Ann. rheum. Dis. (1965), 24, 174

HEBERDEN SOCIETY

ANNUAL REPORT, 1964

At the Annual General Meeting held on December 4, 1964, the President, Prof. E. G. L. Bywaters, was in the Chair.

Prof. J. Goslings and Dr. E. Lewis-Faning were unanimously elected Honorary Members.

The following new members were elected:

Ordinary Members (from Associate Members):
Dr. J. N. McCormick, (from Dr. Cosh, Dr. E. Sever, Mr. D. R. Sweetnam, Dr. M. Wilkinson, Dr. D. P. Page Thomas, Dr. Joan M. Brenner.

Associate Members: Dr. M. McMahon, Dr. E. N. Coomes, Dr. S. D. Roberts, Dr. J. H. Bayliss, Dr. P. Boardman, Dr. D. Burley.

Overseas Members: Prof. B. Cruickshank, Dr. G. Bencze, Dr. H. E. Jasmin.

Continental Members: Dr. J. J. Bode. Dr. F. Françon, Dr. W. H. de Haas.

Temporary Visitor Members: Dr. P. Blasco-Marín (Buxton), Dr. B. A. Castillo (Postgraduate Medical School), Dr. El Sahib (Postgraduate Medical School), Dr. M. T. Espiritu (Postgraduate Medical School), Dr. J. Franks (Postgraduate Medical School), Dr. C. Fürst (Taplow), Dr. J. Kenney (University College), Dr. D. Palmer (Postgraduate Medical School), Dr. H. Roth (Manchester), Dr. J. E. Seegmiller (University College Hospital), Dr. B. Tait (St. Stephen's Hospital, London).

The President recorded with regret the deaths of Sir Francis Fraser, an Honorary Member of the Society, and of Prof. Douglas Collins, a former Member.

Activities
The first Clinical Meeting of the year was held on April 24, at the Wolfson Institute, Postgraduate Medical School (Annals, 23, 505). Papers were presented by Drs. J. S. Lawrence and J. M. Brenner (Manchester), Drs. W. H. de Haas, M. J. Kingma, and F. Drucker (Amsterdam), Dr. T. M. Chalmers (Edinburgh), Drs. R. Gandy, M. Smith, and R. Consden (Taplow), Drs. D. E. Caughhey, B. M. Ansell, Prof. E. G. L. Bywaters, and Dr. C. A. Reading (Taplow), Drs. A. Hall, V. P. Holloway, and J. T. Scott (Hammersmith), and Drs. A. J. Popert, J. Sharp, S. M. Laird, and A. J. Gill (Manchester). Demonstrations were presented by Dr. G. Harris (Postgraduate Medical School), Drs. G. Loewi, B. M. Ansell, and Prof. E. G. L. Bywaters (Taplow), Drs. J. E. Scott and J. Dorling (Taplow), Profs. E. G. L. Bywaters and D. V. Davies (Taplow and St. Thomas's), Drs. E. J. Holborow and G. D. Johnson (Taplow), Drs. L. E. Glynn and J. M. Phillips (Taplow), Dr. A Howard (Taplow), Drs. G. Loewi and J. Dorling (Taplow), Drs. V. P. Holloway, F. M. McCallum, and J. T. Scott (Postgraduate Medical School), Drs. A. Hall, and J. T. Scott (Postgraduate Medical School), Drs. P. Bennett and J. T. Scott (Postgraduate Medical School), Dr. G. D. Johnson (Taplow), Dr. D. J. Ward (Taplow).

The Heberden Round was conducted by Prof. G. A. Smart and Dr. Malcolm Thompson at the Royal Victoria Infirmary, Newcastle upon Tyne, on June 5 (Annals, 24, 175). Papers were presented by Drs. P. N. Robson and P. J. van Miert (Newcastle), Drs. M. Thompson and G. L. Leathart (Newcastle), Dr. J. S. Percy (Newcastle), Drs. M. Thompson, J. R. G. Edwards, and A. J. Watson (Newcastle), Drs. M. Thompson and J. S. Percy (Newcastle), Drs. L. P. J. Holt and C. F. Hawkins (Birmingham), Drs. F. Dudley Hart and P. L. Boardman (Westminster), and Drs. A. St. J. Dixon and J. Wanka (Chelsea and Kensington).

A most interesting and enjoyable combined meeting of the Heberden Society and the Belgian Branch of the International League against Rheumatism was held in Brussels on October 3 (Annals, 24, 176). Papers were presented by Prof. L. Michotte and Dr. Van Bogaert (Brussels), Dr. R. François (Louvain), Dr. J. Vanslype (Antwerp), Dr. J. A. Cosh (Bath), Drs. J. Wanka and A. St. J. Dixon (London), Dr. G. Bencze (Taplow and Szeged), Dr. G. Blanshard (London), and Dr. F. M. Andrews (Stoke Mandeville).

The Heberden Oration for 1964 was delivered by Dr. Morris Ziff on December 4, at the Wellcome Foundation, London. He took as his subject “Immunopathologic Aspects of Connective Tissue Inflammation” (Annals, 24, 103).

The Annual Dinner was held on December 4, 1964, in the new Royal College of Physicians. Among the guests
present were the Minister of Health (The Rt. Hon. Kenneth Robinson, M.P.) Dr. Ziff, Prof. and Mrs. McMichael, and Sir Charles and Lady Dodds.

The Annual General Meeting was held on December 4 and 5, at the Wellcome Foundation. The clinical meeting is reported below (Annals, 24, 178).

Grant-in-Aid

The Society acknowledged with appreciation the renewal of a grant from the Arthritis and Rheumatism Council.

Annals of the Rheumatic Diseases

Full reports of the Society’s activities had appeared regularly in the Annals of the Rheumatic Diseases. The Society was indebted to the Editors for their continued co-operation in furthering the work of the Society.

Library

The Honorary Librarian, Dr. W. S. C. Copeman, reported that the Library, which had been housed in the Apothecaries’ Hall during the past few years by the courtesy of the Faculty of the History of Medicine and Pharmacy, had been removed to the “Heberden Room” in the new building of the Royal College of Physicians in Regent’s Park. The Librarian of the College, Mr. L. M. Payne, had generously offered to undertake the general custody of the collection. Dr. F. N. L. Poynter, Director of the Wellcome Historical Museum, had also promised to continue the help, advice, and maintenance of the books, for which the library had been indebted to him for the past 6 years.

The library would now be more easily available to members, and it was hoped that members would continue to present books, manuscripts, prints, and other material concerned with the historical aspects of rheumatology.

After the Annual Dinner held in the College, a selection of “Heberdeniana” and of books from the library were displayed by the Hon. Librarian and Mr. Payne, and aroused considerable interest amongst the guests.

The following additions had been made to the library:

- Proposal for establishment in Edinburgh of a newly improved apparatus ... in the cure of rheumatism. (1820). (Rebound by courtesy of Wellcome Foundation.)

OFFICERS, 1965

President:
Prof. E. G. L. Bywaters, F.R.C.P.,
Postgraduate Medical School of London, Hammersmith Hospital, Ducane Road, London, W.12.

President-Elect:
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Junior Hon. Secretary:
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Hon. Auditor:
Wilfrid G. Wilks, Esq., F.C.C.S., F.R.Econ.S.

General Secretary:
M. C. G. Andrews
Faraday House, 8-10 Charing Cross Road, London, W.C.2.

PROGRAMME FOR 1965

Clinical Meeting at the Wellcome Foundation, London, on February 26.

Clinical and Laboratory Meeting at the Canadian Red Cross Memorial Hospital, Taplow, Maidenhead, Berks., on April 3.

Heberden Round at the Devonshire Royal Hospital, Buxton, by invitation of Dr. J. Sharp on June 25 and 26.

Heberden Oration, Annual General Meeting, and Dinner on November 12 and 13.

Titles and short programme notes of original communications which Members wish to make to the Society during 1965 should be sent to the Senior Hon. Secretary (Dr. J. T. Scott, Postgraduate Medical School of London, Hammersmith Hospital, W.12) at least one month before the date of the meeting. Abstracts for publication in the Annals of the Rheumatic Diseases (approximately 300 words) should be sent in advance or handed to the Secretary at the Meeting. Additional meetings will be arranged if necessary.
Heberden Round, 1964

This was given at the Royal Victoria Infirmary, Newcastle-on-Tyne, by Prof. G. A. Smart on June 5, 1964. He presented eight patients who showed various combinations of auto-immune diseases, and discussed the inter-relationships of rheumatoid arthritis, thyroiditis, systemic lupus, Sjögren's syndrome, hepatitis, and myositis.

The following papers were also given:

Use of Cobalt 60 in Osteo-arthritis of the Hip. By P. N. ROBSON and P. J. VAN MIERT (Newcastle): One of the most serious problems with osteo-arthritis of the hip is that only a very limited proportion of cases can be helped by surgery, because of the age and general unfitness of many of these patients. This paper reports a method which does not involve major surgery but has given successful pain relief. The work of Truea and his colleagues demonstrated that in osteo-arthritis there was a considerable increase in the blood supply to the femoral head in many cases and suggested that increased tension in the femoral head might account for some of the features of arthritic pain. Experimental work was carried out by injecting fluid under slight pressure into the femoral head in arthritic subjects, which reproduced the pain which they normally associated with their arthritic hips. This report is of the first hundred cases treated by interstitial gamma irradiation with a Cobalt 60 source, in an attempt to decrease the blood supply and relieve tension pain in the femoral head. The patients have now been followed for 5 years and upwards and satisfactory pain relief has occurred in approximately two-thirds of them. The work has reduced greatly the number of patients requiring major hip surgery for their arthritic condition, and it has enabled us to extend relief to many patients who could not otherwise be helped. The operation of Cobalt implant is less than Smith Petersen pinning. A short film was shown to illustrate the operative technique.

Discussion.—Mr. ROBSON agreed with DR. SAVAGE that a control series would have been useful in a study of this sort. Such an investigation was now being carried out, although he considered that osteo-arthritis usually ran a progressive course if the patient lived long enough.

PROF. E. G. L. BYWATERS asked how quickly pain relief occurred and Mr. Robson replied that relief was either immediate or delayed for some weeks. Sometimes indeed, there was an initial exacerbation.

Chronic Diffuse Pulmonary Infiltration complicating Rheumatoid Arthritis. By M. THOMPSON and G. L. LEATHART (Newcastle): Chronic diffuse interstitial fibrosis is a rare pulmonary disorder. While the majority of cases are idiopathic in origin, a significant proportion have been reported in patients suffering from rheumatoid arthritis. Previous descriptions of this association have been restricted to isolated case reports or short series, and the condition was now reviewed with the addition of a further twelve cases. The clinical features, radiological findings, course, prognosis and response to treatment were discussed. An account was also given of the histological findings in three patients and of the results of tests of pulmonary function.

Discussion.—In reply to questions, DR. THOMPSON said that there were no other obvious factors such as smoking, occupation or dust which were related to the development of pulmonary fibrosis in this series.

DR. J. T. SCOTT (London) asked about the incidence of peripheral vascular disease and peripheral neuropathy in these patients and Dr. Thompson replied that none showed any evidence of peripheral vascular disease; there was one patient with polyneuritis and one with a diaphragmatic palsy.

PROF. E. G. L. BYWATERS (Taplow) enquired about the relationship between lung histology and compliance. Dr. Leathart replied that one patient had shown pulmonary infiltration with a normal lung compliance. During the period of observation of these patients, he had seen some sixty or eighty other patients with idiopathic pulmonary fibrosis.

Immono-conglutinin in Rheumatoid Arthritis. By J. S. PERCY (Newcastle): Immono-conglutinin (I.K.) is an antibody to adsorbed complement, i.e. to complement which has been consumed in an antigen/antibody reaction. Comombs and his co-workers showed that I.K. is elevated in acute viral infections and also in acute and chronic bacterial infections. They found comparably high levels in rheumatoid arthritis and ankylosing spondylitis. That immono-conglutinin is found in raised titres in patients suffering from rheumatoid arthritis has been confirmed. It has been shown to be correlated with the clinical assessment of the degree of inflammation present, but it does not correlate with other parameters of disease activity. It has also been measured in non-infective conditions involving tissue damage in an effort to exclude the possibility that it is related to this factor rather than to the prime cause of the disease.

Discussion.—There was some discussion about the optimum time for the development of maximum titre of immono-conglutinin.

DR. J. S. LAWRENCE (Manchester) wondered if 3 weeks after trauma or infarction was not too late for the maximum titre.

PROF. E. G. L. BYWATERS (Taplow) questioned whether the injuries were severe enough. Dr. Percy replied that most of them were fractures of large bones, often involving joints. There was no rise in titre in chronic pyelonephritis. There was no correlation between immono-conglutinin and C-reactive protein.

Leg Ulceration in Rheumatoid Arthritis with particular reference to Ulceration complicating Steroid Therapy. By M. THOMPSON, J. R. G. EDWARDS, and A. J. WATSON (Newcastle): Whereas leg ulceration as a specific feature of rheumatoid disease is a rare finding, bruising of the limbs is now a common feature in patients receiving predni-steroid therapy. Such bruising is usually slight...
and scattered but may occasionally become confluent. The occurrence of large haematomata, sometimes associated with ulceration after trivial trauma, is reported. This has been noted in seven patients and the bruising and ulceration have occurred in a characteristic situation overlying the musculo-tendinous junctions of the anterior tibial group of muscles. The reasons for this anatomical location are discussed and the clinical appearances and course are described. The differential diagnosis of prenidi-steroid ulceration from that of other forms of leg ulceration complicating rheumatoid arthritis is discussed.

Discussion.—Several speakers agreed that there were two types of ulcer, namely those due to vascular lesions and those associated with steroid therapy, skin atrophy and trauma.

DR. O. SAVAGE (London) stressed the severe skin atrophy which could occur with steroid treatment and which could make surgery difficult: this did not occur with ACTH therapy.

Symposium on Indomethacin. Indomethacin in the Treatment of Rheumatic Disorders. By M. THOMPSON and J. S. PERCY (Newcastle): Indomethacin is a rapidly acting, non-steroid, anti-inflammatory, and analgesic compound. Its use is described in the treatment of various rheumatic diseases involving:

(a) A pilot trial, employing 100 mg. tablets in a dosage of 300 mg. or 400 mg. daily (23 patients);
(b) A controlled trial, comparing Indomethacin 200 mg. daily (given in divided dosage using 50 mg. tablets) with phenylbutazone 300 mg. daily (24 patients);
(c) Continuous therapy with 50 mg. tablets employing initial low dosage and gradually increasing dosage by 25 mg. or 50 mg. increments (78 patients);
(d) A similar progressive dosage regime using 25 mg. capsules of Indomethacin (43 patients);
(e) 35 patients on the progressive dosage regime (c) with 50 mg. tablets have since been transferred to treatment with capsules.

Subject to limitations imposed by side-effects, Indomethacin has proved to be a useful agent in the rapid control of acute gout, in the relief of severe spondylitic pain, the management of rheumatoid arthritis in certain cases, and the treatment of degenerative joint disease, especially osteo-arthritis of the hips.

Rectal Absorption of Indomethacin: Clinical Effects and Serum Levels. By L. P. J. HOLT (introduced) and C. F. HAWKINS (Birmingham): Reports of adverse gastrointestinal effects from Indomethacin prompted a study of its absorption from the rectum. The levels of Indomethacin in the serum after 100 mg. suppositories were slightly lower than those after the same dose by mouth. DRS. A. ST. J. DIXON and J. WANKA (Chelsea and Kensington) gave a paper in this symposium which has already been published in the Annals (Ann. rheum. Dis.) (1964), 23, 288. They drew particular attention to the lack of therapeutic effect in six cases of psoriatic arthropathy, in contrast to the good results obtained in gout and osteo-arthritis of the hip.

DRS. F. DUDLEY HART and P. BOARDMAN (London) also contributed to this Symposium.

Clinical Meeting.—A meeting was held on October 3, 1964, at Brussels, when the following papers were presented:

Thermography in Rheumatoid Arthritis. By Dr. J. A. COSH (Bath): Thermography is the technique of recording a pictorial image of a warm body by detection of infra-red radiation from that body. The "Pyroscan" is an instrument for this purpose which uses a scanning device and a sensitive cell of Indium antimonide. The scanner reflects an image of the body, line by line, on to the cell, which produces an electrical signal in response to the infra-red radiation received. From this signal a pictorial image is recorded, line by line, the warm areas being shown as white and cooler areas as black.

The use of the "Pyroscan" in the study of patients with rheumatoid arthritis is described. It has an advantage over simple measurements of surface temperature in that it produces, within a minute, a "thermal plan" of a limb or a joint, showing the warmest areas. It is sensitive to differences in surface temperature of less than 0.5° C. Relatively gross inflammation on or near the body surface can be reliably detected and major changes, e.g., in response to treatment, can be recorded. Minor degrees of inflammation are detected with less certainty. Techniques of improving temperature discrimination are being developed by the manufacturers.

Discussion.—In reply to a question by DR. O. SAVAGE (London), DR. COSH said that inflammation could be assessed at an early stage, and that there was no limit to the frequency of readings. In reply to another questioner he said that all the cases had active disease.

Altérations dans la fonction rénale après traitement prolongé avec Indomethacin pour ostéarthrose de la hanche et pour arthrite rhumatoïde. By Dr. J. WANKA and DR. A. ST. J. DIXON (Chelsea and Kensington): Early reports from Norcross and his group drew attention to the deterioration of renal function which followed Indomethacin therapy. Special attention was paid to this aspect of toxicity in patients attending the Chelsea and Kensington Rheumatism Unit.

In two double-blind controlled trials, the first in rheumatoid arthritis on a weekly crossover basis, and the second in osteo-arthritis of the hip on a monthly cross-over basis, no variations were recorded in blood urea and uric acid levels, or in the appearance and protein content of the urine during treatment with Indomethacin which were not also seen in control periods. This was true both in subjects whose blood urea was normal and in those whose blood urea was already raised before treatment. Patients who responded to Indomethacin were therefore given long-term treatment with this drug, and the renal function was assessed as above, but with serial 4-hour creatinine and uric acid clearance studies in addition. Some patients on high doses of Indomethacin showed a tendency to progressive deterioration in creatinine clearance. Other patients, receiving the lower doses of
50-100 mg. of Indomethacin per day which are now customarily employed, did not reveal this tendency.

Discussion.—PROF. L. MICHOTTE (Brussels) drew attention to gastric side-effects during Indomethacin treatment. Fifty cases had been treated daily with 75 mg. Indomethacin and haemorrhage into the gastrointestinal tract had occurred four times, with one fatality. Dr. WANKA replied that, although their patients had received 300 mg., there had only been one case of minor haemorrhage.

Clinical Evaluation of the L.E.-Cell Test. By Dr. G. BENCZE (Szeged, Hungary): Various types of L.E.-cell tests were compared. Zinkham and Conley's rotation method was found the most successful. By avoiding significant morphological changes in cells, the method lessens the incidence of false positives. Sensitivity is increased by use of the patient's own leucocytes. L.E.-cell production was greatly reduced when leucocytes of normal subjects were used. In 5,500 L.E.-cell examinations in 2,000 patients, L.E.-cells were found in systemic lupus erythematosus, in some cases of rheumatoid arthritis, and in some relatives of patients with connective tissue diseases. The possibility of positive L.E.-cells in asymptomatic relatives of systemic lupus erythematosus patients should also be considered as an explanation for "false" positive L.E.-cell tests.

For L.E.-cell tests to be pronounced positive, many typical cells should be found on at least two occasions during repeated tests. Morphological criteria should be strictly observed. One negative test has no diagnostic significance. Other workers have also found pseudo-L.E.-cells, haematoxylin bodies, and (rarely) rosette forms in L.E.-cell positive smears. The presence of the latter forms together or alone but without typical L.E.-cells has no diagnostic significance, but in such cases serial L.E. tests should be made. In some cases, when many pseudo-L.E.-cells have been observed, typical L.E.-cells have been found subsequently.

Osteo-arthritis of the Hip Joint. By Dr. G. BLANSHARD (London): 92 patients with idiopathic osteo-arthritis of the hip seen consecutively at the Arthur Stanley Institute for Rheumatic Diseases, London, were observed for 2 years by the same team of clinician, radiologist, and physiotherapist. The clinical details were analysed, objective measurements of the degree of incapacity made, and the radiological appearances studied. A new simple method of measuring power at the hip joint was developed. An assessment of the natural history of this condition was made and the clinical, radiological, and objective measurements correlated.

Discussion.—PROF. L. MICHOTTE (Brussels): pointed out that differences in the position of the limb when x-rayed could account for apparent differences in the width of the joint space.

Dr. BLANSHARD said that this had been controlled as far as possible, but agreed that it might have produced the varied appearances in some cases. In answer to another questioner he said that the treatment of these patients had consisted of analgesics and physiotherapy only.

Dr. A. G. S. HILL (Stoke Mandeville): asked whether the apparent upward "wandering" of the acetabulum and adduction of the femur, together with a pelvic tilt, had altered the relationships in such a way as to mimic the effect of subtrochanteric osteotomy, in producing an increase in joint space.

MR. G. PLATT (Aylesbury) wondered whether one could find a similarity here to the creeping necrosis seen in Perthes' disease of the hip. He further stated that, if one removed the articular cartilage, an increase in joint space subsequently developed.

PROF. E. G. L. BYWATERS (Taplow) remarked that cysts occurred in the bone by protrusion of tissue from the joint cavity into narrow spaces after loss of hyaline cartilage. Cartilage regeneration often took place with fibro-cartilage deposition and metaplasia, leading to healing of the cyst.

Polymyalgia Rheumatica. By F. M. ANDREWS (Stoke Mandeville): A study of the syndrome called polymyalgia rheumatica is described. In acute cases, despite a greatly raised erythrocyte sedimentation rate no primary muscle disease was found. The disease was associated with a bronchogenic carcinoma in one case and with rheumatoid-like histology in a second. In follow-up cases three examples of peripheral acrosclerosis and a number of cases of sero-negative polyarthritis were found.

Discussion.—DR. A. ST. J. DIXON (Chelsea and Kensington) remarked that, in a series of temporal artery biopsies in cases of polymyalgia, he had found a high incidence of giant cell arteritis. He pointed out that polymyalgia might antedate the temporal arteritis by as much as 18 months.

DR. G. D. KERSLEY (Bath) considered that polymyalgia could still be classed only as a syndrome; he had never seen a patient younger than 50 years.

PROF. E. G. L. BYWATERS (Taplow) wanted to know how long the erythrocyte sedimentation rate had remained raised in these cases.

Dr. ANDREWS replied that, among all cases seen 3 years after onset, only one had a raised erythrocyte sedimentation rate whereas all the acute cases had normal rates 6 months after the start of treatment.

Dr. J. H. GLYN (London) said that in his experience the erythrocyte sedimentation rate could continue to be significantly raised for more than 2 to 3 years after an apparently complete clinical remission. One of his patients who had subsequently assumed the full clinical picture of disseminated lupus erythematosus had originally been diagnosed as a case of benign polymyalgia rheumatica, and had been treated with very small doses of steroids given last thing at night. He wondered if this artificial fluctuation of the level circulating steroids could in any way have been responsible for the dissemination of the disease. Dr. Glyn also asked if griseofulvin was as useful as had been claimed in the treatment of polymyalgia and if so how it worked.

PROF. L. MICHOTTE (Brussels) answered this by stating that Griseofulvin was useless in this condition and that he did not favour the use of steroids either, but preferred gold.

DR. R. J. FRANCOIS (Louvain) questioned the wisdom of using late-evening doses of steroids, since this would tend to inhibit the patient's own nocturnal steroid secretion.
HEBERDEN SOCIETY

but Dr. Andrews and Dr. Hill considered this was unlikely to occur if the dose was small enough.

Microradiographic Study of the Syndesmophytes of Ankylosing Spondylitis and the Normal Sacrum. By Dr. R. J. FRANÇOIS (Louvain): Five dorsal and five lumbar intervertebral disks obtained at the autopsy of a case of ankylosing spondylitis, and three sacrums from control subjects aged 38, 45, and 54 years were studied by micro-radiography. The syndesmophytes of ankylosing spondylitis result from the same calcification and ossification processes as the bony bridges between the sacral vertebrae of normal subjects.

Discussion.— PROF. E. G. L. BYWATERS (Taplow) made the suggestion that, since the processes of calcification and ossification shown were similar to those seen during the normal ageing process, the changes might be due to prolonged immobilization (“muscle splinting”) such as often occurred with painful inflammation in the apophyseal joints. In answer to other comments, Dr. FRANÇOIS said that, in one case, there had been vascularization of disks in all regions, but that he had not examined the joints in any of his own series.

Presence of Rheumatoid Factor (R.F.) in Periarthritis of the Shoulder. By Dr. J. VANSLYPE (Antwerp): In 215 cases of periarthritis of the shoulder, R.F. was found thirteen times (6 per cent.).

Gold therapy was successfully applied; at the same time the R.F. disappeared in four cases (31 per cent.) and diminished in four other cases (31 per cent.), but the treatment did not prevent the appearance of transitory arthritis in four cases (31 per cent.) and lasting arthritis in one case (7 per cent.).

The author compared his figures with the incidence in a population sample of 196 healthy workers, aged from 40 to 75 years, in which R.F. was found in 11·2 per cent. of those examined.

Discussion.— PROF. L. MICHOSTE (Brussels) pointed out that polyarthitis in adults often started in the shoulder and that the term “periarthritis” was misleading since the condition was always present in cases with shoulder involvement. He agreed that arthrography was frequently helpful, but not only in selected cases, as Dr. Vanslype had suggested. In reply to his question about age distribution, he was told that the average age of all the patients in the study was the same as that of the thirteen with rheumatoid arthritis. In answer to another question Dr. Vanslype said that the inhibition test of Ziff (latex modification) had often been positive when other tests for rheumatoid factor had been negative.

Inhibition of Rheumatoid Factor in vivo and in vitro. By L. J. MICHOSTE and PH. VAN BOGAERT (Brussels): Incubation of serum containing rheumatoid factor (R.F.) with 0·1 M penicillamine or cysteine caused a diminution of the haemagglutination titre. Patients were, therefore, given up to 1 g. penicillamine per day, and the R.F. titre was tested by the latex test for 2 months. After 6 weeks there appeared to be a slight, statistically insignificant fall in titre. Various theoretical considerations of effects of agents on disulphide bonds as found in macroglobulins were discussed.

Acute Inflammatory Dislocation of the Atlantoaxial Joint. By H. VAN KERCKHOVE, P. COUTELLIER, and T. VANGYSEL (Hasselt): A case of dislocation of the atlas on the axis of inflammatory origin was described. The authors considered that the various clinical presentations of this lesion had a common characteristic and a common explanation in the existence of arthritis involving the odontoid process and the atlas. This arthritis may be septic, rheumatic, or non-specifically inflammatory. A classification of the different atlanto-axial dislocations was presented.

Clinical Meeting.— At the Annual General Meeting on December 4 and 5, 1964, the following papers were presented:

A Controlled Trial of Intra-articular Thiopeta in Rheumatoid Arthritis*. By H. L. F. CURREY (London).

6-Mercaptourine (6 M.P.) in the treatment of Rheumatoid Arthritis and Related Conditions. By A. B. MYLES (West London Hospital): Chemical suppression of the immune response can sometimes be achieved by cytotoxic drugs. Of the eight cases selected, seven had severe rheumatoid arthritis, either not responding to normal doses of steroids or with a steroid side-effect. Three of these either had a positive A.N.F. or showed the presence of L.E.-cells. Two had evidence of arteritis. One case of systemic lupus erythematosus was included. The intention was to give 6 M.P. in a dose of 2·5 mg. per kg. bodyweight per day for 28 days or until a significant fall in white blood cells occurred, and then to reduce the dose to 1 mg. The criteria for assessment were clinical findings, erythrocyte sedimentation rate, and differential sheep cell agglutination test. All showed some improvement in one or more of these criteria. Toxic effects were common. Six developed anaemia. Five were unable to complete the 28-day course because of anaemia, leucopenia, or thrombocytopenia.

There were two deaths, in both of which leucopenia had developed immediately before. One death was due to septicemia. The immediate cause of the other was not established; the clinical diagnosis of septicemia was not supported either by blood culture or autopsy. When 6 M.P. was stopped or used in the lower dose some cases relapsed. Although it appears that 6 M.P. may have a suppressive effect on rheumatoid disease, it seems that the rheumatoid narrows is unusually sensitive to doses of 6 M.P. which are usually tolerated for long periods in other cases.

Discussion.— DR. J. J. R. DUTHIE (Edinburgh): We have had a brief experience with Imuran, which is said to be less toxic. We suppressed disease activity with ACTH and gave Imuran under this cover for 6 weeks, but withdrawal of ACTH was followed by an exacerbation of symptoms and there seemed to have been no benefit.

DR. V. WRIGHT (Leeds): It may be that there are no published toxic effects of 6 MP in psoriasis, but I have

* This paper and the discussion thereon will be published in full in a future issue of the Annals.
ANNALS OF THE RHEUMATIC DISEASES

seen patients treated like this bleeding and oozing from the psoriatic lesions.

Dr. A. J. POPERT (Droitwich): You mentioned bacterial infection as a complication of steroid-treated rheumatoid arthritis. It would have been more correct to say that it was a complication of rheumatoid arthritis—it is just as common in untreated cases.

Dr. W. A. BOURNE (Brighton): I have treated three patients with severe rheumatoid arthritis with methotrexate, with no obvious effect.

Dr. A. ST. J. DIXON (London): A number of competent observers have described occasional benefits from this sort of therapy. We have tried several patients—of whom one did very well. We gave Melphalan to another in which the result was disappointing despite necrotic changes on synovial biopsy.

These patients present a tremendous problem and two deaths should not deter us. There is need to define a clinical state of malignant rheumatoid arthritis suitable for such treatment, which should be set up as a multi-centre trial.

Steroid Myopathy. By E. N. COOMES (Royal Infirmary, Manchester)*:

Therapeutic Trial of Three Intra-articular Steroid Preparations in Rheumatoid Arthritis. By C. G. BEARDWELL and B. L. J. TREADWELL (West London Hospital):
The preparations used were prednisolone acetate (PA) in a dose of 25 mg., and prednisolone trimethylacetate (PTMA) in doses of 27·6 mg. and 200 mg. The object of the trial was to determine whether the slow-release preparations had any advantage over PA and whether 200 mg. PTMA had any advantage over 27·6 mg.

The subjects were patients with active rheumatoid arthritis of the knees and each patient was his own control, each in turn receiving all three substances in randomized order, using a double-blind technique. Intra-articular injections were given whenever the clinical state justified it, but never at less than weekly intervals. The degree of inflammation of the knee joint was assessed clinically at each attendance and graded from 1 (quiescent) to 4 (severe). Range of movement, degree and duration of pain relief, and number of weeks between each injection were also recorded. It proved impractical to assess improvement by study of synovial fluid.

58 patients were admitted to the trial. Complete records were obtained from forty and, with others partially complete, permitted comparisons between 200 mg. PTMA and 25 mg. PA, between 200 mg. and 27·6 PTMA, and between 25 mg. PA and 27·6 mg. PTMA in the same patients.

Judged by the interval between injections and the duration of pain relief after injection, 200 mg. PTMA was significantly more effective than 25 mg. PA and probably better than 27·6 mg. PTMA, though the difference did not attain statistical significance. There was no significant difference between 25 mg. PA and 27·6 mg. PTMA. Assessment of clinical activity gave similar results, in that 200 mg. PTMA produced significantly greater improvement than either of the other preparations at both 1 and 5 weeks after injection. 27·6 mg. PTMA appeared slightly more effective than 25 mg. PA at 5 weeks after injection, but again statistical significance was not attained. Improvement in range of movement after injection confirmed these results.

Discussion.—Dr. J. H. GLYN (London): This is an important paper if only because of the vast difference in cost of the two preparations assessed. It is possible that, if 200 mg. PA had been used in direct comparison with 200 mg. PTMA, the results would have been about equivalent and the cost decimated—an important point in relation to the vast quantities of these preparations which are now being used. I am not convinced that single, spaced injections of these steroids even in such high dosages are absorbed systemically in quantities liable to produce deleterious clinical effects. I have never encountered such problems despite 15 yrs' experience of giving at least 100 mg. hydrocortisone acetate into the large joints, frequently injecting two or three joints at a time. The risks appear to be more hypothetical than real.

Dr. BEARDWELL: The cost of 50 mg. hydrocortisone is 8d. and that of 50 mg. prednisolone trimethyl acetate 10s. 8d. Several studies have shown a rise in 17-hydroxycorticosteroids after the injection of hydrocortisone into a knee and also an effect on the opposite knee.

Dr. R. M. MASON (London): There are two variables here—dose and substance. I am not clear how a difference can be established between two substances when the doses are different.

Dr. BEARDWELL: We compared equivalent doses of the long-acting and quick-acting preparations and found no significant difference. We then showed the greater effect of 200 mg. prednisolone trimethyl acetate over the lower dose of 27·5 mg.

Dr. A. G. S. HILL (Stoke Mandeville): How did you maintain double-blind conditions? Was the same volume always given?

Dr. BEARDWELL: Yes, doses were made up in the same volume and appeared almost identical though one could sometimes tell which was which because the higher dose was more viscous. Patients and assessors did not know which was given until the end of the trial.

Occurrence of Rheumatoid Factor in Serum of the Aged. By J. J. DE BLECOURT, F. W. BOERMA, and E. O. VORENKAMP (Gröningen): Several workers have suggested that the incidence of rheumatoid factor in patients with rheumatoid arthritis and also in "normal people" increases with age.

Heimer and co-workers (Amer. J. Med., 1963, 352, 175) reported that they found in a group of 121 inhabitants aged 65 to 93 years, in a home for the aged in the city of New York, a positive latex fixation in 42 per cent. and a positive sheep cell agglutination test in 2 per cent. Patients known to be suffering from rheumatoid arthritis were excluded.

We have investigated 195 people in the same age group and found the latex fixation positive in 8 per cent. and sheep cell agglutination test in 8·7 per cent.

100 people were living in an urban home for the aged and 95 in a rural institution. There were no statistically significant differences between the two groups.

* To be published in full in the Annals with Discussion.
We cannot explain the differences between the results of our investigation and that of Heimer (and other authors cited by him) following the same serological techniques.

**Discussion.**—**Prof. E. G. L. Bywaters (Taplow):** What races were involved in Heimer’s study?

**Dr. De Blecourt:** They were all white people.

**Prof. J. H. Kellgren (Manchester):** There are many reports confirming a high incidence of sero-positivity in old age. There are two possible reasons for this: it may be a function of longevity, or it may be a cohort effect, people over 65 having had an experience of disease in childhood or earlier adult life not shared by younger people.

**Prof. Bywaters:** There is a third possibility, that people remaining in homes for the aged are selected survivors.

**Dr. De Blecourt:** We shall have to wait for many years to answer these questions. I do not think there is much difference between old age institutions in New York and those in Europe. Nutritional state may come into it. Perhaps rural nutrition is not as good as urban—but we could find no significant difference.

**Dr. W. R. M. Alexander (Edinburgh):** Had 100 per cent. of the rural home population lived in the country all their lives?

**Dr. De Blecourt:** Yes.

**Dr. J. S. Lawrence (Manchester):** Prof. Bywaters, survival theory is interesting, but the results of population surveys do not support it. If correct, the percentage of sero-positive people would rise with age but not the actual numbers. In fact the actual numbers go up.

**Prof. Bywaters:** There is also an increased incidence of a positive titre with age in rheumatoid patients themselves.

**Dr. J. Ball (Manchester):** Prevalence of sero-positivity increases with age in most surveys. Wensleydale was an exception to this—we found no male over the age of 40 with a positive test.

**Skeletal Aspects of Haemoglobinopathies.** By Dr. J. H. Middlemiss (Bristol): A general account of the haemoglobinopathies and their geographical distribution was followed by a detailed description of the bone and joint abnormalities which occur in these disorders.

In children with homozygous SS disease, the hands and feet were most commonly affected. Infarcts in the phalanges, metacarpals, and metatarsals with an accompanying non-inflammatory periosteal reaction were followed by aseptic necrosis and absorption of bone. Marrow hyperplasia, a reaction to severe haemolysis, led to wide inter trabecular spaces, expanded medullary bone, and narrow cortices. Pathological fractures and coxa vara were common sequels. Vertebrae became compressed and the skull showed a characteristic radiological blurring of the inner, middle, and outer tables. Improvement in growth following treatment with folic acid suggested that folic acid deficiency was partly responsible. If there was rickets in addition, exuberant osteoid tissue could be seen along the shafts of long bones. There was a high incidence of *Salmonella* osteomyelitis without enteric fever. With haemoglobin SC disease haemolysis was less severe, and the chances of attaining adult life were greater than with SS disease. Bone infection and infarcts were common and childbirth was often followed by aseptic necrosis in the vertebral. The anaemia of thalassaemia major was incompatible with adult life. Marrow hyperplasia and bony swelling were so gross that they prevented aeration of the paranasal sinuses, while bone became scalloped by tumours of extramedullary haemopoiesis.

**Discussion.**—**Prof. E. G. L. Bywaters (Taplow):** You have the congratulations and thanks of the Society. We are now beginning to see patients from these areas and are not yet very well aware of this sort of problem. Have you found painful crises occurring in sickle-cell anaemia without any radiological change—a sort of forme fruste?

**Dr. Middlemiss:** Yes, and this is so with other clinical manifestations. Sometimes there are symptoms of mesenteric thrombosis, but nothing is found at laparotomy.

**Prof. Bywaters:** Were there any damages in alkaline phosphatase?

**Dr. Middlemiss:** We found none.

**Prof. Bywaters:** The pattern of necrosis seems a little different from that of other conditions, caisson disease for instance. Can you explain this?

**Dr. Middlemiss:** Not really. The changes in children are always more exuberant. In adults infarction in the femoral head is often segmental. I do not see why the lesions should be different from those of caisson disease.

**Dr. J. E. Seegmiller (Bethesda, U.S.A.):** I should like to point out that these conditions are often associated with hyperuricaemia and that there is also the possibility of secondary gout.

**Dr. G. R. Fearnley (Gloucester):** Have low-molecular-weight dextrans been used in sickle-cell crises?

**Dr. Middlemiss:** I do not know. There is much research going on in an attempt to prevent sickling and prolong red cell survival. An animal factor has been isolated which will do this, but it is highly dangerous to humans.

**Dr. A. St. J. Dixon (London):** With the increased interest now in surgery, it should be pointed out that these people do not tolerate tourniquets.

**Dr. D. A. H. Yates (London):** We have been screening patients at St. Thomas’s Hospital for haemoglobin abnormalities. Is it a fact that the sickle-cell trait is not accompanied by joint pains?

**Dr. Middlemiss:** Oh, no. People with sickle-cell trait can get crises from time to time, particularly under conditions of stress.

**Rheumatoid Arthritis in Kenya.** By L. Hall (Manchester): Over a 2-year period in a provincial hospital in Kenya detailed records were kept of all African patients suffering from polyarthritis. 108 patients were seen, of whom the majority had acute rheumatic fever and only eight had “classical” or “definite” rheumatoid arthritis. The writer has been able to trace only three previous accounts of such cases in tropical Africa though the disease is common in American Negroes.
A slide latex-fixation test for rheumatoid factor was carried out on 100 African controls and only one weakly-positive result was found.

The reasons for the apparent rarity of the disease were discussed. One factor is the relative youth of the population; analysis shows that this would be expected to reduce the incidence to about one-third of that in England.

Discussion.—DR. J. S. LAWRENCE (Manchester): I think Dr. Hall’s remarks on the age distribution in tropical populations are very much to the point. In a survey at Ibadan under 13 per cent. of females were aged 40 or over, compared with 50 per cent. in Wensleydale. I recently had the opportunity of examining patients in hospital in Lagos, and I found more Still’s disease and Reiter’s disease than rheumatoid arthritis, presumably because of the age distribution. But in a survey in Jamaica with Dr. Bremner, where population was stratified by age so that there were the same numbers in each group, we found the same prevalence of rheumatoid arthritis as in Wensleydale. There were no severe cases in this survey, but the actual prevalence was the same.

DR. J. BREMNER (Manchester): There were no patients with severe rheumatoid arthritis in the survey population in Jamaica, but I did see two extremely severe cases, completely crippled. They lived in the country and stayed there.

PROF. L. MICHOTTE (Brussels): In the Belgian Congo the most important reason for loss of work is rheumatic complaints, but the patients do not reach the hospitals.

DR. C. E. QUIN (Lewes, Sussex): I believe that Masai diet differs from that of the Kikuyu. The Masai eat more meat, drink more milk, and suffer more from arterial disease and rheumatic complaints, while the Kikuyu have more infections and gastro-intestinal trouble.

DR. HALL: In Nakuru we saw patients from many different tribes—they were mainly Kikuyu and Masai and I agree about the diets. But I saw rheumatoid arthritis in both tribes.

DR. W. HUMANS (Leiden, Netherlands): There are several approaches to this problem. One can go out to the country concerned and study the people, but face facilities which are not adequate. One can do it by remote control and get the material to one’s own laboratory, but then one does not see the patients. Or one can bring the patient to one’s own centre. This happened recently when a patient arrived from Liberia. We called her disease rheumatoid arthritis and she was surprised that we were surprised; she said the disease was quite common in Liberia, and she should know because she was the head nurse in a hospital. Do you think this is a new disease in Africa or has it been in existence for a longer time?

DR. HALL: There is no information on this—no doubt it will receive more attention as medical services develop.

PROF. E. G. L. BYWATERS (Taplow): Is there any ankylosing spondylitis? It would be noticeable with a preponderance of young males.

DR. HALL: I saw one patient and one other has been reported from tropical Africa.

Antinuclear and Precipitating Auto-antibodies in Sjögren’s Syndrome. By J. S. BECK, J. R. ANDERSON, W. W. BUCHANAN, K. J. BLOCH, and J. J. BUNIM (Glasgow and Bethesda)*.

Immuno-histological Studies of Connective Tissues in the Adult and Embryonic Rat. By D. G. SCOTT (Leeds): Antisera were raised in rabbits against connective tissues, including renal glomeruli separated from the kidneys of adult rats, and against connective tissues derived from 8 to 11-day rat embryos. The anti-tissue specificities of these antisera were compared in a series of immuno-histological procedures involving direct staining, cross-inhibition, and cross-absorption experiments. Anti-adult antisera contained antibodies reactive with the basement membranes of adult renal glomeruli. Anti-embryonic antisera did not react with these structures. Both antisera contained antibodies reactive with basement membranes of adult renal tubules, with adult renal interstitial tissue, and with the epidermal basement membranes of 8 to 11-day and 12 to 15-day rat embryos. The basement membrane of adult renal tubes and of the 12 to 15-day embryonic epidermis contained additional constituents reactive with antibodies present only in anti-adult antisera. The dermis of the 8 to 11-day rat embryo contained cellular and fibrillar components reactive with antibodies present only in anti-embryonic antisera, while that of individual 12 to 15-day embryos contained fibrils reactive either with anti-adult or with anti-embryonic antisera. These observations have been taken to indicate that adult basement membranes and reticulin differ antigenically from each other and that embryonic connective tissues undergo antigenic modification during development. The antigenic relationships existing between adult and embryonic connective tissues, however, remain to be elucidated.

Discussion.—DR. G. LOEWI (Taplow): Were any conventional in vitro serological studies done?

DR. SCOTT: No.

DR. LOEWI: I have found a rather similar phenomena with antibody to chondromucoprotein which also gives basement membrane staining. There are differences between embryo and adult, particularly in the embryo basement membrane which stains much less strongly.

DR. J. BALL (Manchester): It is possible that apparent loss of antigen in adults may result not from lack of constituents but from unavailability of reactive sites due to molecular reorganization.

DR. W. HUMANS (Leiden, Netherlands): What was the age of these embryos? Were they immunologically competent?

DR. SCOTT: They were taken 8 to 11 days after mating, up to 1 cm. long. Would they be immunologically competent then?

* This paper and the discussion thereon was published in full in Ann. rheum. Dis. (1965), 24, 16.
HEBERDEN SOCIETY

Dr. Humans: Yes, if comparable to man. One could envisage that the mother had antigens to which the embryo formed antibodies.

Dr. A. G. S. Hill (Stoke Mandeville): Would Dr. Scott risk postulating how this situation could produce connective tissue disease?

Dr. Scott: If embryonic determinants disappear in adult life and then, perhaps during the formation of granulation tissue, they reappear, they may be regarded as new and foreign determinants. Persisting antigen is necessary to maintain tolerance.

Differential Staining of Acid Glycosaminoglycans. By J. E. Scott and J. Dorling (Taplow): The application of the "critical electrolyte concentration" (CEC) concept to the differentiation of acidic glycosaminoglycans (mucopolysaccharides) was described. Alcian blue 8GX stains with increasing selectivity as increasing amounts of magnesium chloride are incorporated into the dye solution. Model experiments with pure polyanions, or artifically carboxylated, phosphorylated, and sulphated liver sections, showed that binding of dye to carboxylate or phosphate groups ceased at low electrolyte concentrations (<0.3M) whereas dye continued to be held by sulphate ester groups at concentrations five to ten times as high. The similarity to the well-established cetylpyridinium system for polyanion fractionation was discussed.

Sections of tissues chosen to contain predominantly or characteristically carboxylated mucins and/or sulphate ester polyions showed a staining pattern entirely similar to the model sections. Goblet cell mucin in rat ileum stained at <0.4M MgCl₂, cartilage at <0.6M MgCl₂, mast cells at <0.75M, and corneal stroma at <1.0M. These results are in agreement with the known contents of sialomucin, chondroitin sulphate, heparin, and keratosulphate, respectively. The conditions in which this principle can be used in a practical technique were described.

Observations on the Carbohydrate Content of the Matrix of Ageing Cartilage. By R. A. Stockwell (London): The localization of high molecular weight keratosulphate has been studied in normal human costal and articular cartilage, with particular reference to the changes with age, using the Alcian blue technique of Scott, Dorling, and Quintarelli (Biochem. J., 91, 48, 1964). A critical electrolyte concentration of 0.4M MgCl₂ was used to stain chondroitin sulphate and keratosulphate, and 0.9M MgCl₂ to stain keratosulphate alone.

In infant cartilage there is a negligible staining reaction at the high critical electrolyte concentration. From the second decade onwards, keratosulphate is localized in the inter-territorial matrix of both types of cartilage. In the central region of mature costal cartilage, however, there is a much stronger staining reaction for keratosulphate in the territorial matrix than inter-territorially. A similar territorial predominance is seen round the deepest cells of articular cartilage from about the beginning of the fourth decade.

These results are in agreement with quantitative measurements on the changes of keratosulphate concentration with age, made by Kaplan and Meyer (Nature, 183, 1267, 1959). It is suggested that the territorial distribution of keratosulphate in the central region of ageing costal cartilage, and in the deepest parts of ageing articular cartilage may be related to the efficiency of nutrition of the cells of these zones, as much as to their age.

Discussion.—Dr. J. Ball (Manchester): I should like to congratulate Drs Scott and Dorling, and Dr. Stockwell. This work seems to be an important advance in localizing connective tissue constituents. It may be the first truly histochemical method for the detection of hyaluronic acid other than those involving the use of enzymes. How valuable has it been for this constituent in practice? It is difficult to find evidence in the literature for the presence of hyaluronic acid in synovial membrane. Can the method be used in areas of mineralization?

Dr. Scott: We are much interested in the localization of hyaluronate, which is the most difficult polysaccharide of the whole group to demonstrate because the critical electrolyte concentration is close to that of background protein. We have not been able to demonstrate hyaluronate in synovial membrane. With regard to calcification—when the dye is taken up it is clear that in those regions calcification has had no effect on the staining mechanism, but it is conceivable that it might prevent the uptake of dye in certain situations.

Prof. D. V. Davies (London): Might it be possible to replace the copper atom in Alcian blue with something else of higher atomic weight, so that staining could be visualized under the electron microscope?

Dr. Scott: It is possible to replace the copper with a variety of different metals—thirty or more. Unfortunately those with high atomic numbers do not seem to stay there.

A Speaker: How far does molecular weight affect the staining of kerato-sulphate?

Dr. Scott: The relation of molecular weight to critical electrolyte concentration is a logarithmic one. Low molecular weight kerato-sulphate has a low critical electrolyte concentration. It is not present in large amount and I do not think interference is very serious.

Prof. E. G. L. Bywaters (Taplow): I should like to ask Dr. Stockwell more about the effects of ageing. Growth stops at about 18 and one would think that some changes were due to actual increase in size of cartilagenous rudiments. From examining the age range has it been possible to tell when these changes come into effect?

Dr. Stockwell: As far as costal cartilage goes, these are really maturation rather than age changes, and the pattern becomes much more obvious in the very old than round the age of 18. In articular cartilage I am inclined to believe this is a true age change. One does not get chondroitin sulphate around the superficial cells, nor territorial staining in deep region of kerato-sulphate, until middle age.

Prof. E. G. L. Bywaters (Taplow): As clinicians we are interested in pathological calcification. Calcification occurring in articular cartilage might be well worth while...
looking at. No doubt the authors would be grateful for specimens taken under the right sort of conditions for their examination.

**Localization of Chondromucoprotein in Cartilage and Other Connective Tissues by the Fluorescent Antibody Technique.** By G. Loewi (Taplow): Antibody to chondromucoprotein from pig laryngeal cartilage has been obtained after injection into rabbits. Hyaluronidase treatment of chondromucoprotein reveals additional antigen sites, the antibody reacts with the protein rather than the polysaccharide part of the molecule, and shows extensive cross-reaction with chondromucoprotein from other species including human. By the fluorescent technique, this antibody has been used to localize chondromucoprotein in connective tissue of the heart and aorta. In cartilage, various zones of staining have been demonstrated, and the pattern has been compared with that produced by the controlled Alcian blue technique (see preceding papers) for acid polysaccharide. Zones have been found which are stained by Alcian blue, but not by the antibody, and vice versa; hyaluronidase treatment of cartilage led to general increase of antibody staining, while largely abolishing Alcian blue uptake. The antibody also cross-reacted with a constituent present in basement membranes of various organs.

**Discussion.—Dr. J. E. Scott (Taplow):** I should like to suggest perhaps other explanations which would fit. It could be a problem of penetration of various territories. With colleagues I am working on a problem in which demonstration of this phenomenon of difficulty in penetration is the central theme. Laurent and Ogston (Biochem. J., 89, 249 (1963)) demonstrated that polysaccharides have excluded volume. Alcian blue is a small molecule compared with antibody, and it demonstrated a region of polysaccharide concentration which must be very high round chondrocyte. It follows that this region will have excluded volume which is very high and I should like to suggest that this dark region may be due not to the absence of protein but simply to the fact that antibody cannot penetrate in order to bind with chondromucoprotein.

**Dr. Loewi:** I agree. I have only drawn up this provisional scheme to summarize my data, not as an explanation of the findings.

**Dr. M. Ziff (Dallas):** What of the lacunar staining round chondrocytes? Could this be due to the cut edge of the lacuna allowing penetration? How old was cartilage which was treated with hyaluronidase?

**Dr. Loewi:** Hyaluronidase seems to have similarly marked effect on the embryo and on the adult cartilage. This was fully grown pig. Ability of the antibody to penetrate a cut edge was a very real problem. Surface staining was seen at natural surfaces, such as the surface of articular cartilage, as well as at cut edges.

**Prof. E. G. L. Bywaters (Taplow):** Would artificial cuts in cartilage section give locally increased staining?

**Dr. Loewi:** I have not done this.

**Dr. A. G. S. Hill (Stoke Mandeville):** Do you get any staining with irrelevant antibody followed by conjugate on cut edges?

**Dr. Loewi:** Usually not.

**Dr. Galjaard (Leiden):** Have you compared your results with those published by Karnovsky, who described a “specific” stain for “chondromucoprotein”? He used quite a small molecule which would have less difficulty in penetrating the various territories of the cartilage.

**Dr. Loewi:** Are you sure Karnovsky’s method would not stain collagen in any of its forms?

**Dr. Galjaard:** They carried out some model experiments and these did not show any staining of collagen.

**Dr. D. G. Scott (Leeds):** I should like to offer my congratulations on the slides. To what do you attribute the distribution of staining? The effects of exclusive phenomenon? This means that chondromucoprotein molecules would have to be orientated in such a way that protein was always inside.

**Dr. J. E. Scott (Taplow):** Exclusive phenomenon is shown by polysaccharides, which have no protein there.

**Dr. D. G. Scott:** If protein was sticking out, would you get combination?

**Dr. J. E. Scott:** Provided it can stain only the surface layer, the amount of visible stain would be quite small. Excluded volume does not depend on whether protein sticks out or not.

**Dr. D. G. Scott:** To what do you attribute the incomplete staining of the glomerular tuft?

**Dr. Loewi:** I think basement membranes contain several materials, perhaps with regional differences in composition, and that this might explain the staining distribution.

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**NEW ZEALAND RHEUMATISM ASSOCIATION**

**ANNUAL REPORT, 1964**

The XVI Annual Conference of the New Zealand Rheumatism Association was held at the Memorial Hospital, Hastings, on October 28 and 29, 1964.

The President Elect, Dr. J. Moore Tweed, outlined the progress made towards the formation of the New Zealand Branch of the Arthritis and Rheumatism Council. Incorporation was likely to proceed in 1965. Great help had been given in the past year by Dr. Barclay (Wellington), who had offered further help in medical liaison.

During the meeting the New Zealand Rheumatism Association approved the donation of £500 towards the Council on its formation.
Heberden Society: Annual Report, 1964

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