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**Clinical Meeting** held at the White Hart Hospital, Harrogate, on May 20 to 21, 1966.

**Dr. T. G. REAH (Harrogate)** opened the proceedings by giving a short paper concerning a family where grandfather, father, and son all suffered from rheumatoid arthritis.

**Discussion.—Dr. J. S. LAWRENCE (Manchester):** A family of three generations of males all suffering from rheumatoid arthritis is clearly unlikely to occur by chance. It provides, moreover, convincing evidence that sex linkage on the X-chromosome is not involved in any genetic cause which may be present.

Dr. REAH presented the case of a woman with a destructive lesion of the bones, particularly affecting the hands. Biopsy of a gland showed it to be a reticulum cell sarcoma.

**Discussion.—Dr. J. V. WILSON (Harrogate):** I should think that the age of the patient was of interest here, as well as the distribution of the disease. Was the serum uric acid estimated?

Dr. REAH: The patient attended another hospital 6 months ago, when the serum uric acid was found to be 7.3 mg./100 ml. She was given colchicine and the level fell to 5 mg./100 ml. While she has been here, the serum uric acid has been around 5 mg./100 ml. The diagnosis at the other hospital was said to be “atypical gout”.

**Pleural Lesions and Pulmonary Infections in Rheumatoid Arthritis, by Dr. W. C. WALKER (Leeds):** 516 patients with classical or definite rheumatoid arthritis were studied clinically, radiographically, and serologically and were compared from the respiratory point of view with 301 patients with degenerative joint disease. The incidence of pleurisy, pleural fibrosis, and pleural effusion was determined and measures in the diagnosis of rheumatoid pleuritis assessed. Features of the arthritis, other systemic complications, results of serological and haematological tests, and radiographic changes in those with rheumatoid pleural effusions were compared with the remainder of the rheumatoid population. The incidence of respiratory infections in the two groups was compared, and their significance in rheumatoid arthritis discussed.

**Discussion.—Dr. J. V. WILSON (Harrogate):** Has any body found RA cells in pleural effusions?

Dr. WALKER: We have looked for them only once and they were not present.

**Prof. J. H. KELLGREN (Manchester):** Do these patients come from urban or rural areas?

Dr. WALKER: They came mostly from the polluted atmosphere of Leeds; some came from urban areas around Leeds and a few from rural areas.

**Prof. E. G. L. BYWATERS (Taplow):** This excellent paper contains much material for discussion. When Aronoff, Fearnley, and I* investigated lung lesions in rheumatoid arthritis, we used a control series both in the x-ray series of 130 rheumatoid patients and in the post-mortem series of 42 rheumatoid patients, and in both there was a relative preponderance of lung lesions in the rheumatoid series, involving bronchitis, pulmonary fibrosis, and pleural thickening in the radiological series and bronchitis, pleural adhesions, and bronchiectasis in the autopsied series. We concluded, however, that there was no specific lung lesion common enough to appear in this small post-mortem series. The controls were chosen on a random basis for both series.

**Dr. J. S. LAWRENCE (Manchester):** I have recently had occasion to review patients with positive sheep cell tests and a control group with negative tests. They had chest x-rays and then a forced expiratory volume test. A high proportion of positive sheep cell tests was found in those with a low expiratory volume. The chest x-rays did show more pleural thickening in the sero-positive group. In this, as in most population samples, few of the sero-positive people had evidence of rheumatoid arthritis. Nevertheless, we found that pleural thickening was more common in those with arthritis than without. Of course, positive sheep cell tests are more common in urban populations, so we cannot be sure to what extent this has interfered with the conclusions. It does rather support Dr. Walker’s contention that these pulmonary infections...
Green Serum in Rheumatoid Arthritis, by Dr. K. D. Shah and Dr. V. Wright (Leeds): Certain patients with rheumatoid arthritis were found to have green serum. This could be seen, but not measured spectrophotometrically. The colour moved with albumin, and did not appear to be due to free verdoperoxidase. It was photosensitive and was not reproduced by dilution of serum or bilirubin. It appeared to be due to a relative absence of yellow pigment. The phenomenon was correlated with the clinical, serological and radiological manifestations of the disease.

Discussion.—Prof. E. G. L. Bywaters (Taplow): You say it is easy to recognize: presumably all these readings were done blind?

Dr. Wright: It is easier to see the green when the serum is frozen. The readings were done by three observers independently without knowledge of the diagnosis; the definite yellows and definite greens were always put into the right category, but the intermediate group had a definite observer error in calling them either intermediate or yellow.

Prof. E. G. L. Bywaters (Taplow): How did you categorize them?

Dr. Wright: We took the definite green group and compared them with the rest.

Dr. M. Jeffrey (Harrogate): I wonder if Dr. Shah tried to correlate this finding with the serum iron. We know that serum iron may be low in active and chronic rheumatoid disease. I wonder if the green colour is simply due to a lack of the normal pink of siderophyllin.

Dr. Shah: We could not do this investigation on many patients because of technical difficulties, but Mr. Clough, our biochemist, demonstrated in some the point you make. However, iron is bound to the globulin fraction not the albumin.

Investigation of Morning Stiffness, by Dr. T. G. Plunkett (Leeds): As an extension of the investigation of morning stiffness of rheumatoid arthritis, a clinical and physiological study was undertaken. A self-recording pneumatic dynamometer was designed and a portable arthograph constructed. An inter-relationship of diurnal variation of strength of grip and physical stiffness was suggested. Evidence was presented to show that weakness of grip is insufficient of itself to account for the phenomenon of morning stiffness. The effects of sleep (natural and induced), immobilization, exercise, and temperature were studied.

Discussion.—Dr. O. Savage (London): You measure your strength of grip in lb. per sq. in. Most of us test grip in mm. Hg. Could you tell us what are the equivalent scales?

Dr. V. Wright (Leeds): The average rheumatoid patient would grip in the region of 5 lb. per sq. in. compared with 200 mm. Hg.

Dr. D. A. Brewerton (London): There are two points about the measurement of grip that have always bothered me. One is that muscles and joints were mentioned, but not the tendons in between. The other is the habit of talking about strength as if it were a single entity. It all depends on how you measure strength. For instance, when measuring a static muscle contraction in the presence of a painful joint, it makes a considerable difference whether the muscle is attempting to shorten against a fixed resistance or whether it is holding an external force.

Dr. J. T. Scott (London): It is difficult to relate morning stiffness to other factors. A few years ago I studied morning stiffness in a few patients with rheumatoid arthritis, estimating passive stiffness in a metacarpophalangeal joint with an extension spring.* Objective joint stiffness was greater in the morning than later in the day. Strength of grip was also weaker in the early morning, and hand volume, measured by water displacement, was greater. However, a similar variation in hand volume and strength of grip, but not in joint stiffness, was found in normal subjects.

Dr. Plunkett: I am in fact looking into the effect of immobilization and oedema on strength of grip. I had a little difficulty in measuring hand volume, but I have now devised a method of doing it more accurately than by water displacement. I am using an alginate gel that the Dental Department use for making impressions of the mouth. I take a cast of the hand, which sets in about 1 to 2 minutes, and measure the volume of this.

Dr. V. Wright (Leeds): May I make a point on the question of tendons. It is obvious that tendons do contribute to stiffness at certain phases. Working with the cat wrist joint, which is comparable in stiffness to the metacarpophalangeal joint of a child, we found that in the normal physiological range of joint motion tendons contribute little to overall stiffness. Their effect is in checking inaction at the extremes of joint movement. On the point of static muscle contraction, I entirely agree that the two modes Dr. Brewerton has described will yield different results, but in the case of strength of grip the method Dr. Plunkett has used seems to be the nearest to the physiological situation.

Dr. D. A. Brewerton (London): But cats don't have rheumatoid arthritis!

Dr. V. Wright (Leeds): That is correct.

Antibody Response in Patients with Rheumatoid Arthritis, by Dr. R. B. Payne, Dr. J. W. Czekalowski, and Dr. V. Wright (Leeds): There is evidence to suggest that an aetiological factor in the production of rheumatoid arthritis might be a deranged antibody response of such patients. To test this hypothesis the antibody response to particulate and soluble antigens was tested over a period of 52 days in a group of patients with rheumatoid arthritis and in a control group with osteo-arthritis, and the results were reported. Preliminary results showed that in a patient with Felty's syndrome there was no immunological response to the injection of antigen. The other results at this stage were inconclusive.

Study of Lumbar Disk Degeneration, by Mr. A. Naylor (Bradford): The natural history of intervertebral disk herniation and degeneration shows that the symptomatology is characteristically phasic. The development of our hypothesis of disk prolapse and the biochemical and biophysical changes in disk degeneration were outlined, and possible auto-immune factors discussed. Results of our biochemical and biophysical investiga-
tions, which showed effects of changes on elasticity of disk and its mechanical efficiency, were reviewed. More recent investigations particularly concerned variations in non-collagenous proteins. Enzyme breakdown of polysaccharide/collagen complex was briefly outlined and its possible clinical significance discussed.

**Discussion.—**DR. V. WRIGHT (Leeds): First, has Mr. Naylor found that in the lumbar spine biochemical changes occur in the disks at each level as well as the one which is prolapsed? Secondly, if there is an age distribution of the biochemical changes, does he find that a relatively young subject with disk protrusion does in fact have changes in the disks? How does he explain protrusions at a younger age?

MR. NAYLOR: We take the protruded nucleus of these patients and part of the annulus fibrosus and examine the specimens biochemically. These show changes you expect in a much older patient. I only remove the prolapsed portion. We note that herniations in animals often occur at various levels of the spine. These herniations are usually seen in animals with disks which have aged prematurely. Certain breeds of dogs, such as the pekinese and dachshund, are very prone to disk degeneration; these breeds show intervertebral disk degeneration at about 3 or 4 months of life, though relatively resistant breeds do not show these changes. The biochemical changes I have described may well be the result of the process, not the cause.

**Rheumatoid Peripheral Neuropathy, by Dr. T. G. PLUNKETT and Dr. J. R. GOLDING (Harrogate):** A series of 64 patients with rheumatoid peripheral neuropathy was presented (28 males and 36 females), of whom 28 were dead, 26 alive, and ten untraced. Most had been diagnosed in the years 1959-60, very few being seen after then. The onset of peripheral neuropathy in males was at an average age of 54, and in females at an average age of 51. The average survival time in the fatal cases after the diagnosis of neuropathy was 1 year in males and 2 years in females. The average age of the males was 63 and of the females 61 at the time of follow-up. The relationship to corticosteroid therapy and stress was discussed. Fatal cases and the post-mortem results were also reported.

**Discussion.—**DR. J. S. LAWRENCE (Manchester): I was interested in the histogram of the change in incidence. Have you looked into the relationship to gold treatment?

DR. GOLDING: As far as we can tell more gold is being used in this region than 5 years ago, although the incidence of cases of rheumatoid peripheral neuropathy has diminished over the years. Not much was used in 1959-60 when most of the patients were alive. However, two French authors consider that widespread severe peripheral neuropathy may appear immediately after gold injections.

DR. V. L. STEINBERG (London): My findings in a similar number of cases confirm this trend in incidence in 1959-60, i.e., and in the last year I have only had one or two patients. All my findings are similar to those of Dr. Golding and I agree that gold is not used in these patients more than in others. Were we using large amounts of new steroids in the 1960s?

DR. GOLDING: We were probably using larger doses in 1960 than we are using now.

**Reduced Incidence of Osteo-arthritis in Weight-bearing Joints after Anterior Poliomyelitis, by Mr. G. F. WALKER and Dr. J. H. GLYN (London):** The legs of 98 patients over 35 years old, who had suffered an attack of anterior poliomyelitis at least 10 years previously and in whom one leg was more severely paralysed than the other, were examined.
There was difficulty in assessing laxity by palpation, and the clinical examination of the hip was by Trendelenberg's test, with emphasis on those considered to have muscle weakness.

**Rheumatoid Arthritis after Poliomyelitis, by Dr. E. N. GLICK (London):** Thompson and Bywaters (1962) described unilateral rheumatoid arthritis in the non-paralysed limbs after hemiplegia. They noted that paralysis of both upper and lower motor neurone type has been reported as protecting against degenerative arthritis, but there was no information regarding the effect of lower motor neurone paralysis on rheumatoid arthritis.

In five patients who developed rheumatoid arthritis after having had poliomyelitis, arthritis changes were more marked in non-paralysed limbs. The combination of rheumatoid arthritis and polio may be rarer than might be expected from the prevalence of these two conditions.

**Discussion.—** PROF. E. G. L. BYWATERS (Taplow): I would like to congratulate you on the paper. I was wondering if perhaps Dr. Lawrence might have any figures on the separate incidences of these two diseases in the population, and whether perhaps Dr. Glyn might comment on the incidence of rheumatoid arthritis in the polio population. From his 98 cases there ought to be something like one or two cases.

DR. D. R. L. NEWTON (Middlesbrough): Having regard to the anatomy of the hip, I think this would create a realignment of the weight-bearing area involved.

PROF. E. G. L. BYWATERS (Taplow): How do you assess osteo-arthritis? I do not quite see why Dr. Glyn felt there was no evidence from his figures that lack of weight-bearing was responsible for the relative immunity of the paralysed side.

DR. GLYN: Taking the second question first. The degree of weight-bearing did not vary in the different groups. The incidence is identical in patients who are walking and even doing a normal day's work and in those who are partially chair-bound. The arthritic changes therefore seemed to bear no relationship to the degree of weight-bearing activity, but they did bear a relationship to the degree of paralysis. With regard to the assessment of osteo-arthritis, we used both the conventional clinical criteria and the six radiological parameters mentioned earlier. If two or more of these radiological parameters were positive, we diagnosed osteo-arthritis.

DR. V. WRIGHT (Leeds): What are the vascular changes in poliomyelitis? It could be that this is the major factor in producing the changes of osteo-arthritis and certainly in producing symptoms. There is a good deal of evidence, particularly from phlebography before and after intertrochanteric osteotomy, that alteration of vasculature is responsible for some symptoms in osteo-arthritis.

DR. D. A. BREWERTON (London): There certainly are profound changes in the vasculature in poliomyelitis and this may be bound up with changes in sympathetic function.

DR. GLYN: We feel that the explanation of our clinical observations may possibly lie in these vascular changes.

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DR. J. GLYN (London): There was one, but I was unable to follow him up.

DR. J. S. LAWRENCE (Manchester): One out of 98 is rather a low prevalence. The patients were over 35 years of age.

DR. GLICK: I actually tried to contact this man, but did not get any reply. He was over 80 years old. As regards the incidence figures of polio, I tried to find out what proportion of the population between the ages of 20 and 60 had paralytic polio, but there are no figures.

DR. W. WATSON BUCHANAN (Glasgow): Dr. Glick's observations perhaps lend support to Dr. Duthie's view that rest, and in particular proper splintage, has an important place in the treatment of rheumatoid arthritis.

**Evaluation of the Relative Roles of Hereditary and Environmental Factors on Autoantibody Production, by Drs. W. W. BUCHANAN, J. A. BOYLE, W. R. GREIG, M. BARR, R. M. ANDREW, R. B. GOUDIE, and J. R. ANDERSON (Glasgow):** A study of 145 healthy twin pairs was undertaken in an attempt to define the role of heredity and environment in the production of autoanti-
bodies in normal people. Five autoantibodies were studied, including rheumatoid factor by the Hyland agglutination technique and antinuclear factor using rat liver nuclei as antigen.

Comparison of autoantibody concordance rates in mono- and dizygotic twins showed no evidence of significantly raised concordance in the monozygotic twins for any of the autoantibodies studied. These results suggested that in normal persons heredity is much less important than environment in autoantibody production.

Discussion.—Dr. J. S. Lawrence (Manchester): This is a fascinating study. Certainly Dr. Ball did find aggregation of the sheep cell factor in the populations of Leigh and Wensleydale. When we came to divide the relatives into parents, siblings, and offspring, we found that most of the aggregation was occurring in the offspring. The siblings had a slight increase, and the parents had no more than the expected rate. This in turn did not seem to fit any genetic hypothesis. Recently Professor Collard of Manchester has been looking at the Salmonella and Brucella antibodies in persons with positive sheep cell tests in Leigh and Wensleydale, and he found some increase of antibodies in the sheep cell positive persons, suggesting that it is bacteria rather than genes which are handed down in these families.

Flufenamic Acid (CI-440) in the Treatment of Rheumatoid Arthritis, by Dr. K. T. Rajan (Stoke Mandeville): Flufenamic acid is a stable weak carboxylic acid, rapidly acting, anti-inflammatory, and analgesic compound with the chemical name of N-(a,a,a-trifluoro-m-tolyl) anthranilic acid.

A double-blind double-cross-over trial compared the relative analgesic properties in rheumatoid arthritis of flufenamic acid, aspirin, and phenylbutazone. Thirty patients were admitted to the trial; complete records were obtained from 26 patients and a partially completed record from one.

Discussion.—Dr. J. T. Scott (London): One hesitates to criticise such a carefully conducted trial, but do you not think it might have been a useful control to include a period of placebo tablets in your design?

Dr. Rajan: We did not feel justified in putting these patients who were suffering from active rheumatoid arthritis on inert tablets for 2 weeks.

Dr. N. Cardoe (Norwich): We have just completed a similar trial in which we compared flufenamic acid and aspirin. We doubled the dose to 600 instead of 300 mg. At the end of the trial we did give an opportunity for these patients to continue on the drug, and we have now two patients who have had it for 18 months. They are both satisfied that they are doing well, but radiologically they have got worse. Three of the patients on this dose had to stop it because of diarrhoea.

Dr. A. G. H. Hill (Stoke Mandeville): It seems to me that, because no inert drugs were used, the result is open to the two alternative interpretations, that none of the drugs had any analgesic potency, or that all were of similar potency. This trial was designed to answer the question, does flufenamic acid have greater analgesic power than aspirin or phenylbutazone.

Dr. J. T. Scott (London): Yes, but it is conceivable that an advantage of one analgesic over the other might not be demonstrated because the techniques were not sufficiently sensitive. You would suspect this if you found no advantage of either drug over the inert tablets.

Dr. T. M. Chalmers (Edinburgh): The daily dose of aspirin used in the trial was slightly smaller than commonly used in routine treatment.

Dr. D. R. L. Newton (Middlesbrough): The advantage of a placebo is surely to show up placebo reactors. These are fairly well known statistically, and may show up when one drug of known effectiveness is compared with another.

Dr. Rajan: I would have thought the placebo factor would equally affect patients on each drug. They were all compared individually.

Tomography of the Sacro-iliac Joints, by Dr. M. Wilkinson and Dr. J. A. K. Meikle (Perth): Tomograms of the sacro-iliac joints in various disease groups were compared with those of elderly non-arthritic controls and with post-mortem radiological studies of younger non-arthritic subjects.

Tomography confirmed the frequency of varying degrees of joint fusion, especially in the anterior part of the joint, in elderly non-arthritic and osteo-arthritic subjects. Similar though more extensive changes were observed in younger paraplegic patients.

Rheumatoid arthritic patients showed more frequent and more severe degrees of joint narrowing and fusion, but a minority also showed minor grades of para-articular sclerosis and small erosions. In ankylosing spondylitis marked degrees of sacro-iliac joint narrowing and fusion were found at an early age, but of more use in diagnosis was the demonstration of para-articular sclerosis, marginal erosions, and occasionally pseudo-widening of the joint space, all of which tended to be more prominent than in rheumatoid arthritis.

Compared with antero-posterior radiographs of the sacro-iliac joints, tomograms were more useful for demonstrating joint narrowing and fusion but only slightly better for sclerosis, erosions, and osteophytes.

Discussion.—Dr. V. Wright (Leeds): I think this is an excellent piece of work, and am interested to see that Dr. Wilkinson did not find the changes of ankylosing spondylitis in the paraplegic patients. As you know, we presented before this learned Society evidence that the sacro-iliac changes in these patients differed from the sacralilitis of ankylosing spondylitis with which they had previously been confused. It is reassuring to have Dr. Wilkinson's confirmation.

Dr. D. R. L. Newton (Middlesbrough): Some 10 years ago I was very dissatisfied with antero-posterior views, and I agree that oblique views are not generally helpful. Have we any information about comparison of tomograms with postero-anterior views?

Dr. Wilkinson: We do not have any information on this. We felt it was not justified to expose the patients to further radiation. I agree it would be useful for comparison.

Dr. M. Thompson (Newcastle-upon-Tyne): I should not wish to see the complete rejection of oblique views of the sacro-iliac joints. I have found them useful particularly in discriminating between osteitis condensans ili and ankylosing spondylitis in doubtful cases. An experienced radiographer can produce satisfactory views. We had an interest at one time in sacro-iliac tomograms, but our radiologist had reservations about the amount of radiation to the pelvic area, especially as many of these doubtful cases occur in women of child-bearing age.