EMPIRE RHEUMATISM COUNCIL

EIGHTEENTH ANNUAL REPORT

The eighteenth annual report of the Empire Rheumatism Council was presented by the Chairman, Dr. W. S. C. Copeman, at the Annual General Meeting held on April 27, 1955, at the Royal College of Surgeons.

The Chairman first recorded with regret the loss of a most distinguished colleague, Dr. Frank D. Howitt, whose wise and able guidance would be sadly missed, and of the Rev. H. Heberden, a direct descendant of Dr. W. Heberden, the distinguished 18th-century physician, after whom the Heberden Society is named.

During the year under review a further meeting had taken place with the Minister of Health to amplify what had previously been presented by the E.R.C. Deputation. The Council's views had been favourably received and the Minister had promised that, in the new Ministry Circular regarding senior appointments, Rheumatology would be considered as a subject in which a senior medical registrar could be employed during his training. This was considered an important step towards the ultimate recognition of Rheumatology as a medical specialty.

The Rheumatism Research Centre in the University of Manchester had been started in 1947 as an experimental ten-year scheme financed by the Nuffield Foundation; the Empire Rheumatism Council's action in financing the establishment of a Chair of Rheumatology in the University of Manchester had been largely instrumental in transforming the original experimental scheme to an established department within the university. During 1954 the Nuffield Foundation had offered the university a further grant of £70,000 to develop research in rheumatism, so providing the professor with the assured support of a well-endowed department.

Research.—Since the departure of Dr. A. A. Henly, the laboratory at the Hospital of St. John and St. Elizabeth had not remained idle, but had been used for follow-up work by Miss I. H. M. Muir, one of the Empire Rheumatism Council Fellows, new equipment and apparatus having been installed.

The following reports had been received from the E.R.C. Fellows:

(1) From Dr. Norymberski, Director of Medical Research within the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases:

"Dr. J. K. Norymberski, Miss J. I. Appleby, Mr. G. Gibson, Dr. Jean McKenna, Mr. R. D. Stubbs, and Dr. G. F. Woods, have carried out the following work at the Chemical Research Laboratory of the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases. "The methodology of steroid analysis has received further attention. The combination of reductive and oxidative operations performed on the analytical sample (e.g. urine or urine extract) was found to provide a simple means of:

(i) estimating all 17-hydroxycorticosteroids (17-OH CS);
(ii) selectively estimating 21-deoxy-17-hydroxy-20-oxosteroids;
(iii) partially characterizing or, in some cases, identifying individual 17-OH CS.

"The determination of 21-deoxy-17-hydroxy-20-oxosteroids in the urine disclosed a certain type of adrenocortical dysfunction which was found in the adrenogenital syndrome, but, contrary to previous indications, not in rheumatoid arthritis. "Work was continued on the chemistry of steroid sulphates. Conditions were found for the solvolytic fission of such compounds. Methyl esters of steroid sulphates were prepared and this new and interesting class of compounds was studied in some detail. Synthetic work was commenced with the aim to prepare new derivatives of steroid hormones and to test their biologic activity."

(2) From Prof. A. W. Pickering, Director of the Medical Unit at St. Mary's Hospital, Paddington:

"Miss I. H. M. Muir's work in the past year has been devoted to the study of connective tissue polysaccharides; firstly, because relatively little is known about their structure in normal and diseased states, and, secondly, because recent isotopic work has shown that their turnover rates are very much higher than that of the collagen of the same tissues. It therefore seems a possibility worth investigating that it is the metabolism of polysaccharides that is deranged in connective tissue diseases. Work was therefore undertaken on the following lines:

(i) Assay of Glyco-sulphatose.—An accurate and, possible, rapid method of assay would allow such an enzyme to be identified and its distribution in normal and diseased tissues to be determined. The assay depends on the estimation of inorganic sulphate in tissue homogenates. A method that will estimate 5-25 µg. has been developed. The activity of cells free homogenates, so far assayed, is small, when pure chondroitin sulphate or heparin were used as substrates.

(ii) Improved Methods of preparing and identifying Acidic Polysaccharides.—

(a) Nearly all current methods of preparing acidic polysaccharides cause some degree of depolymerization because contaminating protein is extremely difficult to remove. An improved method of preparing chondroitin sulphate, heparin and hyaluronic acid has been found, which makes use of their insoluble salts with basic dyes. These can more easily be freed of contaminating protein.

(b) Acidic polysaccharides have been identified after
paper electrophoresis or chromatography by staining with metachromatic dyes. A method which greatly increases the sensitivity of their stain has been found, so that 0.5 µg. can be detected on paper.

(iii) Investigation of the Structure of Undegraded Chondroitin Sulphate—The difficulty of obtaining undegraded polysaccharides from connective tissue has so far prevented much investigation of their structure. Depolymerization of polysaccharides, which is a facile and irreversible process, may account for some of the physical changes of diseased connective tissue. The depolymerization, homogeneity, and composition of chondroitin sulphate of high molecular weight is being investigated. Preliminary work has shown that it may not be a simple polymer of the degraded material, and that in the tissues at least part of the chondroitin sulphate may be combined with peptide or protein. It has been found that the quantity of chondroitin sulphate which can be extracted from cartilage after very careful digestion with papain is at least five times greater than that obtained by methods which do not break down protein to any great extent. This material has a very low viscosity and therefore a relatively small molecular weight. It is only partially precipitated by cobraic hexamene chloride which precipitates high molecular weight chondroitin sulphate quantitatively from dilute solutions. The effect of purified papain on cartilage and on highly polymerized chondroitin sulphate is being investigated.

Through the generosity of Geigy Pharmaceutical Co. Ltd., it had been possible to found a “Geigy Travelling Fund” to finance travelling fellowships for (a) senior medical graduates interested in rheumatism, for short periods, and (b) relatively junior men or women (e.g., of registrar or senior registrar level, but not excluding non-medically qualified personnel) for a minimum travelling period of nine months with a maximum of one year. The conditions governing these Fellowships had been based upon those of the Medical Research Council.

The first Geigy Travelling Fellow to be appointed was Dr. Malcolm Thompson of the Rheumatic Unit, Northern General Hospital, Edinburgh, who would be leaving for the U.S.A. in November next, to continue his studies in America under Prof. Walter Bauer at the Massachusetts General Hospital and Harvard Medical School, Boston.

A second fellowship has been awarded to Dr. J. Sharp, Lecturer in Rheumatic Diseases, Manchester University, who will visit the U.S.A. for a period of eight or nine months commencing in the spring of 1956, to study certain aspects of ankylosing spondylitis in New York, possibly under Dr. R. Freyberg.

A third fellowship has been awarded to Dr. J. Ball, also of Manchester University Rheumatism Research Centre, for a three-months’ educational tour in the United States to enable him to visit leading educational institutions there during 1955.

The council had decided to continue to support Dr. E. Wittkower, Assistant Professor of Psychiatry in McGill University, Canada, in his “Study of Rheumatoid Arthritis in Two Contrasting Communities”. This study had been planned to investigate the reciprocal relationships between the rheumatic patient and his illness and between the patient and his social environment, as the disease ran its course over a period of years.

The nine selected centres in England and Scotland had continued the therapeutic trial of cortisone acetate and aspirin in cases of established rheumatoid arthritis of all grades of severity. Although the results of the first year’s treatment were not yet fully analysed, a preliminary analysis made in 1954 showed that there was little obvious difference between the two methods over a period of one year. This conclusion might not be valid for the analysis of the whole series which was expected to be presented at a meeting of the Heberden Society with an analysis of the concurrent x-ray changes.

In the hydrocortone trials referred to in the last report, which had been carried out at ten selected centres in England and Scotland, there was unanimity of opinion that some patients appeared to respond well, and others not at all; that a good effect was perhaps more commonly seen in rheumatoid arthritis than in osteo-arthritis or soft tissue lesions; but that relapses after treatment were also very common.

Dr. Margaret Holroyde had been conducting a small-scale survey to determine the number of patients with various types of rheumatic disease referred to a typical physiotherapy department of a suburban hospital, serving a fairly well-defined light industrial and semi-rural area. It had been found that 78 per cent. of patients had been referred because of their rheumatism. Just under one-quarter of them had rheumatoid arthritis (152 new cases occurring in the year) and one-third had osteo-arthritis, most of the latter being “middle-aged housewives”.

These detailed figures provided valuable factual data for the Regional Hospital Board authorities in planning the long-term investigation and treatment of this group of diseases.

Certificates of good order had been received in all instances where equipment and apparatus had been purchased by the council for various rheumatism centres out of the Hormonal Research Equipment Fund.

In view of the importance of the American Rheumatism Association Meeting, held in California in June, 1954, the council had sent Dr. H. F. West, of Sheffield University, as a delegate. In addition to reporting on the M.R.C. trials, Dr. West had also given a resumé of the long-term cortisone-aspirin trials.

Education.—The Education Sub-committee of the Scientific Co-ordinating Committee had met regularly, under its chairman, Dr. W. S. Tegner. The report of the Royal College of Physicians’ Committee on Chronic Rheumatic Diseases had been fully discussed. Reports received from selected Regional Hospital Boards on facilities, or lack thereof, for treatment, diagnosis, and research were condensed into a concise tabulated statement, which was circulated to professors of medicine, senior administrative medical officers of Regional Hospital Boards, and to directors and deans of postgraduate schools. It was felt that the furnishing of such information to these officials might help to emphasize the need for the inauguration or increase of such facilities.

From this information there had emerged a discussion on specialist training in rheumatism, and the sub-committee had agreed that it was desirable to define clearly the council’s policy in this respect. It was affirmed that the registrar level was not a suitable stage
for specializing in rheumatism; that such specialized training should not commence until the senior registrar level, or above; that it would be more satisfactory if junior posts in rheumatism were annual, and senior house officers appointed for two-year periods at registrar level; and that it would be most valuable to have some form of orthopaedic training at senior house surgeon's level by an interchange in centres with both orthopaedic and rheumatic units.

Over 15,000 free copies of a handbook on rheumatoid arthritis has been distributed. It was not designed for issue direct to patients, but for general practitioners who might pass them to patients at their discretion. Five impressions had been printed and bulk quantities had been supplied to the Northern Ireland General Health Services Board, America, the New Zealand Rheumatism Council and Grey Hospital, the West Indies, and even beyond the "iron curtain". Permission had been granted to a health education journal in Yugoslavia to translate the text for local reproduction. Further copies would gladly be supplied gratis, on application to the General Secretary of the E.R.C.

The popularity of this Rheumatoid Arthritis Handbook had led to the planning of a pictorial handbook for patients suffering from osteo-arthritis.

It had been felt that it might be advantageous to organize refresher courses at consultant level, and Sir Francis Fraser (Director of the British Post-Graduate Medical Federation) had agreed that such a course should be held under the aegis of the University of London; the first Consultants' Three-day Lecture Course had already been held at the Middlesex Hospital.

The Heberden Society had arranged a comprehensive series of educational lectures and demonstrations.

To stimulate interest in the rheumatic field, the Council had made an annual grant of £25 each to the libraries of the British Medical Association and the Royal Society of Medicine, for the purchase of books on rheumatism, arthritis, etc. Suitable book-plates had been inserted in all books so purchased, indicating their source.

The *Annals of the Rheumatic Diseases* continued to be the official medium through which the activities of the Empire Rheumatism Council, the Heberden Society, the British Branch of the European League against Rheumatism, and kindred organizations in Europe and America, were published for the benefit of those interested in the field of rheumatology throughout the world.

During the year, Dr. C. W. Buckley had retired from the post of chief editor of the *Annals of the Rheumatic Diseases*, in which capacity he had served since the foundation of the Journal in 1936. The Chairman had felt proud to be elected to succeed him as editor, and had been encouraged to accept this onerous office in the knowledge that his burden would be eased by the cooperation of Dr. Oswald Savage as assistant editor, and of a hard-working and learned editorial committee.

Correspondence had taken place during the year with leading American rheumatologists regarding the possibility of the foundation of a rheumatism journal in the U.S.A. No definite decision had been arrived at.

*Commonwealth.*—Close collaboration had been maintained with the council's affiliated branches, and vigorous steps were being taken to stimulate teaching, research, and treatment.

Dr. J. E. Grant had been nominated by the Canadian Arthritis and Rheumatism Council to serve on the Scientific Co-ordinating Committee and Commonwealth Sub-Committee, as their liaison officer. Dr. Watson, the Australian representative, had been recalled to Australia, and the loss of the benefit of his valuable advice was much regretted.

The Chairman had accepted invitations from the Australian Rheumatism Council and the University of Sydney, and from the New Zealand Rheumatism Council and the New Zealand Ministry of Health to attend their Annual General Meetings in the autumn of 1955.

*Funds.*—The past year had been characterized by an all-out effort to increase finances, and the generous contributions of many friends and supporters had made possible the significant developments reported. Special appeal to industry had been launched at a dinner at the Mansion House on October 13, by kind permission of the Lord Mayor (the Rt. Hon. Sir Noel Bowater, Bt.), and the occasion had been graced by the presence of the President, H.R.H. the Duke of Gloucester. A very generous response to this appeal had been received, and funds had also been raised by a B.B.C. Sunday evening appeal, and a film premiere at the London Casino, by courtesy of the Variety Club of Great Britain.

**REPORT OF THE WILLIAM MARSDEN TRAVELLING PROFESSOR, 1953-54**

This tour started in August, 1953, and ended in September, 1954.

Starting with the Eighth International Congress of Rheumatic Diseases, held at Geneva in August, 1953, the tour went through Zürich and Berne, continued in Paris, the Netherlands, Copenhagen, Malmö, Stockholm, and Uppsala, and reached the U.S.A. in March, 1954.

*Europe.*—A most friendly and hospitable welcome was received in all of the countries mentioned. I was particularly struck by connective tissue research and by research into the mode of action of the adrenocortical and pituitary hormones. Rehabilitation is taking a more important place than was the case a few years ago. A point of special interest was the university work in Paris, Amsterdam, Copenhagen, and Sweden. It was difficult to pick out one particular aspect, but perhaps Tashum's work in Copenhagen on amyloidosis and Asboe-Hansen's work on mast cells were outstanding. During the European tour I gave two papers to the International Congress on viscosity of synovial fluid and...
electrophoresis of serum proteins in rheumatoid arthritis. In addition I gave lectures to the University of Lund and to the Dutch and Swedish medical societies.

United States.—Here I visited centres in New York, Boston, Philadelphia, St. Louis, the Mayo Clinic, Chicago, Ann Arbor, Cleveland, Washington, San Francisco, and Vancouver, B.C., and gave eight lectures. Perhaps Ann Arbor was the most interesting centre, but I also saw much good work in New York and Chicago.

In San Francisco I gave a talk to the American Rheumatism Association. Finally I visited the University of Vancouver.

A tour of this sort gives the opportunity of seeing many different points of view and many different ways of tackling the same problems. I am grateful to the Board of Governors and the Endowment Fund Sub-Committee of the Royal Free Hospital.

ERNEST FLETCHER.

CONSULTANTS COURSE ON MODERN ASPECTS OF RHEUMATIC DISEASE

This course, which was held on March 24 to 26, 1955, at the Middlesex Hospital and the Postgraduate Medical School of London, was attended by fifty consultants. The opening address by Sir Francis Fraser was followed by a series of papers and discussions:

Prof. J. H. Kellgren: Differential diagnosis of polyarthritis.
Prof. D. H. Collins: Pathology of rheumatoid arthritis.
Dr. E. G. L. Bywaters: Rheumatoid arthritis and its variants.
Dr. J. J. R. Duthie: Anaemia and rheumatoid arthritis.
Dr. O. Savage, Dr. J. J. R. Duthie, and Dr. H. F. West: Cortisone and ACTH in rheumatoid arthritis.
Dr. Ifor Williams: Recent advances in the radiology of rheumatoid arthritis.
Panel discussion on the management of the rheumatoid arthritic, conducted by Prof. Kellgren, Dr. Tegner, and Dr. Duthie.
Dr. F. Dudley Hart: Ankylosing spondylitis.
Dr. J. Sharp: Atypical ankylosing spondylitis.
Dr. R. M. Mason: Uric acid and acute gout.
Dr. F. G. W. Marson: Treatment of chronic gout.
Prof. J. H. Kellgren: Clinical syndromes of osteoarthritis.
Mr. M. H. M. Harrison and Mr. G. C. Lloyd-Roberts: Discussion on osteoarthritis.
Panel discussion conducted by Prof. Hartfall, Dr. Kersley, Dr. Harrison, Dr. West, Mr. Lloyd-Roberts, and Mr. W. D. Coltart.
Series of demonstrations and discussions on the Use and Interpretation of Serological Tests in the Rheumatic Diseases.
Clinico-pathological conference conducted by Dr. Fearnley, Dr. Gilliland, Dr. E. G. L. Bywaters, and Dr. M. H. M. Harrison.

HEBERDEN SOCIETY

At a Clinical Meeting held at the Royal Free Hospital, London, on February 18, 1955, the following papers were given:

DR. J. H. JACOBS (Royal Free Hospital): Studies on Hyaluronic Acid of Synovial Fluid.

By means of exact viscosity studies (Scott, Blair, and others, Biochem. J., 1954, 56, 504), a comparison was made between the degree of polymerization occurring in the synovial hyaluronic acid in cases of rheumatoid arthritis and non-generalized osteoarthritis.

Two different aspects of molecular complexity were investigated as measured by anomalous viscosity and limiting viscosity. From the results of such measurements, it appeared that there were no essential differences between these two aspects of molecular structure in the synovial hyaluronic acid of rheumatoid arthritis and osteoarthritis.

A significant difference was found in the specific viscosity of synovial fluids in the two conditions, but this could be accounted for by the higher concentration of hyaluronic acid found in osteoarthritis, and it was unnecessary, therefore, to assume different degrees of polymerization to account for this difference in specific viscosities.

DR. F. CLIFFORD ROSE (Royal Free Hospital): Masked Pneumonia occurring during Cortisone Therapy.

This paper reported three deaths from pneumonia in patients under treatment with cortisone or ACTH. In all cases the mode of onset of the pneumonia was unusual and the relationship between the physical signs and the clinical duration of the disease atypical. The pathological findings in the adrenals could be correlated with the hormone therapy received. In one, who had received continuous cortisone for 6 weeks before death, there was evidence of atrophy and conspicuous degenerative changes and haemorrhage in all three zones of the cortex. In spite of the possible enhancing effect of cortisone on invasion by organism, the drug should not be stopped on the diagnosis of infection, as such patients when undergoing extra stress, may develop a relative hypo-adrenal state and therefore require a higher dosage of cortisone.