GEIGY TRAVELLING FELLOWSHIPS

Prof. W. G. Spector, M.A., M.B., M.R.C.P., visited rheumatism centres in Australia and the United States (see Report, p. 68).

Dr. Helen Muir, M.A., D.Phil. attended congresses in the United States (see Report, p. 67).

Dr. E. T. Owen (*Australia*) is to work for a year in Great Britain.

Drs. I. C. Isdale and G. A. Q. Lennane (*New Zealand*) is to visit centres in Great Britain in 1965.

EDUCATION

During the year the Council continued to send its *Reports on Rheumatic Diseases* to all general practitioners in the National Health Service as it has done during the past 5 years. Three reports were issued: "The Painful Knee", by Dr. A. St. J. Dixon, M.D., M.R.C.P., and Mr. Alexander Kates, F.R.C.S.; "Still's Disease", by Dr. Barbara M. Ansell, M.R.C.P.; "Complications and Extra-articular Manifestations of Rheumatoid Arthritis", by Dr. A. G. S. Hill, F.R.C.P.E.

A new handbook for patients, *Ankylosing Spondylitis*, brings the total to six, other subjects being *Rheumatoid Arthritis*, *Osteo-arthritis*, *Gout*, *Rheumatic Fever*, and *Lumbar Disk Disorders*. The booklets are available only to doctors for issue to patients. The Council is very grateful to Mr. Leslie Starke for his kindness in illustrating them.

To help gardeners disabled by arthritis and rheumatism the Council has published and put on sale at 1*s.* 6*d.* an illustrated booklet entitled *Your Garden and Your Rheumatism*. This was written by Dr. C. B. Heald, and nearly 20,000 copies have already been sold.

The Council encourages research workers to publish their results in the *Annals of the Rheumatic Diseases*.

COMMONWEALTH

A full report of the work of the autonomous affiliated Associations in Canada, Australia, and New Zealand is included in the *Annual Report*, pp. 23-26.

THIRD CANADIAN CONFERENCE ON RESEARCH IN THE RHEUMATIC DISEASES

Toronto, 1965

The Third Canadian Conference on Research in the Rheumatic Diseases was held in the Royal York Hotel, Toronto, from February 25 to 27, 1965, under the auspices of the Canadian Arthritis and Rheumatism Society and The Canadian Rheumatism Association; 41 papers were presented, and the Proceedings will be published by the University of Toronto Press early in 1966.

The present understanding of the pathogenesis of rheumatoid arthritis was described by two specially invited guest speakers, Dr. R. C. Mellors (*New York*) and Dr. Morris Ziff (*Dallas, Texas*). The pathological lesion in the synovial membrane is characterized by a lymphocyte and plasma cell infiltration, often giving rise to actual lymphoid follicles. These findings are the hallmarks of an immune reaction and in fact the rheumatoid lesion has a similar appearance to a stimulated germinal centre. The earlier studies of Dr. Mellors had demonstrated the production of rheumatoid factor in the plasma cells of the infiltrate and this could be demonstrated even in sero-negative cases. Further evidence of an immunological stimulus was the marked production of the three types of immunoglobulins (γG, γM, and γA) in rheumatoid arthritis. Thus both the histological appearances and the serological findings supported the concept that the pathogenetic mechanism of the disease was immunological. Moreover, the decrease in serum and synovial fluid complement provided additional evidence. The antigenic stimulus was evidently a persistent one and this was indicated, not only by the histology, but by the existence of rheumatoid factor which was probably a non-specific sequel to any continued antigenic stimulus.

The aetiological event leading to this immunological response was, of course, quite obscure at present. No new information was available to support the autoimmune hypothesis of Burnet, in which aberrant forbidden clones of immunologically competent cells have the perverted capacity for immunologically attacking normal synovial antigens. Similarly, explanations of aetiology based on variations in tolerance of the immune system for synovial antigens had no direct support. Dr. Ziff noted that the synovial cell layer itself was not infiltrated with lymphocytes and plasma cells and that this indicated that the antigen responsible for the immune response probably did not lie in these cells. The possibility that a foreign antigen resided in the synovium and was responsible for evoking the immunological reaction kept alive the suggestion that an infectious agent could be the eliciting factor; but no such agent had yet been discovered.

The inflammatory reaction of rheumatoid arthritis had recently been arousing greater interest through the studies of lysosomes. It now appeared that the phagocytosis of macromolecular antigen-antibody complexes by polymorphs could activate the lysosomal granules of the polymorphs and that many of the secondary manifestations of the inflammation, such as cartilage destruction, could be explained on the basis of lysosomal enzyme activity. The demonstration by Hollander of "inclusions" of rheumatoid factor in synovial polymorphs had provided a further stimulus for the interest in lysosomes.

Electron microscopic studies of normal guinea-pig and human rheumatoid synovia, performed by M. D. Haust, J. C. Wyllie, and R. H. More (*Kingston*), confirmed the existence of both phagocytic type A synovial cells, characterized by pinocytic and lysosomal vacuoles, and also type B cells showing evidence of secretory activity. R. B. Salter and R. McNeil (*Toronto*) had made the clinical observation that articular cartilage becomes atrophic when it is not in contact with opposing articular cartilage. They had pursued this observation by immobilizing the knee joints of rabbits in acute flexion. Articular cartilage over the femur above the point of contact with the patella then showed degenerative changes within a period of 3 weeks' immobilization. After several months of such immobilization, the articular cartilage of the femur not in contact with the patella or tibia had virtually disappeared. The change was not reversible and secondary osteo-arthritis was subsequently seen.

The nomenclature of the immunoglobulins was reviewed by G. E. Connell and R. J. Painter (*Toronto*) who described the structural composition of the gammaglobulin from light and heavy chain polypeptides. The effects of plasmin, papain, and trypsin treatment of the gammaglobulin were compared. D. A. Gordon and colleagues (*Toronto*) had applied immuno-diffusion, Sephadex separation, ultracentrifugation, and C^{14} labelling techniques to urinary gammaglobulins and demonstrated that the urinary gammaglobulin reflected predominantly the anabolic phase of gammaglobulin metabolism.

A method demonstrated by R. Baumal and I. Broder (*Toronto*) for studying soluble antigen-antibody complexes in sera would seem to have many possible applications. Soluble antigen-antibody complexes may be separated from serum by passage of the serum through Sephadex G-200. These complexes can be assayed by an isolated perfused guinea-pig lung technique and the sensitivity of the method should permit application to clinical problems.

Lysozomes and their place in the inflammatory action were outlined by W. B. Chodirker (*Rochester, N.Y.*, and *Toronto*). The recent report that streptolysins will disrupt lysozomes and also cause a chronic type of arthritis in rabbits when repeatedly injected intra-articularly was provocative. The possible roles of polymorphonuclear leucocytes, their granules and lysozomal enzymes in the inflammatory action were further amplified by H. Z. Movat and colleagues (*Toronto*). M. F. Glynn, J. F. Mustard and colleagues (*Toronto*) discussed the importance of platelets and suggested that platelet aggregation with the release of certain platelet factors was of importance in causing increased capillary permeability and other vascular phenomena of the inflammatory response.

A. Lussier (*Montreal*) described further experiments, based on Hollander's original observations, to support the concept that the phagocytosis of complexes of 7S gammaglobulin and rheumatoid factor might be the event initiating the inflammatory process in the synovial cavity. The intra-articular injection of autologous 7S gammaglobulin resulted in an inflammatory reaction in five of six trials in rheumatoid subjects. The injection of homologous gammaglobulin or non-rheumatoid autologous gammaglobulin did not result in an inflammation. Further work along these lines might demonstrate how the immune reaction of the rheumatoid process leads to inflammation.

D. K. Ford (*Vancouver*) described repeated failures to demonstrate a viral or mycoplasmal aetiology for Reiter's syndrome and rheumatoid arthritis. He described the main characteristics of the microbiological species, Mycoplasma and noted that seven distinct strains could be isolated from humans. He presented evidence that the T-strain of Shepard was probably a main cause of non-gonococcal urethritis but currently no evidence related this or other strains to Reiter's syndrome. Specifically a recent claim that mycoplasmas were isolatable from joint fluid of patients suffering from rheumatoid arthritis, Reiter's syndrome, and systemic erythematosus by blind passage through tissue culture was not yet supported.

J. B. Houpt and colleagues (*Toronto*) discussed tryptophan metabolism; 3-hydroxyanthranilic acid, hydroxy-kynurenine, and zanthurenic acid excretion were studied in the urine. Metabolic studies were performed on two patients with rheumatoid arthritis while they took low tryptophan diets.

An electron microscopic study of the skin lesions of experimental delayed hypersensitivity to ovalbumin was described by J. C. Wyllie (*Kingston*). The

breakage of tolerance to autologous hepatocellular antigens in rats was induced by the repeated immunization with homologous or heterologous liver by A. U. Sargent and colleagues (*Montreal*). Runt disease was produced in 200 newborn mice by K. Arakawa and J. W. Steiner (*Toronto*); the livers of the runted animals became enlarged and showed necrosis, but no lymphoid infiltration was found in the region of dead or dying liver cells. The authors therefore doubted that lymphocytes were responsible for this lesion of the runting syndrome. Complement was investigated by C. K. Osterland (*Winnipeg, St. Louis*) and H. J. Müller-Eberhard (*St. Louis*) and the eight distinct components of complement were described. Cell membrane damage was observed only after the seventh stage of the serial 7-stage reaction had occurred.

C. S. Hanes (*Toronto*) reviewed the biochemistry, of connective tissues and R. A. Anwar and R. G. Donovan, gave papers on Elastin.

Elastin was also discussed by D. P. Thornhill and F. S. LaBella (*Winnipeg*). Bovine maxillary mucin (R. Lawford and H. Schachter, *Toronto*) and plasma seromucoid and haptoglobin levels of rats (M. Maung and colleagues, *Toronto*) were also discussed.

Pulmonary fibrosis was found in four of 44 rheumatoid patients by Soon Ok Kim and colleagues (*Montreal*); 20 per cent. of the 44 patients, however, had some decrease in maximal ventilatory volume or expiratory flow rate. Only two of the four patients with pulmonary fibrosis had serum intermediate complexes sedimenting between S9 and S13, and there was no good correlation with the level of rheumatoid factor or serum gammaglobulin. C. A. Gordon and J. F. L. Woodbury (*Halifax*) had seen thirteen rheumatoid patients who suffered from pulmonary disease. Both pleural and parenchymal lesions, including parenchymal nodules, were found, and both cavitation and calcification in the absence of pulmonary tuberculosis were demonstrated.

The anti-inflammatory activity of alkoxyglycerols, particularly batyl and selachyl alcohols, was studied in rats by R. G. Burford and C. W. Gowdey (*London, Toronto*) and effects comparable to acetylsalicylic acid and phenylbutazone were obtained by some of the methods employed for measuring anti-inflammatory activity. During the discussion of this paper, however, two groups reported that there was no significant clinical response to selachyl alcohol in patients with rheumatoid arthritis. Some effects of intravenous EDTA in rheumatoid arthritis were discussed by L. Leipzig and colleagues (Detroit). Abnormalities in liver function tests and the appearance of cholestatic jaundice were noted in rheumatoid patients given Norethynodrel (Envoid) at a dose of 30 mg. per day (R. Demers and others, *Montreal*). Radioactive gold (AU^{198}) was used in the treatment of fifty patients with persistent knee effusions of varying aetiology (J. R. Topp and colleagues, *Toronto*); it was thought that in some of the cases improvement could be related to the treatment. The effect of short-term glucocorticoid administration on pituitary-adrenal function was studied by E. J. Pinter and colleagues (*Montreal*).

Two papers discussed rehabilitational methods. An ischial weight-bearing brace (C. M. Godfrey, *Toronto*) seemed to have potential value for those with persistent active arthritis of the knee. L. H. Truelove (*Winnipeg*) described group methods for handling patients with arthritis in the Manitoba Rehabilitation Hospital.

NEW YORK RHEUMATISM ASSOCIATION

At the Annual Meeting of the New York Rheumatism Association held on April 6, 1965, the following officers were elected: *President:* Dr. Charles L. Christian, *President-Elect:* Dr. David Hamerman, *Vice-President:* Dr. Jerome Simson, *Secretary-Treasurer:* Dr. Arthur I. Snyder.

EUROPEAN LEAGUE AGAINST RHEUMATISM

The delegates of the European League against Rheumatism will meet on October 3, 1965, at 4 p.m. in the Kurhaus in Baden-Baden, Germany. A Symposium prepared by the German Branch of the European League against Rheumatism will be held in Baden-Baden on October 4 and 5, 1965.