adjacent dermis is exposed to material from the lesion,[32] and this may account for the ease with which the tumours can be cured by any means which disrupt them.

The disease is probably world-wide. Early epidemiological studies described the incidence in Britain,[33 34] where considerable local variations occurred. Subsequent experience[35] has shown geographical differences in the incidence and distribution of the eruption according to age and sex. It seems likely that local conditions influence the pattern of the disease profoundly. This idea is supported by an interesting comparison between Aberdeen and Fiji.[36] In both populations the main factor determining transmission appeared to be the opportunity of being exposed to infection. This came early in Fiji, where the peak incidence of cases was in children aged 2–3, but later in Aberdeen, where the peak incidence was at 10–12, when attendance at swimming-baths offered appropriate conditions for spread. A preponderance of male patients in Aberdeen was not entirely explained by supposing that boys bathed oftener than girls, since there was no sex difference between bathers and non-bathers. Lesions in Fiji tended to be on the limbs, whereas in Aberdeen the axillae were the favourite site. While differences in clothing habits may be responsible (the question of sharing towels and clothing was not mentioned), the authors' findings suggest that the Aberdeen molluscs may have been sheltering from the cold.

Lesions should be treated by destruction. Pinching with forceps is simple but painful, working in phenol with a sharpened stick more humane but unsuitable for use near the eyes, the electro-cautery elegant but requiring anaesthesia. Large crops of lesions pose a numerical problem,[37] and treatment with a sulphonamide or tetracycline has been recommended. Results are inconsistent, and a second course of a tetracycline apparently provoked an explosive outbreak of new lesions in one case.[38] Conjunctivitis or keratitis require treatment of the (often insignificant) lesions on the lid margins.

Prophylaxis should depend on limiting opportunities for physical contact with infected persons. In Britain swimming-baths seem to be the most frequent source of infection, and it is desirable that schoolchildren should be inspected and excluded from them until clear of lesions. It is important not to share towels or clothing. These measures might reduce the number of cases, but they might also breed a more susceptible adult population. It is doubtful whether the disease could ever be eliminated by these means, since minimal infections[20] would be missed.

[1] Henderson, W., *Edinb. med. surg. J.*, 1841, 56, 213.
[2] Paterson, R., *Edinb. med. surg. J.*, 1841, 56, 279.
[3] Bateman, T., *A Practical Synopsis of Cutaneous Disease*, 3rd ed., p. 271. 1814. London.
[4] MacCormac, H., and Scarff, R. W., *Brit. J. Derm.*, 1936, 48, 624.
[5] Riggio, T., *Arch. ital. Derm.*, 1952-3, 25, 423.
[6] Béchet, P. E., *Arch. Derm. Syph. (Chic.)*, 1938, 37, 897.
[7] O'Donnell, J. M., *Med. J. Aust.*, 1958, 2, 536.
[8] Low, R. C., *Edinb. med. J.*, 1946, 53, 657.
[9] Mehregan, A. H., *Arch. Derm.*, 1961, 84, 123.
[10] Baxter, D. L., and Carson, W. E., *Arch. Derm.*, 1964, 89, 471.
[11] Randazzo, S. D., *Arch. ital. Derm.*, 1955, 27, 555.
[12] Tobias, N., *Arch. Derm. Syph. (Chic.)*, 1951, 64, 208.
[13] Tzanck, A., Sidi, E., and Melki, G., *Ann. Derm. Syph. (Paris)*, 1950, 10, 263.
[14] DeOreo, G. A., Johnson, H. H., and Binkley, G. W., *Arch. Derm.*, 1956, 74, 344.
[15] Duke-Elder, S., *System of Ophthalmology*, Vol. VIII, p. 376. London. 1965.
[16] Blank, H., and Rake, G., *Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man.* London. 1955.
[17] Burnett, J. W., and Neva, F. A., *J. invest. Derm.*, 1966, 46, 76.
[18] Postlethwaite, R., *Virology*, 1964, 22, 508.
[19] Epstein, W. L., Conant, M. A., and Krasnobrod, H., *J. invest. Derm.*, 1966, 46, 91.
[20] Paton, E. P., *Westminster Hosp. Rep.*, 1909, 16, 11.
[21] Gudgel, E. F., *U.S. armed Forces med. J.*, 1954, 5, 1207.
[22] Andrews, G. C., *Diseases of the Skin*, 3rd ed. Philadelphia. 1946.
[23] Casazza, R., *Dermosifilografo*, 1931, 6, 461.
[24] Nardi, G., *Dermosifilografo*, 1934, 9, 110.
[25] Juliusberg, M., *Dtsch. med. Wschr.*, 1905, 31, 1598.
[26] Wile, U. J., and Kingery, L. B., *J. cutan. Dis.*, 1919, 37, 431.
[27] Sutton, R. L., and Sutton, R. L., jnr., *Diseases of the Skin*, 9th ed. London. 1935.
[28] Ehrmann, *Second Int. Derm. Congr., Wien*, p. 284. 1892.
[29] Barrack, B. B., *Aust. J. Derm.*, 1951, 1, 60.
[30] Solomon, L. M., and Telner, P., *Canad. med. Ass. J.*, 1966, 95, 978.
[31] Epstein, W. L., Senecal, I., Krasnobrod, H., and Massing, A. M., *J. invest. Derm.*, 1963, 40, 51.
[32] Henao, M., and Freeman, R. G., *Arch. Derm.*, 1964, 90, 479.
[33] Little, E. G., *Brit. J. Derm.*, 1910, 22, 181.
[34] Walker, N., *Brit. J. Derm.*, 1910, 22, 284.
[35] Overfield, T. M., and Brody, J. A., *J. Pediat.*, 1966, 69, 640.
[36] Postlethwaite, R., Watt, J. A., Hawley, T. G., Simpson, I., and Adam, H., *J. Hyg. (Lond.)*, 1967, 65, 281.
[37] Kaye, J. W., *Arch. Derm.*, 1966, 94, 454.
[38] Baran, M. L.-R., *Bull. Soc. franç. Derm. Syph.*, 1958, 65, 343.

Paraproteinaemia

The first insight into the complexity of the plasma proteins occurred when Tiselius[1] separated a number of fractions by applying an electrical current to them in solution. He labelled a diffuse band of protein with little mobility γ-globulin. It soon became apparent that this fraction was concerned with the body's response to infection and that antibodies formed much of its biological activity.

The use of physical and chemical methods of separation has shown a bewildering number of proteins in the plasma. Separation by centrifugation at high speed has shown molecules varying from 140,000 molecular weight with a sedimentation constant of 7S to very large molecules—macroglobulins of 900,000 molecular weight and sedimentation constants of more than 19S. In 1964 the World Health Organization[2] recommended that the slow-moving γ-globulin of 7S type should be called IgG or γG, the faster moving macroglobulins IgM or γM, and a third group of molecules faster than γG but of similar molecular weight IgA or γA. Because of their function as antibodies J. F. Heremans[3] suggested that these proteins should be called immunoglobulins. More recently further additions have been made in the form of the IgD or γD and possibly IgE immunoglobulins.

In response to antigenic stimulation during life a variety of immunoglobulins are produced. Each varies slightly in activity and structure, and this infinite variation is reflected in the diffuse nature of the bands produced by conventional electrophoresis. Electrophoresis of the serum can be combined with the use of precipitating antisera[4] to distinguish the various immunoglobulins. This technique has been of great value in demonstrating similarities and differences in structure between the groups.

R. R. Porter[5] showed by enzymic splitting of rabbit IgG that this immunoglobulin could be represented—at least diagrammatically—as four chains of polypeptides parallel to each other, with the shorter, "light" chains of molecular weight 20,000 enclosing a pair of larger, "heavy" chains of molecular weight 50,000. All four chains are joined at intervals by sulphydryl bonds. Furthermore IgA and IgM were shown to have a similar basic structure to IgG. All the immunoglobulins seem to contain light chains of two antigenic types κ and λ, whereas the heavy chains are antigenically distinct in each immunoglobulin and have been given the names γ, α, μ, and δ in the molecules of IgG, IgA, IgM, and IgD respectively.

Bence Jones in 1848 described a protein with unusual physical properties in the urine of patients with multiple myeloma. This protein has been shown to be almost identical with the light chain of the immunoglobulins; but the

important difference is that Bence Jones protein shows only one type of light chain, either κ or λ, and there is considerable homogeneity within the type. In myeloma of Bence Jones type the myeloma cells produce only one form of light chain, but in other forms of myeloma a complete protein with both light and heavy chain components which will react with antisera to one of the immunoglobulin proteins is formed. This protein cannot perform any of the biological functions of the immunoglobulin which it resembles, and it is called a paraprotein. An example is seen in γG myeloma, in which the patients are prone to infection though there is a considerable amount of γG paraprotein in the serum.

Paraproteins do not show the same variety of structure and function as immunoglobulins. When subjected to the influence of an electric field they migrate with one accord to form a distinct narrow band on electrophoresis—the so-called "M" band.

Otto Kahler in 1889 described the clinical features of myelomatosis and recognized the association of bone destruction, anaemia, cachexia, and Bence Jones proteinuria as a clinical entity. In 1944 J. Waldenström[6] described a more benign condition in which an abnormal plasma protein, a macroglobulin, was formed and the patient was found to have anaemia, a tendency to bleed, and splenomegaly. This condition, called macroglobulinaemia, is, like myeloma, a clinical entity; proliferation of a lymphocytoid cell is its pathognomonic feature. Since then, however, macroglobulinaemia has been seen in conditions such as leukaemia, reticuloses, carcinoma, and non-malignant conditions such as rheumatoid arthritis. The subject is made more confusing by findings of "M" components in the absence of clinical evidence of disease. The results of prolonged and thorough surveys such as those by J. Hallen[7] in 1966 and that recently reported by J. R. Hobbs[8] show clearly that the finding of an "M" component or paraprotein is not synonymous with diagnosing "myelomatosis" or Waldenström's macroglobulinaemia. Since Waldenström[9] described patients in whose plasma "M" components had been present for many years without deterioration in health others with "benign essential hyperglobulinaemia" have been reported.

Hallen found that patients with paraproteins of IgA or IgG type of a benign essential nature tended to have a low concentration of the paraprotein in the plasma, and that this became constant after a time. The absence of light chains in the urine in any excess was another favourable sign. In contrast, patients who eventually developed myeloma showed a steady increase in the level of paraprotein with time. Hobbs has emphasized the sinister significance of Bence Jones proteinuria, particularly in those patients with a γM type of "M" component. A level of 1 mg./100 ml. of urine appears to be significant. Increasing production implies a worse prognosis. In addition, he has shown that maintenance of the level of the other normal immunoglobulins within normal limits suggests a benign course. The mechanism whereby the production of paraprotein in malignant conditions inhibits normal immunoglobulin production is not clear but is of fundamental importance.

[1] Gitlin, D., *Ann. Rev. Med.*, 1966, 17, 1.
[2] Fudenberg, H. H., *Ann. Rev. Microbiol.*, 1965, 19, 301.
[3] Heremans, J. F., *Clin. Chim. Acta*, 1959, 4, 639.
[4] Grabar, P., and Williams, C. A., *Biochem. Biophys. Acta*, 1953, 10, 193.
[5] Porter, R. R., *Biochem. J.*, 1959, 73, 119.
[6] Waldenström, J., *Acta med. scand.*, 1944, 117, 216.
[7] Hallen, J., *Acta med. scand.*, 1966, Suppl. No. 462.
[8] Hobbs, J. R., *Brit. med. J.*, 1967, 3, 699.
[9] Waldenström, J., *Advanc. intern. Med.*, 1952, 5, 398.

Vagotomy in Treatment of Duodenal Ulcer

Though still the subject of debate, vagotomy combined with some type of operation for gastric drainage has become firmly established in many centres all over the world in the surgical treatment of duodenal ulceration. Indeed, the number of patients who have now undergone this treatment must be numbered in tens of thousands. Several long-term follow-up studies have shown that satisfactory results with acceptably low operative mortality can be expected.[1-5] Even gross pyloric stenosis, once considered a contraindication to the operation, has now been shown to respond admirably to vagotomy and drainage.[6]

Two important questions are still debated. Firstly, how does vagotomy compare with the old-established operation of partial gastrectomy with gastrojejunal anastomosis, the so-called Polya operation, with all its many modifications? Secondly, what is the cause of the diarrhoea which may follow vagotomy and drainage, and how is it to be prevented?

J. Goligher and his colleagues[7] have compared vagotomy and gastrojejunostomy, vagotomy with antrectomy, and the Polya partial gastrectomy in a prospective trial in Leeds. The differences in the results of the three operations proved to be small, dumping being commoner in the patients who had gastrectomy and diarrhoea commoner in those who had vagotomy. A. G. Cox[8] has recently studied 55 patients after partial gastrectomy and 51 after vagotomy with a gastrojejunostomy. The latter had marginally better results than the former in terms of alimentary symptoms. Thirteen of the patients with vagotomy and nine of those with gastrectomy had episodic diarrhoea, but the frequency and severity of the attacks seemed about the same among those affected in both groups.

At least some patients develop diarrhoea after every type of gastric operation. Since this is a symptom which requires thorough evaluation, its exact incidence after vagotomy and drainage has been the subject of much discussion. Whittaker and his colleagues[5] report from the Mayo Clinic on 436 patients followed up on an average for seven years after vagotomy and various drainage procedures. Though 61 patients (14%) had mild diarrhoea, only two had diarrhoea so frequent as to require medication. Perhaps the most careful analysis of bowel disturbance after vagotomy was that of Cox and M. R. Bond,[9] who studied 100 patients approximately four years after vagotomy and gastrojejunostomy. Daily bowel frequency was increased in 71, episodic

[1] Holt, R. L., and Lythgoe, J. P., *Brit. J. Surg.*, 1961, 49, 255.
[2] Holt, R. L., and Lythgoe, J. P., *Brit. J. Surg.*, 1965, 52, 27.
[3] Tanner, N. C., *Brit. J. Surg.*, 1966, 53, 185.
[4] Schofield, P. F., Watson-Williams, E. J., and Sorrell, V. F., *Arch. Surg.*, 1967, 95, 615.
[5] Whittaker, L. D., Judd, E. S., and Stauffer, M. H., *Surg. Gynec. Obstet.*, 1967, 125, 1018.
[6] Ellis, H., *Proc. roy. Soc. Med.*, 1967, 60, 745.
[7] Goligher, J., Pulvertaft, C. N., and Franz, R. C., *Conference on Postgraduate Gastroenterology*, ed. T. J. Thomson and I. E. Gillespie, 1966, Chapt. 26. London.
[8] Cox, A. G., *Brit. med. J.*, 1968, 1, 288.
[9] Cox, A. G., and Bond, M. R., *Brit. med. J.*, 1964, 1, 460.
[10] Kraft, R. O., Kirsh, M. M., Kittleson, A. C., Ernst, C. R., Pollard, H. M., and Ransom, H. K., *Surg. Gynec. Obstet.*, 1965, 120, 472.
[11] Williams, E. J., and Irvine, W. T., *Lancet*, 1966, 1, 1053.
[12] Bastable, J. R. G., *Brit. J. Surg.*, 1965, 52, 459.
[13] Kraft, R. O., Fry, W. J., and Ransom, H. K., *Arch. Surg.*, 1962, 85, 687.
[14] Ellis, H., and Pryse-Davies, J., *Brit. J. exp. Path.*, 1967, 48, 135.
[15] Tucker, F. H., Barnett, W. O., and Goodrich, J., *Surg. Gynec. Obstet.*, 1964, 118, 1281.
[16] Wastell, C., *Brit. med. J.*, 1966, 1, 1198.
[17] Wastell, C., and Ellis, H., *Brit. med. J.*, 1966, 1, 1197.
[18] Kraft, R. O., Fry, W. J., Wilhelm, K. G., and Ransom, H. K., *Arch. Surg.*, 1967, 95, 625.