HEBERDEN SOCIETY

ANNUAL REPORT, 1961

At the Annual General Meeting, held on December 2, 1961, the President, Dr. F. Dudley Hart, recorded with regret the death of Dr. Ernest Fletcher, who was the first recipient of the Heberden Medal in 1938 and President of the Society in 1956-57, and also that of Dr. Peter Davis, one of the younger members of the Society.

The following new members were elected:

Ordinary Members: Dr. M. R. Jeffrey, Dr. G. Loewi, Dr. A. J. Popert, Dr. V. Wright.

Associate Members: Dr. B. W. Lacey, Mr. G. Platt.

The total Ordinary Membership was thus brought up to 100 and the Associate Membership to 28.

Activities

At the invitation of Dr. A. Willcox, the first clinical meeting of the year was held on February 10 at the Middlesex Hospital (Annals, 20, 200). Papers were presented by Drs. J. D. Nabarro and R. E. Cotton (Middlesex), Miss M. D. Snelling (Middlesex), Dr. J. W. Stewart (Middlesex), Mr. P. H. Newman (Middlesex), Dr. F. M. Andrews (London), Dr. E. J. M. Campbell (London), Drs. T. M. Chalmers and J. R. Hearns (Middlesex).

On May 27-28 a very interesting meeting was held in Paris at the invitation of Dr. Jacques Forestier, President of the French Branch of the International League against Rheumatism (Annals, 20, 295). Papers were presented by Dr. M. Thompson (Newcastle-upon-Tyne) and Prof. E. G. L. Bywaters (Taplow), Dr. J. Foretiser (Aix-les-Bains), Dr. J. S. Lawrence (Manchester), Drs. G. Cordier, H. Garnier, and M. Darcy (Paris), Drs. F. Françon and G. Le Blanc (Aix-les-Bains), Dr. G. D. Kersley (Bath), Prof. Merle d’Aubigné and Drs. M. Postel and J. M. Vaillant (Paris), Prof. F. Coste and Drs. P. Massias and N. Chatelin (Paris), Drs. H. Colenbrander (Leiden) and B. M. Ansell (Taplow), and Dr. J. A. Liévre (Paris). The President extended to Dr. Forestier and his colleagues the grateful thanks of the Society for their generous hospitality.

The Heberden Round, entitled “Pituitary and Adrenal Hormones in Rheumatoid Arthritis,” was conducted by Dr. Oswald Savage at the West London Hospital on October 6 (Annals, 21, 79).

The Heberden Oration for 1961 was delivered on December 1 by the Rt. Hon. the Lord Cohen of Birkenhead at the Wellcome Foundation, London, on “William Heberden—medicus vere Hippocratics: ultimus Romanorum” (Annals, 21, 1). Lord Cohen was presented with the Heberden Medal for 1961.

The Annual Dinner was held on December 1, 1961, in the Fellows’ Restaurant at the Zoological Gardens, Regent’s Park, London. Among the guests present were Lord and Lady Knollys, Lord Cohen, Dr. E. Abbott (Dean of Westminster), Dr. and Mrs. E. R. Cullinan, Prof. and Mrs. Malcolm Milne, and Dr. J. W. P. Thompson (British Medical Journal).

The Annual General Meeting was followed by a Clinical Meeting which is reported below (page 213).

Grant-in-Aid

The Society acknowledges with appreciation the renewal of a grant from the Empire Rheumatism Council.

Annals of the Rheumatic Diseases

Full reports of the Society’s activities have appeared regularly in the Annals. The Society is indebted to the Editors for their co-operation in thus furthering the work of the Society.

Library

Dr. W. S. C. Copeman reported that there had been a number of rare and valuable additions to the Library during the past year for which they were principally indebted to the continuing generosity of the Trustees of the Wellcome Foundation. The Society continued also to be very much indebted for the time and trouble expended on its behalf by their learned Librarian, Dr. F. N. L. Poynter, who had also recently arranged for a number of volumes to be rebound at no expense to the Society.

It was much hoped that Members would continue to donate books or relics relating to the field of rheumatic diseases prior to 1914.

The following books had been added to the Library during the year:


BAIN, WILLIAM (1855-1930), and EDGEcombe, WILFRID. The physiology and therapeutics of the Harrogate waters, baths and climate applied to the treatment of chronic disease. Pp. xii, 300. 8vo. London: Longmans, Green. 1905.
ANNALS OF THE RHEUMATIC DISEASES


CADOGAN, William (1711-97). A dissertation on the gout, and all chronic diseases, jointly considered, as preceding from the same causes; what those causes are; and a rational and natural method of cure proposed. Addressed to all invalids. 2nd ed. Pp. 99. 8vo. London: J. Dodsley. 1771.

CAMPOLONGO, Emilio (1550-1604). De arthritide liber unus, de variolis alter. ... Nunc primum in lucem editi opera atque industria Richardi Valcheri. 4 l., pp. 74, 4 ll., pp. 63. 2 pts. 4to. Venice: P. Meietus. 1586.


JONES, Henry Bence (1813-73). On gravel, calculus and gout; chiefly an application of Professor Liebig's physiology to the prevention and cure of these diseases. Pp. xiii, 1 l. 13pp. 8vo. London: T. Taylor and Walton. 1842.


SCHAEFFER, Josephus. Disputatio medica inauguralis, de rhumatismo acuto. 3 ll., pp. 30, 1 l. 8vo. Edinburgh: C. Stewart. 1807. (Author's presentation copy.)


WILLIAMS, William Henry (1771-1841). Observations proving that Dr. Wilson's tincture for the cure of gout and rheumatism is similar ... to ... the eau medicinale. Pp. vii, 25. 4to. London: J. Callow. 1818.

OFFICERS, 1962

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General Secretary:
M. C. G. Andrews
(Tel. No.: COVent Garden 0871.)

PROGRAMME FOR 1962
Clinical Meeting at St. Bartholomew’s Hospital, by invitation of Dr. H. Wykeham Balme, on February 16 (see p. 216).
Clinical Meeting at Brighton, by invitation of Dr. W. A. Bourne, on May 12.
The Heberden Round at Stoke Mandeville Hospital, by invitation of Dr. A. G. S. Hill, on September 28.
The Heberden Oration, Annual General Meeting, and Dinner, on December 7 and 8.

Titles and short programme notes of original communications which members wish to make to the society during 1962 should be sent to the Senior Hon. Secretary (Dr. G. R. Newns, M.R.C.P., Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases, 77 Gell Street, Sheffield, 3) 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.

Annual General Meeting, 1961.—This was held on December 1 and 2 at the Welcombe Foundation, and was followed by a Clinical Meeting at which the following papers were given:

The Possible Role of Plasmin in Mesenchymal Disorders, by Dr. C. H. Lack (Royal National Orthopaedic Hospital, Stanmore): Plasmin appears to function as a fibrinolytic agent in the blood: digestion of clot is by activation of the plasminogen incorporated in the clot rather than by the action of free plasmin. Most tissues contain activator of plasminogen.

When plasminogen is injected into an ear vein of a rabbit some loss of cartilage matrix occurs; this is increased if vascular permeability is increased by heat or chemical rubefacients. This change in the ear cartilage coincides with a rise in serum and urinary chondroitin sulphate. Thomas has already demonstrated a similar change following intravenous injection of unactivated papain. It is suggested that both pro-enzymes, if able to reach cartilage matrix, are activated in situ and attack the chondromucin, whereas the active enzymes have little or no effect because they are neutralized by inhibitors in the blood.

The leaching out of chondroitin sulphate from cartilage is sometimes followed by a deposition of fibrin-like material in the renal glomeruli and on vascular endothelium. Certain resemblances to the fibrinoid deposits of the generalized Schwartzman reaction, and the possibility that these deposits result from the complexing of altered fibrinogen with chondroitin sulphate, are considered.

Discussion.—Dr. G. Loewi (Taplow): If fibrinoid is a fibrin-chondroitin sulphate complex deposited from the blood stream, as Dr. Lack has suggested, we should expect to find it particularly in organs such as the kidney, rather than in the relatively avascular connective tissue where it is in fact frequently found.

Dr. Lack: It has not been proved that all fibrinoid deposits are of the same nature and origin as that found in connective tissue diseases. I think a lot depends on where the complex forms. In certain disease it might remain localized to the site of formation, but in others carried to the kidney.

Prof. E. G. L. Bywaters (Taplow): I believe that with papain some rather minor changes have been described in articular cartilage. Have similar observations been made with plasmin?

Dr. Lack: Yes, I demonstrated this at a recent meeting. I do not know whether permanent changes could be produced by repetition of the process.

Dr. G. R. Fearney (Gloucester): Dr. Lack mentioned the pre-treatment of rabbits with cortisone in his experiments. I wonder if he has considered using epsilonaminocaproic acid, which is an inhibitor both of plasmin and plasmin activator.

Dr. Lack: We intend to use it, but have had a little difficulty in discovering the optimal dose. It seems that the dosage required in rabbits is on a very different scale from that described in humans.

Articular Symptoms in Myelomatosis, by Dr. E. B. D. Hamilton (London) and Prof. E. G. L. Bywaters (Taplow).*

Discussion.—Dr. J. H. Glynn (London): I have recently seen two cases of myelomatosis presenting with typical gout and hyperuricaemia, and wonder whether there is a connexion between the two conditions.

Dr. Hamilton: We have seen several such cases and regard the gout as secondary to the high cellular turnover.

Arthroplasty of the Knee, by Mr. G. Platt (Aylesbury): An operation for arthroplasty of the knee in which the femoral condyles are trimmed to receive a stainless steel prosthesis with a central slot to take the cruciate ligaments was described. The technique and results were

* Published in Annals of the Rheumatic Diseases (1961), 20, 353.
illustated with a cinefilm. The results of 27 operations were assessed after a mean follow-up of 41/2 years. Persistent severe pain, the primary indication for operation, was substantially reduced or abolished in all cases. Range of movement was not increased, but sufficient was retained to maintain the patient’s independence for sitting and negotiating stairs.

Discussion.—Dr. A. G. S. Hill (Stoke Mandeville): I have referred some of the patients for operation in the series described by Mr. Platt, and after following them up have no doubt about the value of the operation.

Prof. J. H. Kellgren (Manchester): Is lateral instability of the knee—a common finding in rheumatoid arthritis—a contraindication to the procedure.

Mr. Platt: Posterior subluxation is a contraindication, but while lateral instability in my experience is not common, I am prepared to operate in such cases. I had a case in which there was advanced destruction of the lower end of the femur with instability, and at operation the knee was painless, had about 40° of movement, and was stable. Stabilization appears to be effected by fibrosis after operative trauma.

Dr. A. G. S. Hill (Stoke Mandeville): The remarkable thing about the operation is the stability afterwards.

Prof. E. G. L. Bywaters (Taplow): One of the reasons for laxity of the ligaments may be loss of substance between bone ends; perhaps restoration by insertion of the prosthesis would make the ligaments tighter.

Mr. Platt: I do not think this happens. The prosthesis is only about one-sixteenth of an inch in thickness.

Electrophoretic Studies of Serum and Synovial Fluids in Rheumatoid and Osteo-arthritis, by Dr. M. Wilkinson and Dr. B. S. Jones (London).*

Discussion.—Prof. E. G. L. Bywaters (Taplow): Proteins in general are removed from the fluid by the lymphatics rather than by the blood stream. Might not the increase be due to delay in uptake?

Dr. Wilkinson: It could be due to delayed reabsorption by the lymphatics, but if so it is strange that it affects the γ globulin selectively.

Dr. J. Ball (Manchester): I agree that local production is a possible explanation. As previously reported to the Society, we have found more rheumatoid factor in extracts of skin and synovium of rheumatoid arthritis than can be accounted for by the tissue blood content. Since plasma cell infiltration was not present in the skin, it may be that the connective tissue cells themselves contribute to the extravascular plasma protein pool, including RA factor.

Dr. Wilkinson: We suggest that plasma cells and lymphocytes produce it. Obviously lymphocytes are not confined to the synovia.

Dr. A. G. S. Hill (Stoke Mandeville): Like others, we found rheumatoid factor, detected by an immunohistological method, in synovial tissue and regional lymph nodes. The investigation is being extended to other tissues and until they have been surveyed it is impossible to decide whether rheumatoid factor present in synovial tissue and lymph nodes is being produced in these sites or simply stored therein: the evidence at present favours production in the joints and we have seen the Rose-Waaler test become positive in fluid from a joint before the serum gave a positive reaction. If production does, in fact, take place in the joints, there must be many factors which affect the equilibrium between serum and synovial fluid titres.

Respiratory Function in Ankylosing Spondylitis, by Dr. P. A. Emerson, Dr. I. Gregg, and Mr. D. Strickland (Westminster Hospital): A method for measuring total chest compliance in conscious subjects was used to show that this is reduced in a series of ankylosing spondylitics. The disturbance of pulmonary function in 20 patients was compared with that produced by tight corseting of the chest in normal subjects. The only respect in which the mechanical disturbance to the chest differed in the two conditions was that in ankylosing spondylitis the residual volume tended to be increased (mean 125 per cent of predicted), although there was no evidence of any obstructive lung disease and the lung compliance was normal. In all other respects the mechanical disturbance was similar in both ankylosing spondylitics and tight corseting of the chest; the vital capacity was reduced at the expense of the inspiratory capacity (mean 60 per cent of predicted) and the total chest compliance was similarly reduced in the two conditions.

Discussion.—Prof. E. G. L. Bywaters (Taplow): As I see it the difference between your corseted normal subjects and the ankylosing spondylitics is that the former are corseted in full expiration, whereas the spondylitics are corseted, so to speak, in a median phase.

Dr. Emerson: I think that is right. We know that, in emphysema or conditions where there is difficulty in breathing out, the chest assumes an inspiratory position in order that the chest wall may be stretched and provide more recoil to assist expiration. It has been suggested that this occurs in ankylosing spondylitis.

Prof. J. H. Kellgren (Manchester): Surely spondylitics are not barrel chested; rather the reverse.

Dr. Emerson: It is important to realize that in spondylitics there is a 25 per cent increase in residual volume, whereas in those one would say were barrel-chested the increase might be 300 per cent.

Question: Was it possible to estimate diaphragmatic movement? Some use their diaphragms more than others. Is there not some difference in this respect between the corseted normal subject who had had no need to use his diaphragm very much and the spondylitic who had had a gradually increasing necessity to do so.

Dr. Emerson: We have not studied diaphragmatic movements because it would entail too much exposure to X rays. It is known that these patients do have good diaphragmatic movement, and this is why, we think, they tolerate well operations on the chest wall, but may die from respiratory insufficiency if the surgeon cuts the phrenic nerve. However, their diaphragmatic efficiency is not necessarily greater than that in corseted normal subjects.
Gold Treatment in Rheumatoid Arthritis—Results of a 30-month Multicentre Controlled Trial arranged by the Research Sub-Committee of the Empire Rheumatism Council. Final Report by DR. F. DUDLEY HART (London).*

Discussion.—DR. G. D. KERSLEY (Bath): This trial is heartening because the result is similar to the clinician's impression. One thing we have to realize is that a clinician not taking part in the trial would not have stopped gold for 2 years in those who had improved and watched them slowly deteriorate. He would either have carried on with small topping-up doses or started another course. I do think we have to get more information on longer term treatment with gold, and the risk of toxicity, in particular to the bone marrow.

THE PRESIDENT: We must find this out if we have another trial.

DR. K. N. LLOYD (Cardiff): I support Dr. Kersley's remarks. There has emerged evidence that, if you stop gold, as was done in the trial, some cases will relapse later on, but if you give maintenance doses a high proportion of cases remain in remission.

DR. DUDLEY HART: We cannot take anything for granted, and this remains to be proved. Dr. Jacques Forestier established gold therapy for rheumatoid arthritis: his son is here and we should like to hear what he has to say.

DR. F. FORESTIER (Aix-les-Bains): We have followed up patients for over 10 years and our conclusions meet with those from the E.R.C. trial—gold produces clinical improvement but does not influence the x-ray changes. I am not surprised that improvement was maintained for 12 months after stopping gold; it is the only form of treatment in which benefit can be observed for so long after cessation. Relapse 2 years afterwards is to be expected; Jacques Forestier and his colleagues have realized since the earliest days of chryotherapy that repeated courses or maintenance doses are necessary to prevent relapse, and it is a mistake to delay repetition of the course until this occurs.

DR. J. H. GLYN (London): When we plan such trials as this we should ensure that the drug is used according to current clinical practice. It is the general impression that patients respond less well to a second course of gold than to the first, and that the correct procedure is to use "topping-up doses" when the first course is completed. This was not done in the present series and as a result it seems to me that the trial has yielded only part of the answer we sought.

Lateral Instability of the Knee, by DR. E. N. COOMES (Manchester): An appliance was used for measuring lateral instability of the knee joint held in full extension. Both knees were examined at the same time, the thighs being held together, and instability assessed by the separation of the medial malleoli produced by known weights. 59 normal subjects were examined, 23 of whom were under 20 years of age, and the younger group were found to have either slacker or more elastic ligaments than the older group. Of 57 patients with rheumatoid arthritis, 37 had obvious clinical involvement of the knees and these joints were laterally unstable. The remaining twenty, who had normal or mildly affected knees, behaved in the same manner as the normal group.

In contrast, no instability was found in knees actively involved in ankylosing spondylitis, and it was infrequent in psoriatic arthropathy.

Discussion.—DR. A. ST. J. DIXON (London): How did you distinguish between lengthening of the ligaments and shrinking of the cartilage and menisci?

DR. COOMES: Only about one-third of the patients with obvious involvement of the knee had radiological evidence of narrowing of the cartilage.

PROF. J. H. KELLOGREN (Manchester): If there is gross cartilage narrowing there is deformity of the bone ends, and I would stress the point that the bone ends in the cases studied by Dr. Coomes were not deformed. Lateral rock occurs at a stage when there are no radiological changes, and it would seem there is something interesting taking place in the soft tissues. It could be compressibility of the cartilage, increasing length of the ligament or both, but not joint deformity.

DR. J. BALL (Manchester): During the last few years I have studied the much simpler situation of spontaneous atlanto-axial subluxation in rheumatoid arthritis; and I am satisfied that this is not initiated by a primary intrinsic general change in the transverse ligament. Direct observation shows that the region of attachment of the ligament to bone is remodelled by erosive granulation tissue, the mineralized part of the ligament being thereby replaced by tissue which is easily stretched. Thus the ligament is lengthened. Dr. Coomes’s findings suggest to me that something similar may be happening in the unstable knee.

DR. M. THOMPSON (Newcastle-upon-Tyne): In rheumatoid arthritis tendon lesions are extremely common, in ankylosing spondylitis very rare, and in psoriatic arthropathy half way between the two. Can this be correlated with instability of the joint?

DR. J. T. SCOTT (Taplow): Has Dr. Coomes any observations on the effect of joint effusions on his measurements?

DR. COOMES: Many of the spondylitics had large effusions with stable knees, and the rheumatoids small effusions with unstable knees. Patients with displaced menisci with traumatic effusion have no instability, and it is not likely that effusion could produce instability.

A Family Study in Still's Disease, by DR. B. M. ANSELL and PROF. E. G. L. BYWATERS (Taplow), and DR. J. S. LAWRENCE (Manchester).*

Further Observations on Salicylate-induced Gastro-intestinal Bleeding, by DR. A. ST. J. DIXON and DR. P. H. N. WOOD (London).†

Discussion.—THE PRESIDENT: What dose of Alka-Seltzer was used, and was it well tolerated?

* Published in *Annals of the Rheumatic Diseases* (1961), 20, 315.

† Published in the *British Medical Journal* (1962), 1, 669, under the title "Salicylates and Gastro-intestinal Bleeding", by P. H. N. Wood, E. A. Harvey-Smith, and A. St. J. Dixon.
Dr. Wood: 4 g. a day, and it was well tolerated. Stubbé described diarrhoea with it, but the formula he used was different from ours and contained calcium phosphate and a small quantity of magnesium which may have accounted for the diarrhoea.

Dr. E. B. D. Hamilton (London): Have you measured serum salicylate levels after giving buffered and ordinary aspirin to see whether the absorption is different?

Dr. Wood: No. The evidence advanced to justify the differences between various clinical formulae is based to a large extent on the supposed demonstration of differences in plasma levels within 20 to 30 minutes. I suspect that the analytical techniques that have been employed are insufficiently precise, especially when the concentration of salicylate is small. Our evidence is so opposed to these observations that I would challenge them.

Prof. E. G. L. Bywaters (Taplow): I am not sure whether you have evidence yet that slow absorption was associated with less bleeding; in other words have you done blood level curves?

Dr. Wood: No, we have not, but they have been done by others.

Dr. Dixon: One interesting thing is the dissociation of the therapeutic effect and the effect on bleeding of aspirin anhydride. This substance given in equivalent doses causes the same amount of bleeding as aspirin and yet has much less, if any, clinical action.

Dr. Wood: You will remember that aspirin anhydride consists of two aspirin molecules. We do not know whether it is hydrolysed before absorption; if it is it may be that one of the molecules of aspirin is altered during the hydrolysis, so that in effect only half the dose is being administered. Of course this is only armchair hypothesis.

Clinical Meeting.—The Society met on February 16, 1962, at St. Bartholomew’s Hospital, London, by invitation of Dr. H. Wykeham Balme. The President, Dr. G. D. Kersley, was in the chair, and the following papers were given:

Neuropathic Joints, by Dr. G. O. Storey (London): 52 cases with neuropathic joints were reviewed, the series comprising tabs dorsalis (37), syringomyelia (10), diabetes (4), and sciatic nerve lesion (1). In some, particularly when the spine was involved, the neuropathy was asymptomatic, while in others onset of symptoms was acute or gradual. Radiologically, increased density of the bone ends often preceded disintegration of the joint, and later either atrophy or gross hypertrophic changes predominated. Purulent effusion into the joint or a related synovial pocket occurred in eight cases, half being sterile. Other complications were para-articular calcification, fractures, dislocations, haemarthrosis, and pressure on the ulnar nerve and lumbo-sacral plexus.

Discussion.—Prof. E. G. L. Bywaters (Taplow): I am impressed with the relative incidence of the cases in the series. I very rarely see tabetic arthropathy; diabetic arthropathy more commonly.

It is of interest that gross disorganization of joints may occur in congenital hemiplegia as a result of motor disability. In this condition there is no sensory impairment and I am sure the main causative factor is the uncontrolled use of the affected limb.

One point may be made in connexion with syringomyelia: several joints in the same limb tend to be affected, whereas when multiple joints are involved in tabes the distribution is more haphazard.

Dr. W. A. Bourne (Hove): I recall a case in which a Charcot knee joint resulted from a lumbar disk lesion. Trophic ulcers were so extensive as to necessitate skin grafting.

Dr. H. Wykeham Balme (London): Does synovial biopsy help in the diagnosis of neuropathic joints?

Dr. Storey: I think it may, but we must do more biopsies before being sure.

My series had a preponderance of tabetic because Mr. A. J. King at the Whitechapel Clinic, the London Hospital, has a special interest in them and has collected them over many years. I would have expected a bigger proportion of diabetics, and think that many cases of Charcot’s joint in this condition are not diagnosed.

Alkaptonuria—A Family Study, by Dr. C. F. Hawkins (Birmingham): Three members of a family suffered from alkaptonuria and ochronosis, and the radiological features of the associated osteo-arthritis were demonstrated. The original patient had been unnecessarily treated for diabetes for several years, and his excretion of homogentisic acid was materially reduced by dietetic restrictions only if they were so strict as to be unacceptable. It was demonstrated that nowadays the diagnosis in infancy may be unsuspected since napkins washed with detergents rather than soap are not stained by homogentisic acid.

Discussion.—Dr. Oswald Savage (London): I am sure that Dr. Garrod himself would have liked to hear this paper, so ably and entertainingly delivered in his own hospital. Were there any consanguineous marriages in the family?

Dr. Hawkins: There usually is consanguinity, but I could find no evidence of it in this study.

Dr. W. A. Bourne (Hove): There were three cases of alkaptonuria in one generation, with none in the preceding or consecutive generations, which is characteristic of transmission by a recessive gene—the generally supposed mode of inheritance for this condition.

Dr. H. Wykeham Balme (London): A descendant of one of Dr. Garrod’s cases, until recently a patient here, earned a reasonable living as a small boy and young adult by selling his urine for teaching purposes.

Prof. E. G. L. Bywaters (Taplow): It is very odd that the clinical manifestations do not come on until the age of 30 to 40. Presumably the cartilage takes up the homogentisic acid polymer only gradually. Has anyone studied the cartilage of very young people in affected families?

Dr. Hawkins: Not as far as I know.

Shoulder-hand Syndrome following Herpes Zoster, by Dr. T. R. Littler (Birkenhead): Between August, 1958, and July, 1959, four cases of this syndrome have been
encountered. In each of them was a clear antecedent history of herpes zoster. The occurrence of this form of reflex neurovascular dystrophy following zoster is an acknowledged rarity, very few cases having been reported in the literature. The average age at onset was 64 years and three of the four patients were females. Both upper limbs were equally involved. The sequence of events usually associated with the shoulder-hand syndrome was observed in every case. Initially each patient complained of a painful, stiff shoulder with swelling of the homolateral hand and fingers. During this stage there was clinical evidence of increased blood flow through the limb. The intermediate stage was one of gradual resolution, and was followed by the final stage in which trophic changes were observed. These included flexor tendon contracture, sclerodactyly, and evidence of diminished blood flow through the limb. Three of the four cases were judged to have made a satisfactory recovery, without the aid of stellate ganglion injection or physiotherapy. Treatment consisted mainly of analgesic drugs and physiotherapy. The average duration of the syndrome was about 16 months. X-ray examination revealed varying degrees of osteoporosis of the bones of the affected limb, but the erythrocyte sedimentation rate was normal, there being no evidence of any systemic reaction. Characteristic personality changes were observed in three of the patients.

The internuncial pool theory, based on experimental work by Lorente de Nó, provided the most satisfactory explanation of the underlying mechanism of the shoulder-hand syndrome. Because many diverse conditions may all culminate in the production of this syndrome, it could be regarded as a classical "end-result" syndrome. In this connexion it is interesting to speculate whether rheumatoid disease which shares many common features with it may represent another example of an "end-result" syndrome. Osteoporosis, sclerodactyly, thickening and contracture of tendons, deformity, fusiform swelling of the fingers, and a degree of pain and stiffness sufficient to immobilize a joint were all seen in the patients in this series, yet all these essentially rheumatic characteristics originated in a virus infection of dorsal root ganglia. A renewed study of the autonomic nervous system in relation to the rheumatic diseases might lead to further advancement of our knowledge of them.

Discussion.—Dr. M. Thompson (Newcastle-upon-Tyne): It would be dangerous to attempt to connect the lesions of the shoulder-hand syndrome with rheumatoid arthritis. We certainly know little about the cause of rheumatoid arthritis, but the pathology is very different from that of the shoulder-hand syndrome.

Dr. D. Preiskel (London): Dr. Littler seemed apologetic over not having used stellate ganglion block. My results with this procedure have been very disappointing.

Dr. V. Wright (Leeds): Did brachial pain, such as might be due to cervical osteo-arthritis, precede the onset of herpes? We have observed a high incidence of this condition before the onset of the shoulder-hand syndrome.

I would draw attention also to the possible role of immobilization, particularly in cases in which the syndrome follows coronary thrombosis. Moreover, we know that those who develop the syndrome often have an odd personality.

Dr. Littler: Herpes was, of course, preceded by some pain, but not of the character expected with spinal osteo-arthritis.

Dr. W. S. C. Copeman (London): I understand that viruses of the zoster type tend to be specific, and as this virus is neurpathic I wonder how it correlates with the vascular involvement observed clinically.

Dr. Littler: I think the theory of Lorente de Nó is a good one and fits the facts. Incidentally, it explains why the hip-foot syndrome is so rarely encountered; the connector cells in the grey matter are very plentiful in a small section of the cord in the upper thoracic region, and become progressively less frequent in number as it descends.

Relative Importance of Various Tissues in Joint Stiffness, by DR. V. Wright and DR. R. J. Johns (Leeds): Previously we demonstrated that both normal and rheumatoid subjects show a marked diurnal variation in strength of grip. An apparatus has therefore been constructed to measure directly stiffness at the joint. The torque (force) required to produce passive sinusoidal motion of the joint is measured and related to displacement; and the force on stopping rotation at the limit of oscillation is measured in relation to time.

To ascertain the relative importance of various tissues in joint stiffness, the rheological properties of the wrist of the anaesthetized cat were studied. They closely resembled those of the human metacarpophalangeal joint, being comparable to the stiffness of a child's joint.

Most of the stiffness was due to non-linear elasticity and plasticity, elasticity being twice as great as plasticity. Inertia accounted at most for 6 per cent. of the total torque and viscosity for 2 per cent., and friction was immeasurably small.

The contribution of various tissues to total joint stiffness varied with the amplitude of motion. The tendons, for example, contributed little until the extremes of joint motion were reached. The "check rein" effect of disconnected tendons appeared to be due to their being compressed by their sheath at the extremes of joint motion. The capsule made a marked contribution to the total stiffness at all amplitudes. In the mid-range of joint motion (±0.5 radians) the capsule contributed 47 per cent. of the total torque, passive motion of the muscles 41 per cent., tendons 10 per cent., and skin 2 per cent.

Discussion.—Dr. D. A. Brewerton (London): Is it right to assume that because the cat was anaesthetized the muscles were completely relaxed. Passive movement of a limb normally involves active participation of the central nervous system to give a smooth readjustment of muscle length. It might be that a conscious and perfectly relaxed subject would offer less muscle resistance than an anaesthetized subject.

Prof. E. G. L. Bywaters (Taplow): I wonder if Dr. Wright would say something about the "warming-
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up" process? It is noticeable in animals and humans and even more so in patients with rheumatoid arthritis and sometimes in those with osteo-arthritis. These studies have been carried out in the steady state: have you any observations on the initial response of an immobilized joint?

Dr. WRIGHT: Obviously one cannot give an entirely definite answer as to whether an unanaesthetized animal would behave differently. We have, however, looked into this question in humans, when we find no electromyographic evidence of muscle activity during passive movement of the joint. With regard to the "warming-up" process, if you mean actual increase in temperature we have studied this and find an increase to 45°C will produce a 25 per cent. reduction in joint stiffness. Conversely, a reduction to 19°C will produce a 25 per cent. increase in joint stiffness. If you mean the effects of previous immobilization, our experiments have shown that if you immobilize joints for period of 3 to 24 hours you get both reduction in strength of grip and increased stiffness. Dr. J. T. Scott, in his interesting work, found that frequent extension of the metacarpophalangeal joint to its limit produced an increased range of movement. We have worked within the physiological range of joint mobility, and have found no difference in joint stiffness during oscillation for as long as 3 hrs. Oscillation in hypertension produces decreased stiffness due to plasticity.

Atypical Polyarthritis in Relatives of Psoriatrics, by Drs. D. N. GOLDING, H. BAKER, and M. THOMPSON (Newcastle-upon-Tyne): There is evidence that psoriasis is associated with inflammatory polyarthritis more often than can be explained by mere coincidence. There are wide variations in the clinical picture of psoriatic arthritis and no definition has been universally accepted as diagnostic, but the Rose-Waaler agglutination test is negative in the vast majority of patients with psoriasis and arthritis, and positive in at least 80 per cent. of classical rheumatoids. It has been established that there is an hereditary component in the causation of psoriasis, although the exact mode of inheritance is unknown. It has also been shown that erosive arthritis is significantly more common in the relatives of patients with sero-positive rheumatoid arthritis than in controls, and that clinical arthritis occurs more frequently in the families of patients suffering from sero-negative arthritis than in controls. It is therefore likely that genetic factors may determine the association of psoriasis and arthritis, and if there were reason to believe that a psoriatic factor existed in the genetic constitution of a patient suffering from sero-negative polyarthritis, this would support a diagnosis of psoriatic arthritis. The existence of a psoriatic genetic factor may be inferred from the presence of psoriasis in one or more close relatives. The family histories of 53 patients with psoriatic arthropathy were studied in the light of these observations, and the authors postulate that some cases of sero-negative polyarthritis in close relatives of patients with psoriasis are examples of psoriatic arthropathy before the development or in the complete absence of psoriasis.

Four diagnostic criteria were used in this study:

(1) Exclusion of other causes of erosive polyarthritis;
(2) Consistently negative Rose-Waaler test;
(3) Clinical and radiological features suggestive of psoriatic arthropathy;
(4) Psoriasis in one or more close relatives.

The clinical and radiological features of five patients who satisfied the above criteria were described.

Discussion.—The President: These are important observations and we shall all have to think more about them.

Dr. B. M. ANSELL (Taplow): We have seen psoriasis develop in juveniles, 8, 9, and 15 years after the onset of polyarthritis, and in these cases the arthritis has been particularly mild. I should like to ask the time interval in those who developed joint lesions before the psoriasis.

PROF. E. G. L. BYWATERS (Taplow): I think the relatively mild course is characteristic of these cases whether psoriasis is present at the time or not; the striking thing is the good prognosis. In our long-term follow-up, all who had or who developed psoriasis while under observation between 1949 and 1958 ran a course in the higher functional grades during the first and second 5-year periods.

The only point I would add to the features of psoriatic rheumatism enumerated by Dr. Golding is tendon sheath involvement, particularly of the finger flexors. This, of course, is sometimes seen in rheumatoid arthritis, but in association with psoriasis there is not uncommonly an effusion into the sheath, often recurrent, producing little disability, and sometimes without involvement of the joints.

Dr. GOLDING: We understand that the sausage-shaped fingers sometimes seen are due to involvement of both interphalangeal joints and tendon sheaths.

PROF. E. G. L. BYWATERS (Taplow): Yes, but I stress that tendon sheath lesions sometimes occur alone.

Dr. THOMPSON: Of the 53 patients with sero-negative psoriatic arthropathy, seven developed the polyarthritis well in advance of the psoriasis, in twelve the onset of psoriasis and arthritis was simultaneous, and in the remainder the psoriasis antedated the arthritis. Dr. Baker, our dermatologist, undertook the family survey.

Dr. BAKER: There was a history of rheumatism in eight of the 53 families. Of the 46 who attended for examination, ten were found to satisfy our criteria for the form of arthritis under discussion, and in all these the Rose-Waaler test was negative.

Au186 in the Treatment of Persistent Knee Effusions, by Dr. B. M. ANSELL, MRS. A. CROOK, DR. J. R. MALLARD, and PROF. E. G. L. BYWATERS (London): Attempts to produce a "radiation synovectomy" were reported, using colloidal Au186, a beta-gamma emitter with a half-life of 2-7 days and a range in the tissues of 1-2 mm. Provided there was at least a moderate effusion, intra-articular injection was followed by rapid diffusion and localization on the synovial membrane. 22 therapeutic injections (mean dose 580r) were given to seventeen patients, in ten of whom the better of
bilaterally involved knees was injected with inactive gold and used as a control. At the end of 1 year results in the treated group were classed as good in ten, improved in seven, and negative in five. There was a trend to improvement among the controls, but at the final assessment the treated knee tended to be better than the control. It was suggested that this form of therapy may fail because of inability of Au 198 to penetrate far enough into very thick synovial membrane.

**Discussion.**—**DR. G. R. FEARNELEY (Gloucester):** How much gold was there in each dose?

**DR. ANSELL:** About 0·01 mg.

**MR. W. D. COLTART (London):** One sees large numbers of recurrent effusions into knees, and some are extremely difficult to deal with. Does Dr. Ansell think this is now a practical therapeutic procedure?

**DR. ANSELL:** No. My feeling is that, in a case of recurrent effusion and minimal soft tissue swelling after aspiration, it is worth putting in radioactive gold, but not once there is much thickening of the synovial membrane. Yttrium 90 may give better results, but a colloid preparation has only just become available, and in the soluble form it was not well taken up. Yttrium is a pure beta-gamma emitter and our apparatus was not good enough to detect it, so we had to rely on autoradiographs of biopsy specimens and could not be certain that the sample was representative of the whole knee.

**DR. J. H. GLYN (London):** Has Dr. Ansell used Au 198 in cases of intermittent hydrarthrosis?

**DR. ANSELL:** We asked four patients with intermittent hydrarthrosis to keep a diary for 6 months, and when this was done the development of effusions was much less regular than the history suggested. One patient who previously had swelling every 2 months had no swelling at all during this period. Consequently we did not think assessment in these cases would be easy.

**A SPEAKER:** One feels that the relatively poor results may be due to the chronicity of the disease. The effect of radioactive gold must be similar to that of nitrogen mustard which is not of much use in arthritis of 3 to 4 years’ standing because there is then so much degenerative change.

**DR. ANSELL:** Two final points. We have only attempted to treat patients who showed a good joint cavity on x-ray. The duration of the effusion does not necessarily seem to matter. One of my good results was in the case of a doctor with bilateral knee effusions who had had the disease for 7 years, had been on treatment with steroids for a long time, and had had recurrent haematemesis. Steroid therapy was discontinued and he had recurrences of the effusions; he was having 300 ml fluid removed more or less every 3 weeks and biopsy showed that he had classical rheumatoid arthritis.

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**IV WORLD CONGRESS OF CARDIOLOGY**

*Mexico City, October 7-13, 1962*

The Fourth World Congress of Cardiology will be held in the City of Mexico on October 7-23, 1962, under the presidency of Professor Ignacio Chavaz. Full particulars may be obtained from the Secretary General, Dr. I. Costero, Institute of Cardiology, Avenida Cuauhtemoc 300, Mexico, 7, Mexico D.F.

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**THIRD PAN-AMERICAN CONGRESS OF RHEUMATOLOGY**

*September, 1963*

This will be held in Santiago, Chile, on September 15 to 19, 1963, under the presidency of Dr. Manuel Losada. All enquiries should be made to the Secretary-General, Dr. Oke France, Casilla 23D, Santiago, Chile.