ABSTRACTS

Acute Rheumatism

Experimental Reactivation of Subsiding Rheumatic Fever.


The authors report from Irvington House, Irvington-on-Hudson, and the New York University School of Medicine a further clinical and laboratory study of the relapses which occur after the cessation of salicylate or steroid therapy in patients with rheumatic fever. In their previous studies of this rebound phenomenon (Yale J. Biol. Med., 1961, 33, 259 and 279; Abstr. Wild Med., 1961, 30, 230), evidence was obtained which suggested that such relapses represented the reappearance of the inflammation that had been suppressed during therapy. In the present study, 88 patients aged 4 to 18 years who had not received anti-inflammatory therapy for one month and who then showed no clinical evidence of active rheumatic disease were given experimental re-treatment for a period of 2 weeks. Consecutive patients were allocated to one of three treatment groups which received respectively: prednisone in a dosage of 60 mg. per day for one week and 40 mg. per day for the second week (29 patients); aspirin, 0.75 gr. per lb. (110 mg. per kg.) body weight per day for one week and 0.5 gr. per lb. (70 mg. per kg.) per day for the second week (29 patients); the remaining thirty patients received no therapy and served as controls. On cessation of therapy, clinical relapse was observed in nine of the patients who had received prednisone, in one who had received aspirin, and in none in the control group. Laboratory relapse (shown by a rise either in the erythrocyte sedimentation rate or in the C-reactive protein level) occurred in thirteen, three, and three patients in the three groups respectively. In the prednisone-treated group the incidence of relapse depended to some extent on the nature of the cardiac condition. Thus relapses occurred in three of eleven patients with no valvular involvement, in two of eleven with valvular involvement and no significant cardiomegaly, and in four of seven with significant cardiomegaly. In the aspirin-treated group relapse occurred only in one patient of the seven with significant cardiomegaly. No relapse was observed in the untreated group whatever the cardiac state. Analysis of the case records revealed that clinical relapses after the experimental course of therapy occurred only in those patients who had previously shown clinical or laboratory evidence of disease activity following an earlier course of treatment which had included steroids.

The authors conclude that these findings support their hypothesis that post-treatment relapses are due to a resumption of the inflammatory process previously suppressed and that anti-inflammatory drugs, particularly steroids, should be avoided in patients with rheumatic fever but without acute clinical manifestations.


The authors, working at the Children's Hospital in Essen, have noted that rheumatic fever in German children now runs a much milder course than formerly and that deaths during the first attack are now very rare. On the other hand there is little evidence that rheumatic fever is becoming any less common and the tendency to relapses is as high as ever. It is estimated that a relapse will occur in one out of every three children within 5 years of the first attack. Prevention of these relapses is therefore of great importance and the authors report the effect of oral penicillin prophylaxis on the relapse rate in three groups of patients:

(1) 55 who regularly and daily took 200,000 units of phenoxymethyl penicillin by mouth; in an average period of 2 years follow-up only one suffered a relapse.

(2) 29 patients who were prescribed the same treatment but were irregular in taking the drug; two suffered a relapse.

(3) Seventy patients who were not given any prophylactic treatment; nineteen relapsed.

These findings emphasize the necessity of continuous prophylaxis, which must be enforced even though it is tedious to children.

John Lorber.
**ABSTRACTS**


The authors present six case histories to illustrate the association between rheumatic heart disease and thyrotoxicosis as observed in six female patients between the ages of 20 and 40 treated at the Hospital of the National Institute of Cardiology, Mexico.

The first patient, aged 34, had a history of rheumatic fever at age 5, followed by mitral stenosis with haemoptysis at age 30. Mitral valve-lavulotomy was performed, but she failed to improve and developed evidence of hyperthyroidism, which responded to antithyroid treatment. Histological examination of a thyroid biopsy specimen (illustrated) showed evidence of chronic (Hashimoto's) thyroiditis.

The second patient, aged 29, had a past history of frequent tonsillitis, but no rheumatic fever. She presented with mitral stenosis, atrial fibrillation, and cardiac failure. Mitral commissurotomy resulted in improvement and a return to normal cardiac rhythm, but 6 months later she developed an illness manifested by arthralgia and a raised erythrocyte sedimentation rate, which was treated as rheumatic fever and slowly improved. In the following year she developed a large tender goitre, which responded to antithyroid treatment; a thyroid biopsy examination showed chronic thyroiditis.

Very similar histories were recorded in the remaining four patients, who all had evidence of rheumatic fever and cardiac valvular lesions and later developed thyroiditis and/or thyrotoxicosis.

In all six patients precipitating antibodies against polystyrene latex coated with thyroglobulin were demonstrated. These were not found in sixteen control patients, including some with acute or chronic rheumatic heart disease, chorea, and tonsillitis, or in four healthy control subjects.

[The incidence of this association among women in this age group with rheumatic heart disease seen at the authors' hospital is unfortunately not stated, nor are any findings in regard to L.E. cells or the L.E. factor presented.]

*Allan St. J. Dixon.*


A number of workers have shown that the concentration of lactic acid in capillary, arterial, and superficial venous blood following exercise is greater in patients with heart disease than in normal subjects. It has been assumed that this is due to the influence of lowered oxygen tension on the metabolism of exercising muscle, but lactic acid catabolism may also be impaired owing to the marked reduction in blood flow through other tissues. The purpose of the present study, reported from the University and Queen Elizabeth Hospital, Birmingham, was to investigate more precisely the relationship between the haemodynamic response to exercise and the production of lactic acid, the study including seven normal subjects and 24 patients with rheumatic heart disease, mainly mitral stenosis, of varying severity. The exercise consisted in pedalling a bicycle ergometer for 10 minutes in the recumbent position, the rate of external work being maintained at a constant level. The brachial artery was cannulated in all cases, and a cardiac catheter was placed with its tip in the pulmonary artery and a length of polythene tubing inserted into the femoral vein in fifteen cases. The concentrations of lactic acid in arterial and venous blood were measured during the second 5 minutes of exercise, while at the same time measurements of oxygen uptake and of oxygen saturation of arterial mixed venous and femoral venous blood were made.

These studies showed that the rise in oxygen uptake was very similar in normal subjects and in patients with mitral stenosis, but that the rise in lactic acid concentration in both arterial and venous blood was much greater in the patients with mitral stenosis. There was also a greater difference in femoral arteriovenous lactic acid levels in the patients and the femoral venous oxygen saturation fell to a lower level than in the normal subjects. A subsidiary study carried out on 41 patients at rest in bed showed that the concentration of lactic acid in arterial blood was similar in those who were severely disabled by heart disease and in patients without cardio-respiratory distress.

The authors then calculated the amount of lactic acid produced per ml. of oxygen used by the exercising legs and found that this amount increased considerably as the femoral venous saturation fell. By this means a correlation was established between the concentration of lactic acid in arterial blood, the femoral venous oxygen saturation, and the oxygen uptake, which held good both for normal subjects and cardiac patients. The amount of lactic acid produced by the exercising muscles can be estimated by first determining the blood flow through the leg during exercise. This value correlated well with the observed concentrations of lactic acid in arterial blood. The authors point out that it has now been shown that at rest the combustion of carbohydrate accounts for only a portion of the oxygen uptake of muscle, and hence it is unwise to draw any conclusions from calculations based upon the lactic acid production of muscle until all possible muscle metabolites have been studied simultaneously.

*G. Clayton.*


The author of this paper from the University Medical School, Budapest, draws attention to the lack of quantitative data concerning the serum protein pattern in acute rheumatic fever. He determined the total quantity of circulating proteins by estimating the percentage in the plasma and the volume of the plasma. Electrophoretic
fractionation of the plasma proteins then made it possible to compare the quantity of the circulating albumin and different globulins. These values were determined serially in fifteen children suffering from acute rheumatic fever. The absolute quantity of circulating globulins was found to be increased. As a consequence, the plasma volume increased while the total amount of albumin and the total number of erythrocytes remained unchanged. This haemodilution is considered to be the cause of the anaemia and hypoalbuminaemia which are well recognized features of rheumatic fever.

[A great deal of work is skillfully compressed into very few pages of text and tables.]

John Lorber.


The incidence of mitral valve disease found at post-mortem examination in patients over age 50 is reviewed. In a 13-year period, 2,086 necropsies were performed in patients over age 50. Of these, 64 (3.1 per cent.) had mitral valve disease; in 47 (73 per cent.) death was thought to be due directly to that condition. In four cases the presence of a mitral valve lesion was not suspected during life. The heart was enlarged in 62 cases (97 per cent.). Gross dilatation of the left atrium was found in six cases and gross dilatation of the right atrium in one case. Active rheumatism was present in one case. Emboli were found in thirteen (20 per cent.) cases at necropsy.

A history of rheumatic fever or chorea was found in 27 (42 per cent.). Twelve of the 37 women had borne altogether 27 children. Shortness of breath on exertion was the presenting symptom in 34 (53 per cent.). A mid-diastolic murmur was present in thirty (47 per cent.). There was a record of auricular fibrillation at some period during life in forty (63 per cent.). A blood-pressure of greater than 150/90 was recorded in 22 (34 per cent.).

The possible causes of longevity in mitral stenosis and the significance of the findings in relation to valvotomy and its prognosis are discussed. [Author's summary.]


A case of Sydenham’s chorea with raised intracranial pressure and papilloedema is reported. Investigation revealed no obvious cause, but two lumbar punctures greatly improved the child’s general state and abolished the papilloedema.

W. E. S. Bain.


ABSTRACTS

Chronic Articular Rheumatism (Rheumatoid Arthritis)


From observations made monthly on a group of 274 employed men the severity gradient of rheumatoid arthritis among them has been described in terms of the part of their time that they spend with active disease. This frequency distribution is reasonably well represented by a Pearson Type I function. The Type I frequency distribution can be found from an initial determination of whether a man is in episode, plus a subsequent redetermination for each man not then in episode.

The method developed provides a simple approach to making comparisons of the frequency of rheumatoid arthritis between groups in such a way as to eliminate the uncertainties arising from simple point prevalence measurements. Essentially, the procedure we recommend suggests that the usual point prevalence survey be supplemented by at least one additional examination to see how many additional afflicted persons are found. The second examination is curiously productive in that the two examinations are sufficient to specify the entire situation, if one is satisfied to assume the Type I distribution. Further examinations make it possible to check this point.

From the point of view of immediate results, we have a new view of rheumatoid arthritis as a very common disease that is only occasionally disabling. This position is supported by both data and theory which show how many cases with symptoms of rheumatoid arthritis will be disclosed by long-continued examination. The evidence of these several rheumatoid manifestations suggests that the older notion of a distinct separation between rheumatoid arthritis and fibrositis is probably unwarranted; the continuity of affliction dispels this. The notion now must be that we are dealing with a single continuous gradient of disease from no involvement to severe involvement. The mathematical techniques presented are presumably applicable to the study of other remittent diseases. [Authors' summary.]

Effect of Hyperventilation on Rheumatoid Arthritis.


The investigation herein reported was designed to test the hypothesis that the efficacy of aspirin in the rheumatic diseases is related causally to the results of the hyperventilation it produces, since similar symptomatic improvement in rheumatoid arthritis has been observed with other hyperventilatory conditions such as fever, hot baths, and pregnancy. The effects of aspirin were compared with those of hyperventilation produced by the Drinker respirator in four healthy subjects and nineteen patients with arthritis [specified]. The values assessed were the subjective status of the patient (by replies to questions) and the range of joint motion during aspirin administration, after aspirin had been withdrawn for 48 hours, after 3 to 6 hours in the respirator, and finally after cessation of passive respiration. The alveolar carbon dioxide tension (pCO₂) was measured by an infra-red gas analyzer, and the serum salicylate concentration, the erythrocyte sedimentation rate (E.S.R.), the C-reactive protein value, eosinophil count, and plasma 17-hydroxycorticosteroid levels were determined.

Symptomatic improvement occurred within one hour from the start of hyperventilation in fifteen experiments and was associated with a marked decrease in alveolar pCO₂ in all except one patient who had gout. Active hyperventilation persisted after removal from the iron lung in fourteen out of nineteen experiments for a mean period of 7 hours (0.5 to 29 hours) and was accompanied by continued freedom from symptoms. There was correlation between improvement in the range of motion and the alveolar pCO₂; the clinical state appeared to correlate better with alveolar pCO₂ than with the serum salicylate level. The E.S.R. fell significantly in nine out of thirteen markedly hyperventilated patients. The values for serum C-reactive protein and pain threshold were not significantly altered. Patients with Reiter's syndrome, gout, and ankylolyzing spondylitis also improved. The mechanisms of this effect remain obscure.

E. G. L. Bywaters.

Band-shaped Keratitis in Juvenile Rheumatoid Arthritis.


A 15-year-old girl with rheumatoid arthritis presented a band-shaped opacity across the cornea and chronic iridocyclitis in the right eye impairing vision to 0.5 (10/20); incipient changes of the same kind were seen in the left eye.

G. von Bahr.

"Inhibition Test" in Uveitis of Rheumatoid Aetiology.


The authors studied the diagnostic possibilities by using the "inhibition test of agglutination" in rheumatoid uveitis. In sixteen of 112 cases the sera showed no inhibiting activity. Ten were found to be positive with the "latex fixation test" (rheuma test) specific for rheumatoid arthritis. The diagnostic importance of this test is thus confirmed.

G. Cristini.

Involvement of the Hips in Juvenile Rheumatoid Arthritis.


The clinical and radiological features of involvement of the hip-joint in juvenile rheumatoid arthritis were studied in 85 patients at the Hôpital Reine Hortense, Aix-les-Bains. Of 54 of the patients in whom coxitis developed before age 15, 27 had been examined in childhood and the course of the disease was actually observed for 1 to 5 years in eleven and for 6 to 16 years in a further eleven. Of the 27 with coxitis who first came under observation after age 15, some were examined...
much later, even as long as 45 years after the onset of the disease. The hip joint was usually affected at an early stage—in 29 cases during the first year of the disease. Radiologically, osteoporosis was the first change observed; it was already visible in one case of only 3 months’ duration. The authors state that osteoporosis begins in the cephalic epiphysis and spreads to the femoral shaft and the bones of the pelvis. The outline of the joint, often irregular in childhood, is still more distorted by the disease. Narrowing of the articular space is a late manifestation and may be slight, as in one severe case of 6 years’ duration (of which radiographs are reproduced). Premature fusion of the constituent bones of the acetabulum or upper end of the femur may occur. The fusion may be faulty with persistent cartilage at the lines of union. Accelerated fusion can lead to premature arrest of bone development in the femoral head and in the pelvic bones; such arrest in development is often irregular, producing pelvic asymmetry or marked disharmony between the constituents of the hip joint. In 24 joints there was a marked valgus deformity of the femoral head and in five the deformity was varus. There was some degree of subluxation in twenty hip joints. It is pointed out that bone destruction leads to collapse of the femoral head and accelerates the subluxation. Large osteophytes frequently develop on the upper rim of the acetabulum. In three cases osteoporosis was the only sign of involvement. Bony ankylosis was observed in five cases, but four of these with destructive lesions in the vertebral column were regarded as cases of ankylosing spondylitis.

William Hughes.


The authors of this paper from the University Poly-clinic, Marburg, and the Municipal Hospital, Wiesbaden, stress the difficulty of assessing the efficacy of therapy in a disease such as rheumatoid arthritis in which a remission rate of 48 to 71 per cent. may be obtained in the first year of illness and in which, in the years to follow, 25 per cent. of cases improve spontaneously and an equal number deteriorate in spite of every known form of treatment. The good results claimed for chloroquine must be seen in the light of these facts. Consequently, in carrying out a clinical trial of chloroquine, the authors chose cases which had been under their care for months or years and required corticosteroids, phenylbutazone, and salicylates. Chloroquine was given in a dosage of 250 mg. daily for 3 to 4 months before a decision was reached as to its effect, that is, whether the dose of steroid could be reduced or omitted, or, alternatively, whether relapses had been prevented. Initially 44 patients with chronic rheumatism were thus treated and sixteen were eliminated because of side-effects or for other reasons; finally, only 28 patients (twenty with rheumatoid arthritis) took part in the long-term trial, taking chloroquine for an average of 17 months. Of these, five seemed to have been improved (though the result was not decisive in four cases), eleven remained unaffected, and twelve became worse. It was noted that the Rose-Waaler reaction, positive in twenty cases, was directly affected by chloroquine in ten cases, the titre falling with administration of the drug and rising when it was left off, but the change bore no relation to the clinical state and was only noted with Svartz and Schlossmann’s modification of the above reaction; the result of the latex fixation test was unaffected.

There appears to be no doubt that chloroquine has a special affinity for highly polymerized substances, including elements of connective tissue. Were it possible to exploit this phenomenon clinically, it might lead to a new concept in therapeutics either by variation of the nucleus itself, or by making use of the latter as a carrier of an “anti-rheumatic” substance. In the meantime, the value of the use of chloroquine in chronic rheumatoid arthritis is open to question.

D. Preiskel.


PRESENT POSITION OF SYNTHETIC ANTIMALARIAL DRUGS IN THE TREATMENT OF RHEUMATOID ARTHRITIS. (La place actuelle des antimalaridés de synthèse dans le traitement de la polyarthrite chronique évolutive.) Lacapère, J., Bonhomme, F., and Delaville, G. (1962). Presse méd., 70, 209. 4 figs.


OSTEO-ARTHITIS


SPONDYLITIS


From the University of California Medical Center, Los Angeles, the authors report six cases of benign self-limited spondylitis occurring in five infants and children aged 7 months to 2½ years and one boy aged 13 years. They were all characterized by failure to identify a specific infectious agent, the mild clinical course of the disease, and recovery without the use of antibiotics. The radiological appearances were indistinguishable from those of pyogenic osteomyelitis, consisting in narrowing of an intervertebral space followed by mild destructive lesions on the adjacent surfaces of the vertebral bodies. In two cases an associated paravertebral soft-tissue mass was present. In all six cases spontaneous regression of the changes, with reactive sclerosis and reduction of the irregularity of the vertebral erosions, took place after 2 to 3 months. Though the narrowed disk space became wider it never returned to its former normal width and the affected vertebral plates showed some residual abnormality of shape.

The findings in this series are compared with those in three similar small series reported respectively by Saenger (Amer. J. Roentgenol., 1950, 64, 20), Brenner and Neligan (Brit. med. J., 1953, 1, 856; Abstr. Wild Med., 1953, 14, 408), and Dupont and Anderson (Acta paediatr. [Uppsala], 1956, 45, 361), making a total of 21 cases available for study. These showed remarkable agreement in regard to sex distribution (equal in all four series), age incidence (7 months to 14 years), duration of symptoms on presentation (with two exceptions this was never longer than 2 months), the absence of evidence of systemic infection, and the radiographic appearances, both at the time of first examination and subsequently. The authors conclude that it is not clear whether these cases represent a new aetiological group or are merely variants of infectious spondylitis.

R. O. Murray.


This report from the University of Michigan compares and contrasts the radiological findings in the spine and pelvis in rheumatoid arthritis and ankylosing spondylitis, forty patients with advanced disease of each type being examined. There was a much greater proportion of females among the patients with rheumatoid arthritis (26) than among those with ankylosing spondylitis (7) and the average age was somewhat higher, though the duration of disease in the two groups was comparable.

Sacral-iliac lesions, found in all the cases of ankylosing spondylitis, were present in thirteen of the cases of rheumatoid arthritis. The latter differed in that the subchondral erosions were more clearly defined and showed less reactive sclerosis. Moreover, they were almost entirely confined to the true sacro-iliac articulations, which are shown by a radiograph of any anatomical specimen with a metallic marker outlining the articular surface to be restricted to the lower two-thirds of the joint, the upper third being the site of ligamentous attachments. This upper third was only once involved in the cases of rheumatoid arthritis, although in the late stages of that disease four showed fusion of the lower part of the joint. This was comparable to the fusion seen in the late stages of ankylosing spondylitis, but in
this condition involvement of the dorso-lumbar spine was generally present, a feature not seen in rheumatoid arthritis.

Erosions of the symphys pubis and ischial tuberosities, again more clearly demarcated and with less reactive sclerosis, developed in only three and five cases respectively in the group with rheumatoid arthritis compared with fourteen and nineteen in the spondylitic group.

Spinal changes in rheumatoid arthritis were virtually absent in the dorso-lumbar region, whereas more than half the cases of ankylosing spondylitis showed the classic signs of vertebral squaring, apophyseal joint ankylosis, and decreased disk height. In the cervical spine, on the other hand, vertebral subluxations and erosions affected half the cases of rheumatoid arthritis and were uncommon in ankylosing spondylitis.

R. O. Murray.


Thirty-four patients with ankylopoietic spondylitis and 58 with uveitis are reported, with results the same as noted in the literature. Spondylo-arthritis ankylopoietica was noted in 15-5 per cent. of cases with uveitis, and uveitis in 35-2 per cent. of patients with spondylo-arthritis. Only a mild form of uveitis was noted in spondylitis ankylopoietica. Both rheumatological and ophthalmological examinations should always be carried out in such patients.

W. H. Melanowski.


The authors conclude from their study of six cases that anterior uveitis is often the first symptom of rheumatism. This uveitis is plastic but not granulomatous. X-ray examination of the sacro-iliac joint is essential.

J. Rougier.


Report of a case of iridocyclitis in which routine aetiological research revealed a painless ankylosing spondylitis.

S. Vallon.


While osteosclerosis is frequently observed in several lower dorsal or lumbar vertebral bodies, its limitation to a single vertebral body is a rather unusual finding. This report from the University of Maryland, Baltimore, concerns sixteen examples of a solitary dense vertebral body collected by the author; of these, eight were due to focal Paget’s disease, five to Hodgkin’s disease, one to reticulum-cell sarcoma, and two to metastatic cancer. Other causes of such lesions, although recognized in the literature, were not encountered.

Solitary manifestations of Paget’s disease occur in about one out of ten cases, the spine being most commonly affected. Atrophy of the spongiosa produces coarse vertical trabeculation or subcortical sclerosis, and in this series the appearances were typical of those found elsewhere in the skeleton. A double contour or “picture frame” may result from subcortical sclerosis. Enlargement of the affected vertebral body was noted in six of the six cases, and in four cases confirmatory evidence of the diagnosis was found elsewhere in the skeleton.

Post-mortem evidence of bone involvement in lymphomatous conditions, including Hodgkin’s disease and reticulum-cell sarcoma, is found in approximately 50 per cent. of cases, but in only about half of these there are radiological signs of such involvement. Haematogenous spread commonly produces multiple bone foci often affecting the vertebral bodies. Localized involvement of a vertebral body was found to be associated with invasion of the periosteum and bone from neighbouring lymph nodes which had been involved by the disease. At operation these were surgically inseparable from the affected vertebral body. These bodies presented a dense and amorphous appearance, in two cases accompanied by evidence of extrinsic osteoblastic activity, with irregular bony proliferation externally along one or more margins.

The author regards this appearance as being characteristic of a lymphoma.

Osteoblastic metastases in the spine usually involve several vertebrae and are commonly secondary carcinoma of the prostate, although there may be other causes. Limitation of the lesions to a single vertebral body was found in two cases. The increase in density was like that seen with widespread metastases and consisted of patchy and confluent areas; it was therefore less homogeneous than that found in the other conditions described. The primary lesions in these cases were carcinoma of the nasopharynx and of the colon.

R. O. Murray.


(Miscellaneous)


In this study the relation between rheumatoid arthritis and pleural effusion was investigated at the Royal Infirmary, Blackburn. During a period of 15 to 39 months the two conditions were found to be associated in seven men aged between 25 and 66. In all of these the sheep erythrocyte agglutination test gave a positive result. The pleural effusion preceded the joint changes in two patients, but articular pain was the presenting symptom in three patients; in the remaining two the diagnosis rested almost entirely upon the laboratory findings. The investigations revealed no evidence of any other cause of pleural effusion such as tuberculosis or bronchial carcinoma.

The case records presented include an account of a man aged 50 who had a large right-sided pleural effusion, from which straw-coloured fluid was obtained on aspiration. The fluid contained no malignant cells or acid-fast bacilli, and guinea-pig inoculation of the fluid yielded negative results. Biopsy showed infiltration of the pleura with macrophages. In the 8th week of the illness this patient developed severe pain and swelling in the knee-joints, wrists, finger-joints, and right elbow. At this stage the erythrocyte sedimentation rate (Westergren) was 60 mm. in the first hour. Cortisone therapy was employed and 3 months later the patient was discharged on a maintenance dose of methylprednisolone. Some 28 months after first admission radiological examination of this patient showed erosions in the head of the proximal interphalanageal joint of one finger and also general periarticular demineralization in both his hands.

Another patient, a man aged 57, gave a history of pain in the fingers. He was referred to hospital after an attack of pleurisy. X-ray examination showed a small right pleural effusion; 6 months later the fingers had developed spindle-shaped deformities. A. Garland.


A man developed an attack of urethral discharge followed by fever, conjunctivitis, and migratory polyarthritis at the age of 25, another at 32, a third at 33, and had then at least 23 periods in hospital until he died aged 58 from arteriosclerotic and rheumatic heart disease. There were numerous attacks of iritis ending with blindness of one eye. Autopsy revealed an old yet active iridocyclitis, with numerous plasma cells and lymphocytic aggregations throughout the stroma of the iris and ora serrata. The findings in the other organs were also non-specific. G. von Bahr.


In this study, reported from St. Thomas's Hospital, London, and the M.R.C. Endocrinological Research Unit, University of Edinburgh, the urinary excretion of oestrogen in eleven patients with pulmonary osteoarthropathy (ten with carcinoma of the lung) was compared with that in a control group consisting of seven patients with carcinoma of the lung but without arthropathy (of whom three had digital clubbing), five with clubbing or gynaecomastia associated with other disease, and 24 healthy men. In the patients with pulmonary arthropathy the mean excretion of oestrogens was more than twice that in the controls; eight of the eleven excreted more oestradiol than normal, three more oestrone, six more oestriol, and seven more total oestrogens; the increase was greatest in respect of the oestradiol fraction. Between 4 and 8 weeks after removal of the primary pulmonary tumour in six of the cases, the oestrogen excretion had fallen to less than half the pre-operative levels, and in all had returned to normal.

The cause of this increased excretion of oestrogen is not clear. It could not be due to the tumour itself, as in those patients with tumour but without arthropathy oestrogen excretion was normal, and in one of the six operated cases the level of excretion increased considerably in the first week after removal of the tumour, nor was it associated with clubbing or with gynaecomastia. Further, the conjugation and inactivation of oestrogens were apparently not impaired, since it was found that the recovery of injected oestradiol in the form of the three urinary oestrogens was normal; likewise in the
patients studied there was no clinical or biochemical evidence of adrenal or hepatic abnormality.

A. Gordon Beckett.


A case of Reiter's disease is described in a man aged 26. The patient had been previously treated with quinine for malaria, and the erythrocyte sedimentation rate had been raised for a long time. In the second week skin changes similar to varicella occurred. Hyperkeratosis of the hands and feet was also observed. Eosinophilia (12 per cent.) was noted. The disease had lasted a long time and was resistant to treatment. Improvement was followed by a complete relapse after 2 years. Penicillin and sulphonamide helped only the conjunctivitis and urethritis. Aureomycin caused an exacerbation. Some good effects were observed after ACTH and streptomycin. As bacteriological examination was negative, a viral aetiology is suggested by the authors.

W. H. Melanowski.


Report of a case, emphasizing the severity of the disease when cutaneous manifestations are marked.

S. Vallon.


Report of a case cured by oral chlorocide (20 tablets daily, to a total of 80).

W. Leydhecker.


The Fiessinger-Leroy-Reiter syndrome has been frequently observed in Algeria. Its evolution is unforeseeable but it never has serious visceral localization. Corticotherapy is advisable during the acute phase.

S. Vallon.


The unusual signs of this case were the appearance of the syndrome in a French soldier who had been in North Africa for a long time, severe bilateral keratitis, and late articual complications 40 days after the onset of urethritis and conjunctivitis.

S. Vallon.


Eighty cases of the Fiessinger-Leroy-Reiter syndrome were studied. The disease appears to be of enteroviral origin. Good therapeutic results were obtained with cortisone, ACTH, and (chiefly) Nivaquine. S. Vallon.


A series of letters exchanged by the authors on this question.

W. Leydhecker.


Three weeks after apparent cure, the patient developed a severe inflammatory relapse of chronic evolving polyarthritis; recovery occurred after treatment with gold salts.

S. Vallon.


The authors studied radiographs of 46 patients with Reiter's disease and found a constant pattern. These bones and joints of the pelvis and lower limbs were mainly affected, showing periostal new bone formation and erosion.

W. E. S. Bain.


**Gout**


It is well established that agents which control hyperuricaemia beneficially affect the joint manifestations of gout and bring about a reduction in the size of tophi. Probenecid, which is generally considered to be the most satisfactory drug for prolonged treatment, was used as a standard for comparison of the effects of a newer agent, zoxazolamine, a muscle relaxant with a potent uricosuric action.

At San Patricios Veterans Administration Hospital, San Juan, Puerto Rico, thirty patients in whom the diagnosis of gout was established were assigned at random to one of two treatment groups—probenecid in a dosage of 1·5 g. daily or zoxazolamine 1·5 g. daily; after the first few days the dosage of zoxazolamine was reduced in most of the patients to 0·25 g. twice daily.

The fall in the serum uric acid level which occurred after treatment for one day and 3 days was significantly more rapid when 1·5 g. zoxazolamine was given daily than when the same dosage of probenecid or 0·5 g. zoxazolamine daily was administered. The effect of 0·5 g. zoxazolamine daily on the serum uric acid level and on the uric acid clearance rate was similar to that of 1·5 g. probenecid daily. Minor gastric discomfort occurred in two patients in each group and a drug rash was observed in two patients receiving zoxazolamine and one receiving probenecid. During the first day of treatment with 1·5 g. zoxazolamine, acute pain suggesting a renal or ureteric origin developed in five patients, none of whom passed a recognizable calculus. It is suggested that because pain occurred on the day of maximum uricosuria and abated quickly in spite of continued treatment, it was probably due to crystallization of uric acid in the kidneys. No similar reaction was observed in any of the patients given 0·5 g. zoxazolamine daily.

Probenecid is considered to be a very safe drug. Toxic reactions from zoxazolamine when used as a muscle relaxant have been infrequent, although serious complications have been reported. The author concludes that the clinical choice of drug will be guided by considerations other than the difference in uricosuric activity. 

*Kenneth Stone.*


Until comparatively recently there has been only an occasional reference in the literature to the regular use of small (suppressive) doses of colchicine as a prophylactic measure against acute gouty arthritis. In a preliminary study of the pattern of acute attacks unmodified by prophylactic measures it was found that about three-quarters of a series of 614 patients who could reliably recall the onset of their first attacks had a second seizure within 2 years of the first; in the remaining patients, however, this interval was very variable. In 506 of the cases the number of recurrences and the history were precise enough to discern a pattern of frequency and severity. It was found that in 47 per cent. there was the classic of increased frequency of attacks, in 34 per cent. there was a relatively constant number of attacks year after year, and in 17 per cent. there was no consistent pattern. In the remaining 2 per cent. the attacks decreased in frequency with time. Attacks, as judged by the disability involved, became increasingly severe with time in 24 per cent., were of constant severity in 56 per cent., and were so variable in intensity as to form no regular pattern in 12 per cent. In 8 per cent. attacks became less severe, usually as the result of prompt treatment.

Colchicine was tried in 208 patients (including eight females) who had had regular acute seizures of gout, classified as “severe” or “moderately severe”, for a period of years. The drug was given daily for at least 2 years, the average period of observation being 54 years. Tophi were seen in 95 of these patients at the start of the regimen and appeared in seventeen further patients during the period of observation. Stiffness, pain, and tophaceous involvement of joints indicative of chronic gouty arthritis were noted in 49 patients. The initial dosage of colchicine was 1 mg. daily, and this was maintained throughout in 138 cases. In 45 cases the daily dose was later reduced to 0·5 mg. or less, but in eighteen cases 1·5 to 2 mg. daily was administered. Minor bowel disturbances occurred at the onset of treatment in 4 per cent. of the patients, but tolerance was established by graduating the dosage or by giving the drug in enteric-coated capsules. Extra doses (2 to 3 mg. daily) were given to abort incipient attacks. Chlorothiazide and other drugs tending to incite acute seizures were, if possible, withdrawn, and uricosuric drugs were discontinued at the start of the regimen if the patient had frequent and severe acute attacks. Uricosuric drugs were later given, in addition to the colchicine, to 89 patients.

As a result of this prophylaxis 110 patients became virtually free from attacks and a further 72 had only mild episodes. In 26 patients there were still appreciable symptoms, but many of these patients were young, with disease that was fulminant or was complicated by other factors. No real difference was observed between the group given colchicine alone and the group given colchicine and uricosuric drugs. [These results relate exclusively to the incidence and severity of attacks.] Apart from bowel sensitivity in a few cases no side-effects of colchicine were encountered. The possibility of genetic consequences is considered, but there was no evidence of these in the present series.

The authors consider that colchicine is effective and reasonably safe and is probably preferable to prolonged daily administration of phenylbutazone. They emphasize that the prophylactic regimen described does not prevent the formation of tophi, for which uricosuric agents must be given. It is their practice to withhold the latter drugs until there are symptoms or signs of tophaceous deposits.

*B. E. W. Mace.*
interference with tubular reabsorption This has been attributed.

The authors have studied the uricosuric action of zoxazolamine, a compound which is not related to a wide variety of agents (including probenecid, phenylbutazone, and bishydroxycoumarin) that have previously been found to increase urate clearance in human beings. This pharmacological action is believed to be due to interference with tubular reabsorption of urate in the kidney, but there is no single component shared by these drugs to which one such constant uricosuric effect can be attributed. It has been established that the response to uricosuric agents of non-gouty subjects is essentially the same as that of patients with gout. The effects of zoxazolamine were assessed in 35 healthy volunteers at the Veterans Administration Hospital, San Francisco, by comparing the blood urate clearance values on two successive days. On the first (control) day no medication was given, but on the second zoxazolamine was administered in varying doses. The urate clearance values were paired with those for creatinine which did not change on the successive days. The effective dosage of zoxazolamine was about 50 mg.; below 25 mg. the effects were inconstant. The response to 125 mg. was better than that to 50 mg. and almost as good as the response to 250 mg. Aspirin given simultaneously with zoxazolamine caused a profound fall in uricosuria; the same inhibitory effects of aspirin were demonstrated when the drug was given with probenecid and sulphinpyrazone. "Acetaminophen" (paracetamol), which has analgesic properties similar to those of aspirin, did not interfere with the action of zoxazolamine. A rise in the blood urate level has been observed in patients receiving maintenance doses of chlorothiazide; in the present study neither chlorothiazide nor hydrochlorothiazide interfered with the uricosuric effect of zoxazolamine. The uricosuric effect of the simultaneous administration of probenecid or sulphinpyrazone with zoxazolamine was roughly equal to the sum of the effects of the two drugs. Unlike probenecid, zoxazolamine had no effect on the excretion of penicillin, phenolsulphonphthalein, or 17-ketosteroids. It has been reported that zoxazolamine given as a muscle relaxant in a dosage of 1 to 6 g. daily produces unpleasant side-effects; no such side-effects were observed with the dosage used in this study.

William Hughes.


This article from the Hôpital Lariboisière, Paris, describes the use of a new uricosuric agent, 2-amino-5-chlorobenzoxazole (zoxazolamine) in the treatment of nineteen cases of chronic gout. The average daily dose was 375 mg. and there was a mean reduction in the blood uric acid level by about one-quarter. In over half the patients gouty tophi decreased in size and the number of acute attacks was reduced.

As regards side-effects, in one case the drug caused severe anorexia and had to be discontinued. In other cases mild digestive disturbances did not call for cessation of treatment.

G. S. CROCKETT.

Diagnostic Significance of Hyperuricemia in Arthritis.


The diagnostic significance of raised serum urate levels in patients with gout or rheumatoid arthritis was studied at the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland. All the patients and a group of healthy controls received diets of a known purine content. The mean serum urate level in the controls as determined by an enzymatic spectrophotometric method was 5.1 mg. per 100 ml. in males and 4 mg. per 100 ml. in females.

Small to moderate doses of salicylate caused a rise in the serum uric acid levels in ten of the thirteen male patients with gout and three of the five males with rheumatoid arthritis. The opposite effect was noted in four female patients with rheumatoid arthritis. A similar difference between the response of males and females was observed in the group of healthy subjects. The only female in whom there was an increase in the serum urate level after salicylates was the daughter of a gouty patient. False high values for the serum uric acid level as determined by the colorimetric method were observed when the serum salicylate concentration exceeded 13 mg. per 100 ml., presumably due to chromagen derived from the salicylate; this effect was particularly noticeable in those gouty patients with renal disease.

From a further study of the difference between males and females in the response to salicylate the authors conclude that it may be related to a quantitative difference in the renal mechanism for the excretion of either uric acid or salicylate and that the lower serum urate levels found in females may be a reflection of the same process.

J. Warlick Buckler.


Gout plays no significant role in iridocyclitis. In routine blood uric acid tests in iritis a raised level was found in 3 per cent., whereas in the healthy control group it was 10 per cent. No explanation is given for this discrepancy in blood uric acid levels.

M. KLEIN.


An account of gout in all its manifestations, written primarily for the instruction of general practitioners in a country where this disease is rarely diagnosed. A critical appraisal is given of the value of the various types of drugs used in the treatment of both the acute and chronic phases.

W. S. C. Copeman.
Pararheumatic (Collagen) Diseases


The authors, working at the School of Medicine and Presbyterian Hospital, Pittsburgh, studied the localization of fibrinogen and/or fibrin, albumin, and γ globulin in the renal lesions of three patients with progressive systemic sclerosis (scleroderma) and three with malignant hypertension by the immunofluorescent technique.

The lesions in both groups were similar. The areas of mucoid intimal thickening of the small arteries and fibrinoid necrosis of the arterioles and glomeruli stained with the antifibrinogen serum, indicating the presence of material antigenically like fibrinogen, but contained little albumin or γ globulin. When the serum of one patient with scleroderma was conjugated with fluorescein iso-thiocyanate, staining of nuclei was observed, indicating the presence of antinuclear antibody. Sera from the other patients with scleroderma gave inconstant staining, while those from the patients with malignant hypertension gave negative results.

The authors conclude that the similarity of the renal lesions in these two conditions might reflect a common pathogenesis despite the differing aetiology of the basic disease process. G. L. Asherson.


The authors report from the University of Illinois College of Medicine, Chicago, a study of the level of antinuclear factor in patients with systemic lupus erythematosus (S.L.E.) and in their relatives. Antinuclear factor was measured by a fluorescent technique, using human buccal cells and reproducibility was good, titration of the minimum concentration of serum which gave a positive result showing variations of one tube or less in the ten sera studied. A titre of 1:4 was regarded as positive.

None of the forty healthy control subjects gave a reaction at a dilution of 1:4 and 33 were entirely negative, while of the fifty patients with a variety of diseases not related to S.L.E. only one gave a positive reaction. However, one or more samples of serum from 51 of the 56 patients with S.L.E. gave a positive reaction. Positive reactions were also found in the serum of 24 of the fifty relatives of these patients.

There was a general tendency for the titre of antinuclear factor to be higher in patients with clinical activity of the disease and histologically active renal lesions, but the titre was not consistently related to the serum γ-globulin level. Patients who were first observed during clinical exacerbation showed a fall in titre as their disease responded to large doses of steroids.

Two positive test results were obtained in seventeen patients with rheumatoid arthritis and in three out of ten patients with progressive systemic sclerosis; but in two patients with acute dermatomyositis and eight samples of serum from one patient with thrombotic thrombocytopenic purpura the results were negative.

The authors suggest that in systemic lupus erythematosus there is a breakdown of the mechanisms which normally prevent immune reactions against the patient's own tissues and they regard the occurrence of antibodies against nuclei in the relatives of patients with systemic lupus erythematosus as evidence that this abnormality is inherited. G. L. Asherson.


In this further study [see previous abstract] the authors have investigated the electrophoretic pattern of serum proteins in 49 patients with systemic lupus erythematosus (S.L.E.), observed the relation of this pattern to disease activity, proteinuria, and response to treatment with steroids, and compared it with that in 124 normal control subjects.

In the control group the negro subjects showed significantly lower levels of serum albumin and higher levels of γ globulin than the white subjects (full details of the values for the serum protein fractions are given in a table). In the patients with S.L.E. the total protein value was significantly lower only in patients with proteinuria. The serum albumin level was, however, lower than normal (even in the absence of proteinuria) and was related to disease activity. A rise in the α1-globulin level was associated with proteinuria rather than activity, while α2-globulin levels were raised in patients with inactive disease and proteinuria. The mean β-globulin level was generally unaltered, but showed a slight decrease in patients with active disease. The γ-globulin level was raised to an average of about 2 g. per 100 ml., the level being higher than normal in patients without proteinuria and lower than normal in patients with inactive disease and proteinuria. The authors graded disease activity from 0 to 3 and found that in patients without proteinuria the γ-globulin level rose from Grade 0 to Grade 2, but fell slightly in the patients with Grade-3 disease activity, even in the absence of proteinuria. Patients who died within 8 weeks after the test showed lower γ-globulin levels than those who survived. The ratio of albumin to γ globulin correlated well with disease activity and was less affected by proteinuria than was the γ-globulin value. Treatment with steroids led to a fall in the γ-globulin level and a rise in the serum albumin level in individual patients, this being probably related to the control of disease activity.

The authors raise the question whether there is a hereditary difference in γ-globulin levels in white and negro subjects and emphasize the unexpected fact that the highest γ-globulin levels were found in patients with intermediate disease activity. G. L. Asherson.
Treatment of Systemic Lupus Erythematosus with Steroids. 

The results of treatment with steroid hormones of 107 patients suffering from systemic lupus erythematosus over a minimum period of 2 years are described and compared with those reported by other authors.

The majority of symptoms are rapidly though not permanently relieved, but the effect on the mortality rate is uncertain in the absence of a control group. There is no doubt, however, that in individual patients the drugs are temporarily life-saving. The incidence of side-effects was felt to be remarkably low, and it is suggested that larger doses of steroid than those administered to this group of patients may be given for a longer time in patients not responding to treatment. There appeared to be no therapeutic advantages in using any one form of steroid hormone, but electrolyte disturbances will be less of a problem if the delta analogues are used. The E.S.R. [erythrocyte sedimentation rate] has not been found to reflect accurately the clinical state of the patient, and it is regarded as unwise to insist on maintaining a normal sedimentation rate using larger doses than are needed to keep the patient symptom-free.

At the present time, in the absence of a superior therapeutic agent, it seems imperative that patients ill with systemic lupus erythematosus should be treated vigorously with steroid hormones. [Panel's Summary.]


The authors, working at the Medical College of Alabama and the Veterans Administration Hospital, Birmingham, Alabama, studied sixteen of the 32 patients who had been seen in the Dermatological Clinic with chronic discoid lupus erythematosus of at least 2 years' duration to detect clinical and laboratory evidence of systemic lupus erythematosus.

Ten of the patients were male and one patient had rheumatoid arthritis. The erythrocyte sedimentation rate was raised in nine patients and the haemoglobin value low in one. Two patients had albuminuria. However, only one patient could be diagnosed as having probable systemic lupus erythematosus on clinical grounds.

Nevertheless, nine of the patients had a raised serum globulin content, two gave a positive result in the L.E. cell test and two in Coombs's test, one had a positive Wassermann reaction (with negative Treponema pallidum immobilization reaction), and three gave skin reactions to homologous leucocytes. The latex-fixation reaction was positive in four patients, and ten patients gave a precipitation reaction with deoxyribose nucleic acid.

The authors conclude that many patients with the diagnosis of chronic discoid lupus erythematosus have some of the serological features of systemic lupus erythematosus and raise the question whether those patients in whom the tests give positive results are more likely to develop frank systemic lupus erythematosus than are others. G. L. Asherson.


A long-term study of the therapeutic results achieved with antimalarial drugs in lupus erythematosus (L.E.) was carried out at the Mayo Clinic, the records being reviewed of seventy patients in whom the disease was diagnosed in 1952 and 1953. The patients were treated with quinacrine hydrochloride initially and with other antimalarials later. In two of the patients the original diagnosis was thought to be erroneous and one further patient could not be traced. Of the remaining 67 patients, nine died in under 5 years (three from L.E., four from carcinoma or cardiovascular accident, and two from unknown causes), and 58 were followed-up for 5 years or more.

The group of 67 patients included five with subacute systemic L.E., seven with chronic generalized discoid L.E., and 55 with chronic localized discoid L.E. The maintenance dosage of quinacrine was 100 mg. daily. On the basis of the response the patients fell into three groups:

1. Remission without relapse within 3 to 5 years (7);
2. Improvement but with relapses (50);
3. No improvement (10).

Patients who remitted showed improvement after 4 to 8 weeks, but in some remission occurred only after 4 years' treatment. One case history is reported, that of the only patient with subacute systemic L.E. who went into remission after 3 years of continuous therapy and has now lived 5 years without treatment or relapse. Of the ten patients who failed to respond, eight had discoid and two had systemic L.E. Chloroquine was found to be less toxic than quinacrine. It is pointed out that the effect of these drugs is suppressive rather than curative, relapses being the rule rather than the exception. Some patients responded better to one drug than to another; in subacute systemic L.E. added antimalarials may make it possible to reduce the dosage of steroids.

E. G. L. Bywaters.


Three patients are reported who developed the Stevens-Johnson syndrome after 18 months or more treatment with diphenyl hydantoin or trimethadione for epilepsy.

W. E. S. Bain.


In this paper, which is the first report of this disease to be published in Bulgaria, the author presents five
cases in women. The first patient had sarcoidosis. Histological examination showed granulomata of the lacrimal glands. The second patient had known a history of acrosclerosis. The third had chronic polyarthritis. The other two had rheumatic fever. All five patients had a very high erythrocyte sedimentation rate and considerable hypergammaglobulinaemia. Since the other symptoms differed in nature and severity while the ocular manifestations were typical in all the cases the author believes that the pathogenesis of kerato-conjunctivitis is not founded upon one aetiology.  
N. Blatt.

Affection of the Excretory Glands in Sjögren's Syndrome.  

Kerato-conjunctivitis sicca forms part of a complex syndrome. In three patients, all women, enlargement of the parotid with histological changes as described by Sjögren was found, polyarthritis with raised antistreptolysin titre, raised E.S.R., enlargement of liver, increased gamma globulin, decreased albumin, and normochromic iron deficiency anaemia. In one patient the changes started long before the menopause, Schirmer's test was normal in one case, in the other two tear secretion was almost nil; in one case achylia gastrica and oesophagitis coexisted, in another case a purpura, and again in one case a disturbance of pancreatic secretory function was found. The syndrome seems, therefore, to present disturbances of secretory function not only of the lacrimal and salivary glands but also of the sweat, gastric, and pancreas glands. Another constant feature is the occurrence of processes which can only be termed rheumatic, and are possibly at the root of the disease.
L. Wittels.

Sjögren's Syndrome: Clinical and Histological Aspects.  
14 figs, bibl.

Description of a typical case and extensive review of the literature.
A. Giardini.

Parotid Gland in Mikulicz's Disease and in Sjögren's Syndrome.  
Ann. Otol. (St. Louis), 69, 849.  
6 figs.

Kerato-conjunctivitis Sicca and Sjögren's Syndrome;  
Systemic Manifestations and Haematologic and Protein Abnormalities.  
Bibl.

Syndrome of Oedematous Exophthalamos, Pretilial Myxoedema, and Hypertrophic Osteo-arthritis after Thyroidectomy.  
France méd., 23, 189.
Non-articular Rheumatism

Lancet, 2, 1111. 15 refs.

This paper, from Farnham Hospital, Surrey, describes the clinical features, laboratory findings, and prognosis in twenty cases of the obscure, long-continued illness which had been called "polymyalgia rheumatica", observed by the author between 1952 and 1959. The ages of the patients when first seen ranged from 61 to 78 years and sixteen of them (80 per cent.) were females. The symptoms, which were insidious in onset, included headache, depression, general malaise, and widespread pains, particularly in the neck, back, and limbs, unassociated with arthritis. Night sweats occurred in five patients, of whom three were febrile, and four additional patients were also febrile. In nine patients the widespread non-articular pain was not present. [The author discusses his reasons for including these patients, but there is no evidence that they were suffering from a common disorder.]

The erythrocyte sedimentation rate (E.S.R., Westergren) was considerably elevated in all cases (75 to 138 mm. in one hour). Many of the patients had a normochromic anaemia. In thirteen patients tested the sheep cell agglutination test gave a negative result. In eight cases the patients were treated by rest in bed in hospital, and the remainder at home. Salicylates were given for relief of pain and two patients received phenylbutazone "which seemed to give greater relief than salicylates". Only one patient was given prednisolone. With this regimen all the patients improved, although in a few the E.S.R. remained abnormally high and in only two cases has it been persistently normal. In no case was death attributable to the disorder, the nature of which is unknown. 

Hewett A. Ellis.


In five subjects with symptoms similar to those described in "polymyalgia rheumatica" who were examined at the University of Manchester Rheumatism Research Centre the technique of Kellgren was employed in order to assess the type and distribution of pain after stimulation of a number of central joints and ligaments. The sites included the joints of the shoulder-girdle, the subacromial bursa, the manubrio-sternal joint, the intersosseous sacro-iliac ligaments, and the atlanto-axial interspinous ligament. After intradermal injection of procaine, saline solution was injected into the various sites.

Unilateral occipital headache was experienced by two subjects given the injection into the atlanto-axial interspinous ligament. So far as the acromio-clavicular joint was concerned, pain occurred about 15 seconds after withdrawal of the injecting needle. The area of maximal pain was at the top of the shoulder and from this point the pain spread up the side of the neck and downwards over the deltoid muscle. Injection of the subacromial bursa gave rise to pain in the lower part of the deltoid muscle and at the base of the thumb. Injection into the sternoclavicular joint was followed by pain over the joint, over the sternomastoid muscle, and also over a small area of the trapezius, while injection into the manubrio-ster nal joint produced unilateral pain about two costal spaces lower than the joint.

In all cases the distribution of the pain was similar to that experienced in cases of so-called polymyalgia rheumatica. The investigators conclude, therefore, that the syndrome of polymyalgia rheumatica is probably attributable to arthritis, mainly of the spine and limb girdles. In this context significance is attached to the fact that muscle abnormalities have never been detected in patients with the syndrome. By analogy, muscle pain may occur in ankylosing spondylitis, a disease in which the main pathological processes affect the spine.

A. Garland.

General Pathology


An evaluation to determine the significance of the results of the sensitized sheep-cell agglutination test was carried out on a group of 1,012 patients drawn from an arthritis out-patient clinic, from private practice, and from the wards of Kingston General Hospital, Ontario. The test utilized the euglobulin fraction isolated by dilution with 0·0027 N hydrochloric acid. The group included 217 cases of definite rheumatoid arthritis, 59 of possible or probable rheumatoid arthritis, and 736 cases of other rheumatic disorders. Definite rheumatoid arthritis stood out as having not only the highest incidence of positive reactions, but also a distribution of significantly higher titres than any other group.

Definition of a "false positive reaction", especially in a sensitive test such as this, is discussed. A positive reaction indicates the presence of a reacting macroglobulin which cannot as yet be differentiated into specific forms or specifically related to individual diseases. When positive reactions are obtained with non-rheumatoid diseases such as viral infections the titre tends to fall and the reaction remains positive only so long as the pathological processes concerned are active. The authors suggest that the concept should be discarded that a positive test result is specific for rheumatoid arthritis and that the result should be considered in relation to the total clinical picture. In this respect they grant relatively high priority (in terms of the diagnosis of rheumatoid arthritis) to high-titre positive reactions, the persistence or rise of positivity for weeks or months, and fulfilment of the diagnostic clinical criteria of the American Rheumatism Association. Details of the reactions in the various clinical groups are given [without, however, relation to specific clinical features such as the presence or absence of nodules].

Harry Coke.

The preparation of fresh tanned erythrocytes is time-consuming and therefore often inconvenient. In this paper from the Wellcome Research Laboratory, Beckenham, and the Middlesex Hospital Medical School, London, the authors describe a stable preparation of thyroglobulin-coated erythrocytes which can conveniently be used for detecting autoantibodies in the serum of patients with thyroiditis. Briefly, sheep erythrocytes are treated with tannic acid, coated with human thyroglobulin, and then treated with formalin. The preparation is stored at 4°C, is available for use at any time, and is stable for at least 9 months.

Agglutinin titres obtained with this preparation were fairly well correlated with the absolute levels of serum antibody estimated by quantitative techniques. A better correlation with absolute values could be achieved by the use of a haemagglutination inhibition test in which constant amounts of thyroglobulin were added to serum dilutions before they were titrated against thyroglobulin-treated cells. The application of this and other immunological tests to the differential diagnosis of thyroiditis, thyroid cancer, non-toxic nodular goitre, primary myxoedema, and thyrotoxicosis is discussed.

M. C. Berenbaum.


In this study from the University and Western Infirmary, Glasgow, the antithyroglobulin antibody titres (estimated by Boyden's tanned erythrocyte agglutination technique) in a series of 127 patients with collagen diseases are compared with those in 175 control patients with various conditions whose serum was submitted for blood grouping. Sera giving a positive response were subjected to precipitation tests by the Ouchterlony method, but only four gave a reaction (two from patients with Sjögren's disease and two from controls; three of the four had thyroid disease). All positive agglutination reactions were inhibited by thyroglobulin, but not by pooled γ globulin.

A higher incidence of positive reactions was found in the series with collagen disease than in the controls, the proportions being 27 and 12 per cent. respectively (P < 0.01, using Yates's modification of the χ² test). This increase in incidence is analysed according to age and sex and also in individual disease entities, selected control subjects matched for age and sex being used for this last purpose. There was a significant increase in positivity among 62 cases of rheumatoid arthritis, 26 cases of Sjögren's disease, and seventeen cases of systemic lupus erythematosus, which gave positive results in 24, 38, and 35 per cent. of cases respectively. One patient out of sixteen with discoid lupus, one out of five with scleroderma, and one with dermatomyositis also gave positive results.

The mechanisms of autoantibody formation are discussed and the conclusion is reached that an intrinsic abnormality of the immunity system may be an additional factor in the development of thyroid autoantibodies, particularly in patients who show evidence of other autoimmune phenomena. [However, no attempt is made to relate thyroglobulin antibody to the presence or absence of rheumatoid factor or of the L.E. cell phenomenon, which was present in only thirteen of the seventeen cases of systemic lupus erythematosus.]

E. G. L. Bywaters.


In this paper from the University of Greifswald, the authors report the results of a serological investigation into the occurrence of the so-called rheumatoid factor among patients of various age groups suffering from rheumatic and non-rheumatic disorders. The latex fixation test of Singer and Plotz, with slight modifications, was used, good correlation having been obtained between the results of this test and those of the Waaler-Rose test. A total of 911 sera were examined, of which 38 came from patients with rheumatoid arthritis. Of these, 24 (63 per cent.) gave a positive latex fixation reaction compared with 39 (1.9 per cent.) positive results among the remaining 873 patients.

When the age distribution of positive reactors was analysed a significant rise was noted in the middle of the fourth decade and again at the beginning of the sixth decade, irrespective of the clinical diagnosis. The possible interpretation of these findings is discussed.

H. F. Reichenfeld.


In this co-operative study between the Middlesex Hospital Medical School, the Rheumatism Research Unit of the Medical Research Council, Taplow, and the University Hospital of Leyden the occurrence of a positive L.E. cell reaction, antibodies against nuclei (A.N.F.) as demonstrated by the complement fixation and fluorescent antibody techniques, a positive latex fixation reaction for the rheumatoid factor, antibodies against human liver as shown by the autoimmune complement fixation (A.I.C.F.) test, and antibodies against thyroid tissue as demonstrated by the tanned erythrocyte and other techniques has been assessed in groups of patients with systemic lupus erythematosus (S.L.E.), rheumatoid arthritis (R.A.), and autoimmune thyroid disease or combinations of these. A different
control group of healthy and diseased persons was used for each test.

All the patients with S.L.E. had systemic involvement and a positive L.E. cell reaction. Patients with a clinical picture of R.A. with a positive L.E. cell reaction were not included in this group. The patients with R.A. were all “definite” or “classic” cases as defined by the American Rheumatism Association. Patients with autoimmune thyroid disease were selected because of their high tanned erythrocyte titre. Patients with S.L.E. or R.A. with evidence of thyroid disease were considered separately.

The full results are tabulated. The anti-nuclear factor reaction was positive in all but one of the 65 patients with S.L.E. studied, the A.I.C.F. reaction was positive in 37 per cent., and the level of anti-thyroid antibody was increased in 25 per cent. Of the 79 patients with R.A. alone, 20 per cent. had a positive L.E. cell reaction and 50 per cent. a positive anti-nuclear factor reaction. A low titre of anti-nuclear factor was found in fourteen of the 182 patients with uncomplicated Hashimoto’s thyroiditis. These reactions became negative if performed at 37°C instead of room temperature. Only in nine cases was the A.I.C.F. titre increased. In all the seven patients with R.A. and overt thyroiditis antibodies against thyroid tissue were present, and complement-fixing antibodies to human liver were demonstrated in five. Three of these patients had had positive L.E. cell reactions, but serum taken after prolonged cortisone therapy was negative for the antinuclear factor. In both S.L.E. and uncomplicated R.A. thyroid antibodies occurred only in women. On the other hand the A.I.C.F., latex fixation, and anti-nuclear factor reactions were positive in equal numbers in the two sexes. This suggests that the thyroid antibody may be related to a thyroid abnormality which is commoner in women than men rather than to a general abnormality of the antibody-producing system.

Discussing their findings, the authors suggest that autoimmune disease can be divided into two groups. In “disturbed antigen” disease it is considered that antigen, which fails to reach the antibody-producing system during the critical time for the induction of immunological tolerance, escapes from the tissues and provokes an immune response from a relatively normal antibody-producing system. On the other hand in “disturbed tolerance” disease the immune response occurs against widely distributed antigens to which the normal subject is presumably tolerant. Here a primary abnormality of the antibody-producing system is postulated. In Hashimoto’s thyroiditis the increased familial incidence of various thyroid disorders, including thyrotoxicosis, suggests a primary abnormality of the thyroid gland, while in S.L.E. the familial incidence of hypergammaglobulinaemia suggests a primary abnormality of the antibody-producing system. The antibodies occurring in these diseases may be considered in three groups—the organ-specific antibodies (such as those against thyroid tissue), the A.I.C.F. antibody, which reacts with non-organ-specific cytoplasmic antigens, and the antibodies against nuclei. These anti-nuclear antibodies occur in nearly all cases of S.L.E., many cases of Sjögren’s disease, and some cases of R.A. and hepatitis. The authors suggest that they may provide an index of disturbed immunological tolerance.

G. L. Asherson

Antibody Production in Rheumatic Diseases. The Effect of Brucella Antigen. MEISELAS, L. E., ZINGALE, S. B., LEE, S. L., RICHMAN, S., and SIEGEL, M. (1961). J. clin. Invest., 40, 1872. 3 figs, 20 refs. The possibility that a disordered immune response is related to the development of the rheumatic diseases, regarding which previous reports have been highly conflicting, was investigated at the Maimonides Hospital and the State University of New York Downstate Medical Center, Brooklyn, by observing the production of antibodies in nineteen patients with rheumatoid arthritis, eleven with systemic lupus erythematosus, five with acute rheumatic fever, and six with acute nephritis, following the subcutaneous inoculation of 0.5 ml. Brucella vaccine; a group of 27 hospital patients with miscellaneous disorders served as a control. Blood samples were usually obtained before inoculation and at 1, 2, and 3 weeks afterwards. In addition to the estimations of anti-brucella agglutinin titres, the samples were also examined for L.E. cells, rheumatoid factor, isohaemagglutinin titres, antinuclear antibody titres (using a fluorescent technique), and antithyroglobulin antibodies. Serum proteins were examined by paper electrophoresis and the sedimentation characteristics of the antibrucella agglutinins, rheumatoid factor, and antinuclear antibodies were determined by ultracentrifugal analysis.

Although there was some overlap between individual patients in the various groups, the patients with rheumatoid arthritis and systemic lupus erythematosus showed a significantly greater rise in antibrucella agglutinin concentrations than did the control subjects. Thus the geometric mean of antibrucella titres at 2 weeks was 80 for the 27 control subjects, 555 for thirteen patients with rheumatoid arthritis, and 400 for ten with systemic lupus erythematosus. Some patients with rheumatoid arthritis and systemic lupus erythematosus also showed changes in the titres of certain of the other antibodies studied. Of the eleven patients with systemic lupus erythematosus, four gave a positive result in the direct Coombs’s test, of seven with rheumatoid arthritis three showed a rise in the level of rheumatoid factor. Anti-thyroglobulin antibodies occurred in three of eleven patients with systemic lupus erythematosus and in five of fifteen with rheumatoid arthritis. None of the control subjects showed this abnormal type of response.

The nature of the non-specific response of certain of the patients with rheumatoid disease and systemic lupus erythematosus is unknown. The authors suggest that it may be a basic defect in some so-called “autoimmune” diseases. They consider that the hyper-response to Brucella antigen in these patients may be related to the known predilection the organism has for damaging mesenchymal tissue, which is the “target tissue” in rheumatoid disease. Ultracentrifugal analyses revealed...
that the antibrucella agglutinin, like the rheumatoid factor, belongs to the 19S class or γ-globulin. Further work is in progress to investigate the possibility that all the responding antibodies belong to the 19S class.

Hewett A. Ellis.


This work was undertaken at Cornell University Medical College, New York, in an attempt to determine the number and cellular origin of rheumatoid factors in rheumatoid arthritic synovial membrane by use of the fluorescent staining technique, employing two conjugates of different colours:

1. Apple-green fluorescein isothiocyanate conjugated with bovine serum albumin and its homologous rabbit antibody in the form of a soluble complex;
2. Human γ globulin labelled with orange-red rhodamine B200 which was prepared by heat aggregation, these two reactants being used either simultaneously or separately in sequence.

Synovial and lymph-node tissue was obtained by biopsy from seven adult patients with established active rheumatoid arthritis, while similar tissues from nine patients with various joint disorders but without rheumatoid arthritis served as a control.

By these means rheumatoid factor was found in the cytoplasm of the plasma cells in the synovium. When the two reagents were used simultaneously some cells reacted with one, some with the other, and a few with both. Cells stained entirely by the heat-aggregated globulin reactant were more commonly seen than the other varieties. Prior treatment of the sections with aggregated globulin inhibited subsequent staining by either conjugate, while their treatment with the unlabelled immune complex inhibited subsequent staining by the labelled immune complex, but not by fluorescent aggregate. From the evidence so obtained the authors infer the existence of two rheumatoid factors. In lymph nodes there was staining of the cells of the germinal centres and of plasma cells, similar in quality to that in the synovial tissue. It was noted, however, that in any particular centre the colour of staining was either all apple-green or all orange-red. These reacting factors were found to be present in all the specimens from the cases of rheumatoid arthritis, but not in the control tissues, including those showing other forms of synovitis.

G. Loewi.


In this investigation carried out at Duke University School of Medicine, Durham, North Carolina, after removal by precipitation from human plasma of the euglobulin fraction by the mineral acid dilution method a further precipitate was obtained from the supernatant by the addition of chondroitin sulphate. The precipitate thus obtained is termed the S fraction. It was strikingly increased in quantity by dialysing the plasma against a standard buffer in the first instance. This was reversible by the re-addition to the dialysed plasma of an organic, heat-stable substance in the dialysate. Numerous known dialysable plasma components were examined without identifying the substance active in these procedures. The biological significance of the increased chondroitin sulphate precipitate seemed related to the group of acute-phase reactants. A group of 26 patients with rheumatoid arthritis gave the highest lipid-protein fraction available for precipitation as S fraction in comparison with twenty active inflammatory cases and nineteen non-inflammatory cases. No quantitative differences were obtained by means of electrophoresis or Ouchterlony techniques, the latter showing the S fraction to contain fibrinogen and lipoprotein among its components. The cholesterol element of the fraction was high, especially in rheumatoid plasma. The S fraction inhibiting substance was also demonstrated in urine and cerebrospinal fluid.

Harry Coke.
tests was noted in a group of 104 cases of special diseases; among 43 cases of hepatic disorders there were fourteen positive results, and among 22 of peptic ulcer there were three positive results, while cases of influenza and mumps gave no positive results.

It is concluded that the reduced time for euglobulin fractionation has proved advantageous, while maintaining a comparable satisfactory degree of specificity and sensitivity for rheumatoid arthritis. Harry Coke.


The authors, working at the Aurora Hospital, Helsinki, and the Rheumatism Foundation Hospital, Heinola, Finland, have studied the relationship between clinical and serological findings in rheumatoid arthritis, the series consisting of patients with known rheumatoid arthritis and normal subjects who had been randomly selected during a study of the prevalence of the disease in Heinola, a town with a population of 10,000, in which every 10th inhabitant over 15 years of age was examined. Clinical examination was supplemented by radiography of the hands and feet and a lateral view of the cervical spine, and blood was taken for serological study, the following serological tests being carried out: the latex slide test, the bentonite test using one serum dilution, the latex tube test, and the Waaler-Rose test in which a titre of 64 or more was regarded as positive.

Clinical examination of the 539 persons in the study revealed nineteen with definite and 31 with probable rheumatoid arthritis according to the diagnostic criteria of the American Rheumatism Association. In five of the nineteen cases (26 per cent.) of definite rheumatoid arthritis, at least one serological test gave a positive result. For the group of probable rheumatoid arthritis the corresponding percentage was 23. The titre in the Waaler-Rose test was low (in the range 64 to 128), whereas the patients being treated in hospital for rheumatoid arthritis had a titre in the range of 250 to 500. In the remaining 489 persons the proportion of positive results in the serological tests were as follows: Waaler-Rose test 1-6 per cent., latex tube test 4-1 per cent., latex slide test 4-9 per cent., and bentonite test 1-4 per cent.; the titre in the Waaler-Rose test was low in this group. Only one serological test was positive in the great majority of subjects in the normal group, whereas in cases of rheumatoid arthritis usually several tests were positive concurrently.

C. E. Quinn.


This further investigation [see previous abstract] was carried out on 408 patients treated at the Rheumatism Foundation Hospital, Heinola, Finland, between 1958 and 1960, the diagnosis of rheumatoid arthritis being based on the clinical and radiological findings. As regards functional capacity the majority of the 408 patients, 128 men and 280 women, were in Classes II and III. The Waaler-Rose and latex tube tests were performed on all patients and the bentonite test in 260 cases. A positive Waaler-Rose reaction was obtained in 67 per cent. of cases and a positive latex tube test in 85 per cent. Most of the positive results of the Waaler-Rose test were in the titre range 250 to 500, there being relatively few low positive results. The results of these two tests agreed in 324 cases. Of the cases negative in the latex test, only five had a positive Waaler-Rose reaction, but the later test was positive in 79 cases in which the Waaler-Rose test was negative. The latter test was positive in 41 per cent. and the latex test in 63 per cent. of patients who had had rheumatoid arthritis for less than 6 months; in those in whom the disease had been present for 6 to 12 months the corresponding percentages for the Waaler-Rose and latex tests were roughly the same as in the series as a whole, this latter finding suggesting that the tests may be of some help in early diagnosis of rheumatoid arthritis. Of the 260 patients in whom the bentonite test was performed it was positive in 44 per cent., whereas in these patients the Waaler-Rose test was positive in 65 per cent. and the latex test in 82 per cent.

C. E. Quinn.


In this paper from the University of Zürich the authors report the results of the following serological investigations carried out on 930 patients with arthritic complaints: determination of the antistreptolysin titre, streptococcal agglutination, the antiglobulin consumption test; appearance of the L.E. phenomenon, various agglutination reactions with latex and Fraction II, and the Bentonite flocculation test.

By analysing the percentage of positive reactions obtained in various inflammatory and non-inflammatory diseases the following four types could be distinguished:

1. The streptococcal type; this was confined to cases of rheumatic fever, which all showed a high antistreptolysin titre, but negative results with the other tests.

2. The agglutinating type; this group included cases of rheumatoid arthritis and periarteritis nodosa, and in these there was a high percentage of positive results with various agglutination tests.

3. The L.E. type was seen in cases of lupus erythematosus, which nearly always gave positive results with the antinuclear factors and a high percentage of positive results with the agglutination reactions.

4. The non-reactors. These included patients with osteo-arthritis or gout, and the control group of patients with non-arthritic conditions.
It was noted that scleroderma seemed to fall between Types 2 and 3, giving a high percentage of positive reactions in the antiglobulin consumption test.

H. F. Reichenfeld.


Precipitating auto-antibodies, reacting with extracts of human and some animal tissues, were detected in the serum of nine of 29 patients with Sjögren’s syndrome. Two antigen-antibody systems are concerned, some serum specimens containing both antibodies, others either one alone. Antibodies reacting specifically with lacrimal or salivary gland extracts were not detected, but ten of the specimens of sera contained antibody to thyroglobulin. The results demonstrate that Sjögren’s syndrome is associated with both organ-specific and non-organ-specific auto-immune diseases.

J. Heaton.


ACTH, Cortisone, and Other Steroids


The author reports on the antirheumatic potency of a number of adrenocortical steroids which have been modified by slight deviations in chemical structure and which have been tested clinically at St. Vincent’s Hospital (Medical School of the University of Southern California), Los Angeles. The influence of a single chemical modification in the structure of hydrocortisone or cortisone, such as fluorination at C-9 greatly increases the anti-inflammatory properties of the steroid, but also produces such marked sodium-retaining and potassium-losing effects that it cannot be used systematically as an antirheumatic drug. On the other hand the introduction of a double bond at C-1-C-2 produced prednisone and prednisolone and increased the antirheumatic potencies about fourfold over the parent substances without a corresponding increase in electrolyte activity.

In the present study 32 corticosteroids containing two or more chemical modifications have been tested for antirheumatic activity. The method consisted in treating patients with active rheumatoid arthritis with an established steroid and then with the test substance in order to determine the dosage of each substance required to maintain equivalent clinical improvement. It was found, for instance, that 16α-methyl:9α-fluoroprednisolone (dexamethasone) was approximately seven times as potent as prednisolone. It is stated that the requirements for antirheumatic potency are: a double bond between C-4 and C-5 in ring A; an oxygen atom at C-3, at C-11, and at C-20; and a β-hydroxy group at C-17.

Oswald Savage.


In a study undertaken at the Vanderbilt University School of Medicine, Nashville, Tennessee, to determine whether the spirolactones directly influence the adrenal secretion of aldosterone five normal control subjects, one patient with primary aldosteronism, one with nephrosis, and one with hepatic cirrhosis, all being kept on a fixed daily electrolyte intake, were given spirolactones orally or intramuscularly in a dosage of 400 to 750 mg. daily in divided doses for 3 to 6 days; in two studies 50 μg. (20μc.) tritium-labelled aldosterone was given intravenously in order to determine the aldosterone excretion rates. Samples of 24-hour collections of urine were analysed for radioactive aldosterone, “tetrahydroaldosterone”, 17-hydroxy corticoid, 17-ketosteroid, and sodium and potassium content.

The urinary excretion of sodium and chloride was increased and that of potassium and ammonia decreased in all the subjects with intact adrenal glands. The excretion of radioactive aldosterone and tetrahydroaldosterone was either unchanged or increased. The aldosterone excretion rate, estimated by determining the degree of dilution of labelled aldosterone in the urine over a given time, was unchanged. No consistent alteration in 17-hydroxycorticoid or 17-ketosteroid excretion was observed to result from the administration of spirolactone.

The authors conclude that the spirolactones act by reversing the effect of aldosterone on electrolyte excretion and in the renal tubules, probably by competitive inhibition and do not directly influence aldosterone excretion, metabolism, or excretion by the kidneys. The increase in urinary aldosterone excretion which may follow spirolactone therapy is attributed to loss of total body sodium, which is in itself the physiological stimulus for increased aldosterone secretion by the adrenal glands.

Gerald Sandler.


The authors have described in a previous report seventeen patients in whom posterior subcapsular cataracts were observed in association with long-term steroid therapy. The lens opacities in these cases are considered in the present paper from a morphological point of view.

The cataracts are characterized by small granular subcapsular deposits located near the posterior pole. They can usually be distinguished from diabetic, traumatic, and dinitrophenol cataracts, but may be confused with the cataracts associated with intra-ocular disc ionizing radiation, and occasionally with the posterior cortical cataract of senility. J. R. Hudson.


In this further communication, the authors report an investigation of 72 patients with various rheumatic diseases treated with long-term steroids. All of twelve patients treated with 15 mg. prednisone or its equivalent daily for over a year showed the complications, and of the 72 cases, thirty (42 per cent.) were found to have subcapsular cataracts.

In seven patients with normal biomicroscopic findings on earlier examinations, posterior subcapsular cataracts were eventually found in all, following periods of steroid therapy varying from 1 to 6 years.

Pathological examination of the lenses of a corticosteroid-treated rheumatoid patient with posterior subcapsular lens opacities revealed in contrast to the usual senile cataract, remarkable preservation of the lens border in section and absence of cellular degeneration of the lens epithelium in whole mount. J. R. Hudson.


Forty patients on steroid therapy for rheumatoid arthritis were examined. Two patients only, a man and...
a woman, in the 50 to 59-year age group, had posterior polar cataracts. There was no control series. Both patients had a family history of cataract.

J. H. Kelsey.


This communication from the Mayo Clinic reviews the evidence for an association between Cushing’s syndrome and neoplastic disease. In a survey of the literature the authors have found reports of 58 cases in which neoplasm, other than pituitary and adrenocortical tumors, occurred in patients with Cushing’s syndrome. Of these growths eighteen were thymomata, 22 bronchogenic carcinomata, eight pancreatic carcinomata, and ten miscellaneous tumors. Soon after Cushing’s syndrome was first described its occasional association with a thymoma was noted.

Between 1932 and 1958, 232 cases of Cushing’s syndrome were seen at the Mayo Clinic, excluding those cases due to administration of exogenous corticosteroids or corticotrophin (ACTH). The adrenal glands were explored surgically or examined post mortem in 203 cases, when adrenal hyperplasia was found to be present in 151, benign cortical adenoma in 27, and cortical carcinoma in 25. In this series malignant tumors were noted in thirteen (5·6 per cent) of the cases and benign tumors in nine (3·9 per cent.). Of the malignant tumors, three were thymomata and two were tumors of the pancreas.

It is admitted that the series is too small to provide statistical support for a conclusion of causal relationship, but some features were noted that suggest this possibility, and encourage further study. For instance, it is striking that a high proportion of the malignant tumors associated with Cushing’s syndrome, both in the authors’ series and in the cases reported in the literature, have been tumors of the thymus, lung, or pancreas. One-third of these have been thymoma—a rare tumor. Further, it has been noted that some tumors in patients with Cushing’s syndrome have occurred at an earlier age than would be expected. These and other findings suggest that in some instances the relationship between the syndrome and malignant neoplasm is more than coincidental.

Kenneth Stone.


Other General Subjects


It is pointed out that the “trigger-point phenomenon” is frequently encountered in the practice of physical medicine, trigger-point being defined as a “discrete area of tenderness to pressure or to stretch probably no greater than 1 mm. in radius” which produces a violent reaction to stimulation. It is a point of extreme tenderness to palpation below the skin, in the subcutaneous connective tissue, in muscle, fascia, tendon, or ligament. This phenomenon may occur in a large number of conditions and is considered by the author to be a “pathophysiology” state rather than an anatomic abnormality; it “ceases to exist when removed for biopsy”. Excessively strong stimuli may initiate a vicious circle of impulses in a network of neurones so that a chain reaction is set up. Initially, excessive afferent sensory stimuli coming into the spinal cord may create an abnormal dynamic state of the neurones of the cord and cause a “reverberating circuit” which could prolong the trigger point state for months or years.

Treatment must be directed to breaking the vicious circle and this can be done by accurate infiltration of the area with a local anaesthetic, by cooling sprays, or by “routine” physiotherapy. The author has treated 123 cases which had failed to respond to other measures,
and claims that the results were excellent in 73 per cent.,
good in 17 per cent., and poor in 10 per cent.

This paper fails to convince. In tennis elbow, for
example, which falls within the definition of trigger-
point phenomenon, pain can also be elicited by putting
the forearm extensors into tension; moreover, in a
proportion of such cases (especially if the trouble is
bilateral) in spite of local signs and symptoms the ultimate
cause is found to lie in the cervical spine.

D. Preiskel.

Rheumatism in Cotton Operatives. Lawrence, J. S.

The incidence of rheumatism in a sample of 117 male
and 228 female cotton workers aged 45 and over was
compared with the incidence in a similar number of
control subjects who had never worked in cotton and
who were randomly selected from an urban and rural
population. More of the control subjects (89 per cent.
of males and 85 per cent. of females) than of the cotton
workers (73 and 74 per cent. respectively) gave a history
of symptoms of rheumatism and of loss of work because
of rheumatism. On the other hand the male cotton
workers had more severe osteo-arthritis in the finger
and thumb joints than the controls, as assessed by radiog-
raphy; it is suggested that this may be due to continu-
uous minor traumata. The authors conclude that “in
view of the relatively benign nature of the disease found
in cotton operatives, preventive measures are not indicated”.

John Pemberton.

Possibilities of Physiotherapy. (Möglichkeiten der Physio-
Therapie.) Hirschfeld, P. F., and Longton, J. E.

Contribution to the Problem of “Rheumatic” Back Pains.
(Beitrag zum Problem der “rheumatischen” Rücken-
20, 423.

Nocturnal Painful Acroparaesthesia and the Carpal Tunnel
Reumatismo, 13, 282. 3 figs, bibl.

Use of Baytinal in the Stretching of Contractures of the
Joints. (Über die Anwendung von Baytinal bei der
Streckung von Gelenkkontrakturen.) Riesz, E., and

Sympathetic Syndromes in Rheumatoid and their
Treatment with Hydergine. (Les syndromes sympa-
thiques en rhumatologie et leur traitement par
HyderGINE.) Langeron, L., Vincent, G., and Garry,

Use of a New Combination of Drugs and Steroids in the
Treatment of Rheumatic Diseases. (El empleo de una
nueva asociación con esteroides en el tratamiento de
las enfermedades reumáticas.) Barceló, P., and
3 figs.

Comprehensive Medical Care for Handicapped Children.
Glaser, H. H., Lynn, D. B., and Harrison, G. G.

Musculoskeletal Complaints in an Industry. Annual
Complaint Rate and Diagnosis, Absenteism, and
Arthr. and Rheum., 4, 283. 1 fig., 14 refs.

Dental Treatment of Rheumatic Patients. (Traitement
Méd. et Hyg., 19, 347.

CORRIGENDUM

In the paper entitled “Comparison of Differential
Agglutination Titre (D.A.T.) in Juvenile and Adult Rheumatoid
Arthritis”, by E. G. L. Bywaters, Mary E. Carter, and F. E. T. Scott (Ann. rheum. Dis., 1959, 18, 233), the following
correction should be made to Table III, p. 236:

<table>
<thead>
<tr>
<th>Age at Onset (decade)</th>
<th>0-9</th>
<th>10-19</th>
<th>20-49</th>
<th>50+</th>
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<td>Percentage Change in Functional Status</td>
<td>Improved</td>
<td>100</td>
<td>90</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Unchanged</td>
<td>0</td>
<td>0</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Worse</td>
<td>0</td>
<td>10</td>
<td>17</td>
</tr>
<tr>
<td>Total . . .</td>
<td>3</td>
<td>10</td>
<td>12</td>
<td>19</td>
</tr>
</tbody>
</table>

Bold numerals have been corrected.