5] 'Trans. Path. Soc.,' 1885, p. 199.
[6] Ibid., 1894, p. 66.

Ulcerative colitis is frequent in asylums, and it is well known that the patients in these institutions are often largely fed on pork. On inquiry at a large bacon factory I am told that every part of a pig is consumed except its brain, so that opportunities of acquiring the disease by ingestion must be frequent, as swine fever is widely prevalent in this country.

The facts here adduced, as well as the similarity between the disease in swine and in mankind, both as to morbid anatomy and described clinical symptoms, certainly seem to justify the prosecution of further inquiries as to their possible intercommunicability.

My excuse for the somewhat hasty way in which this preliminary communication has been presented to the Society must be found in the desire to avail myself of the present collective investigation of swine fever by Government. This has enabled me to present a series of specimens from different parts of the country, an opportunity which may never occur again. *May* 21*st*, 1895.

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2. *Boar's tusk growing in a circle.* (*Card specimen.*)

By F. Parkes Weber, M.D.

The specimen is a boar's lower tusk of the left side. Owing to incomplete opposition with the upper tusk, it has overgrown, so as to form a complete circle, the point having entered for one and a half inches into the pulp-cavity. The transverse ridges on the root bear witness to the irritation caused by the entry of the point, and there has been a deposition of new bone between the point and the walls of the pulp-cavity. The left upper tusk cannot have been absent, for its position is marked by a slight polished bevelling, to be seen on the specimen. A very similar specimen has kindly been shown me by Dr. Günther in the British Museum, Natural History Department. *January* 15*th*, 1895.

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