ABSTRACTS

[This section of the ANNALS is published in collaboration with the two abstracting Journals, Abstracts of World Medicine, and Abstracts of World Surgery, Obstetrics and Gynaecology, published by the British Medical Association. The abstracts are divided into the following sections: acute rheumatism; chronic articular rheumatism (rheumatoid arthritis, osteo-arthritis, spondylitis, miscellaneous); sciatica; gout; non-articular rheumatism; endocrinology; general pathology; other general articles. At the end of each section is a list of titles of articles noted but not abstracted. Not all sections may be represented in any one issue.]

Acute Rheumatism


Several authors have described a proliferative endarteritis with occlusion of small cerebral vessels, areas of cortical devastation, meningeal fibrosis, and the formation of nodules composed of mesodermal and glial elements, in acute rheumatic fever.

Four cases are presented here because the neuropathological appearances considered to be typical of chronic rheumatic encephalitis were associated with unusual neurological manifestations.

The first patient, delivered by instruments of a syphilitic mother. At 3 years she had an acute attack of “brain fever” with convulsions. She became “difficult,” had an I.Q. of 43 and an enlarged heart with mitral regurgitation. She died at 35 years of pulmonary tuberculosis. Necropsy showed occlusion of small arteries and capillaries with endothelial and adventitial proliferation; lemon-shaped and butterfly-shaped areas of the cortex were devoid of nerve cells, and small nodules were scattered along the meninges. There was rheumatic endocarditis and mitral stenosis.

The second patient did not talk until the age of 3 years. At 10 she had chorea, became “difficult” with a low I.Q. She died at 21 of tuberculous pneumonia. Necropsy revealed old rheumatic endocarditis and endarteritis of the leptomeningeal vessels, cortical areas devoid of nerve cells, and demyelination and occlusion of vessels in the basal ganglia.

The third patient was normal until an attack of “brain fever” at 19 months, after which she was unable to walk or talk. Torsion and spasm of the muscles of the trunk and neck developed, with choreoathetotic movements of the limbs. A diagnosis of torsion dystonia was made. She died at the age of 19 years of bronchopneumonia. Necropsy revealed rheumatic endocarditis with mitral stenosis. The brain showed acellular cortical areas, endarteritis of meningeal vessels, and nodular thickenings of the arachnoid. The basal ganglia and cerebellum were most affected, and there were heavy deposits of iron in the globus pallidus.

The fourth patient was backward from birth and spoke and walked with difficulty. At 9 there was a right-sided pyramidal defect, and later a left-sided one also. She died at 11; at necropsy large deposits of iron were found in the globus pallidus. There was much glial proliferation, especially in the perivascular areas, around which there were necrosis and demyelination. The leptomeninges were thickened and there were granulomatous nodules along the walls of the lateral ventricles.

The histological findings in these four cases are those of a chronic productive encephalitis. The vascular changes in the brain, associated with similar alterations in vessels elsewhere, especially in the heart, are considered sufficiently specific to establish the meningo-encephalitis. The deposits of iron in the fourth case were far in excess of the amount expected in encephalitis and suggested a diagnosis of Hallervorden-Spatz disease, a familial condition in which extrapyramidal hyperkinesias appears at about 10, with death in the thirties. A large amount of iron pigment in the globus pallidus and substantia nigra is characteristic. The clinical signs also include pyramidal defect, gliosis and thickening of the leptomeninges. It is suggested that Hallervorden-Spatz disease may not be a degenerative morbid entity.

Torsion dystonia is a clinical concept and Hallervorden-Spatz disease primarily neuropathological. The fourth case suggests that torsion dystonia and Hallervorden-Spatz disease are manifestations of rheumatic meningo-encephalitis.


This is the second of two papers by these authors, the first dealing with the antistreptolysin-O titre (A.S.T.) of the blood in acute tonsillitis, and the present one with the titre when acute tonsillitis is followed by rheumatic fever. Serial investigations of A.S.T. and erythrocyte sedimentation rate (E.S.R.) were carried out on 96 patients with rheumatic fever, of whom 72 had a prodomal infection of the upper respiratory tract. The A.S.T. was raised in 90 per cent. of the patients and there was a correlation between this titre and the erythrocyte sedimentation rate. The two curves were of similar shape, the A.S.T. following the erythrocyte sedimentation rate after an interval of 1 to 2 weeks and being highest in the more severe cases. In rheumatic fever the A.S.T. reaches a higher level and the curve, although more gentle, is more prolonged than in throat infections not followed by rheumatic manifestations. In certain cases the A.S.T. remains elevated much longer than the erythrocyte sedimentation rate, and these patients were repeatedly found to harbour the haemolytic streptococcus in the throat.

The authors conclude that the greater production of these antibodies in rheumatic fever compared with uncomplicated throat infection is due to the fact that the patients are “immunized” by the recurrent streptococcal infections which are a feature of rheumatic fever.

Winston M. L. Turner.


The results are reported of prophylactic administration of sulphanilamide in the prevention of relapse
in children who have had rheumatic fever. The recurrence rate in 211 children aged 4 to 14 years who were given small daily doses of sulphanilamide was 3.2 per cent. In a control group in which the age distribution closely matched that in the trial group, the rate was 11.8 per cent. It is considered that this difference is statistically significant. The haemolytic streptococcal carrier rate was also determined, and a reduction in the incidence of group-A streptococci was found in the treated group. There was some increase in the incidence of group-A strains resistant to sulphanilamide in the treated group. It is considered that sulphanilamide prophylaxis is of value, should begin between attacks, and should be continued up to the age of 14 years.

A. Kekwick.


Heparin tolerance tests were carried out on 27 patients with rheumatic fever, sixteen normal subjects, and 26 sufferers from active tuberculosis. In acute rheumatic fever there is an increase in resistance to the anticoagulant activity of heparin. This resistance is related to rheumatic activity, but not to the erythrocyte sedimentation rate. The tuberculous patients showed some heparin tolerance, but this was far below that reached by the rheumatic patients.

Jeffrey Boss.


Two cases of rheumatic fever are described in both of which signs of abdominal disease warranted laparotomy. At operation a segment of the colon was found to be thickened, inflamed, and oedematous. In each case the appendix was removed and histological examination revealed chronic inflammatory reaction in the stroma of the peritoneal coat. There were no specific lesions characteristic of rheumatic infection, but the changes were similar to those found in the synovial membranes in cases of rheumatic fever.

In each case the condition in the colon subsided spontaneously during the week after operation. Investigations for the presence of any specific infective agent proved negative and the authors suggest that the lesions in the large bowel were manifestations of rheumatic infection.

Kathleen M. Lawther.


At the Massachusetts General Hospital an analysis was made of data involving 6,000 consecutive necropsies. The analysis showed that 436 patients had died from rheumatic heart disease and that 513 patients had died from coronary disease. In 32 cases both conditions were present, but in only seven of these cases was the correct diagnosis made before death. Moreover, in 21 of the patients suffering from the two conditions rheumatic heart disease escaped diagnosis during life. Among 10,000 cases of cardiovascular disease the clinical diagnosis of a rheumatic cardiac lesion with co-existent coronary disease was made in 57 cases. The presence of rheumatic disease was recognized in only 2 per cent of patients with lesions of the coronary arteries, whereas the combined lesions were found in 6 per cent of the series of necropsies on cases of coronary heart disease. On clinical examination the majority of combined lesions were discovered in elderly patients. It is not always easy to detect the presence of rheumatic heart disease in these patients, especially when there is no history of rheumatic fever. Even when auricular fibrillation is discovered the arrhythmia may not necessarily be a sequel to a rheumatic lesion. Usually little assistance is to be expected either from the radiological findings or from the electrocardiograms. Auscultation for the characteristic murmurs of mitral stenosis constitutes an important clinical aid. Sometimes the murmurs associated with a lesion of the aortic valve may be attributed to atherosclerosis instead of rheumatic disease.

It is considered that rheumatic heart disease plays no part in the pathogenesis of degeneration of the coronary arteries. This belief is supported by the fact that the series of necropsies did not include a single instance of the occurrence of combined lesions in a patient under 40 years of age. On the other hand, it must be borne in mind that the two conditions may co-exist. A. Garland.


The Q-T interval was studied in 134 cases of acute rheumatism: in one hundred of these cases there was other evidence of active carditis, and in twelve of inactive carditis. The Q-T interval corrected for heart rate (Q-Tc) was calculated from Bazett's formula Q-Tc = \[ Q-T \times \sqrt{C} \] (where C = cycle length). The upper limit of normal for Q-Tc was taken as 0.422 second for men and children, and 0.432 second for women.

Q-Tc was prolonged in ninety out of one hundred cases of active carditis. In two of the ten cases with normal Q-Tc pericarditis was present; this is known to shorten Q-Tc (digitalis also has this effect). In eleven of the 22 patients judged to have no carditis Q-Tc was prolonged, and in four of these cardiac damage was later revealed by the appearance of significant murmurs.

Return of Q-Tc to normal occurred rapidly in those patients with active carditis who made an uninterrupted recovery, but in cases of prolonged activity Q-Tc remained lengthened after active carditis had ceased as judged by other criteria. Development of relapses in some cases, however, suggested that a prolonged Q-Tc occurring alone could be regarded as evidence of persistence of activity. Length of Q-Tc was found to vary directly as the erythrocyte sedimentation rate in patients not suffering from pericarditis or receiving digitalis, except during the later phases of a prolonged attack. The fact that Q-Tc is prolonged in cases of cardiac hypertrophy limits the value of the measurement in longstanding rheumatic heart disease. J. W. Litchfield.


Although it has been amply demonstrated that the \( \beta \)-haemolytic streptococcus is implicated in the causation of rheumatic fever, its exact aetiological role is as yet unknown. Meyer (Physiol. Rev., 1946, 27, 335) has
suggested that hyaluronidase liberated by invading streptococci (which have been shown to produce the enzyme) may damage synovial and connective tissues, which are rich in hyaluronic acid, and this hypothesis is supported by the finding of a raised specific antihyaluronidase titre in the serum of children with streptococcal infection, particularly when rheumatic fever subsequently develops. The authors have now studied, in children with active and inactive rheumatic fever, Sydenham's chorea, and streptococcal pharyngitis, the concentration of the non-specific hyaluronidase inhibitor normally present in the serum and readily distinguishable from the specific antibody against hyaluronidase. [For details of the methods used, the original paper should be consulted.]

Whereas the concentration of hyaluronidase inhibitor in the serum of children with inactive rheumatic fever and with chorea uncomplicated by other rheumatic manifestations was generally lower (by about 40 per cent.) than the average for normal children, it was found to be raised significantly (by an average of 94.5 per cent.) in the serum of those with acute exudative rheumatism and those with streptococcal pharyngitis, the increase in individual cases being roughly proportional to the clinical severity of the attack. A similar rise in hyaluronidase-inhibiting activity of the serum has been reported in acute bacterial and virus infections, in disseminated malignant disease, and during involution of the uterus, and may represent either a non-specific defence reaction or a consequence of tissue destruction. On the other hand, the consistently lower values found among patients with inactive rheumatic fever and convalescents may be of significance in relation to susceptibility to rheumatic disease, although the authors emphasize that further research is necessary before any conclusions may be drawn.

D. J. Crowther.


The authors used heparin in the treatment of eight cases of acute rheumatism which had failed to respond to salicylate therapy (salicylate dosage and blood levels are not given). They observed dramatic improvement in seven cases which included two cases of severe panniculitis. For mild cases 100 mg. heparin was given intravenously 8-hourly for at least 5 to 7 days. In severe cases 300 mg. heparin in 500 ml. normal saline was infused over 24 hours, the daily dosage being gradually increased to 600 mg. and modified so that the coagulation time did not exceed 40 minutes. The course lasted for one week, and was repeated after several days in cases in which response was incomplete. Joint pains and swelling quickly subsided, abnormal cardiac physical signs and electrocardiographic changes disappeared, and erythrocyte sedimentation rates returned to normal; improvement continued after cessation of this treatment. After further observations of this therapy in chronic polyarthritis, pleural and pericardial effusions, pulmonary oedema, and post-phlebitic chronic oedema the authors are of the opinion that heparin has an anti-exudative effect, promoting resorption of exudates and oedema, as well as maintaining blood fluidity.

I. Ansell.


A satisfactory level of penicillin in plasma for about 3 hours after each dose was obtained by giving orally tablets of penicillin, buffered with calcium carbonate and suitably flavoured, in doses of 100,000 units twice a day. In 63 children who received this treatment for 7 months there was no group A haemolytic streptococcal upper respiratory disease, and only one child was found to be a carrier. Of 64 controls, four had group-A haemolytic streptococcal upper respiratory infection and eleven were proved carriers.

It is suggested that this method of treatment is likely to be effective in the prevention of rheumatic fever.

R. S. Illingworth.


Penicillin lozenges, containing 5,000 units each, were given to 22 children one hour after meals. They were found to produce a penicillin level of 0.5 to 2 units per ml. of throat secretion at the second hour, a level high enough to ensure bacteriostasis of susceptible organisms for practically 2 hours. There was no noticeable amount of penicillin in the blood. A control group of 22 children were given dummy lozenges not containing penicillin. Throat swabs from four of the treated children showed a growth of haemolytic streptococci, 34 of *Streptococcus viridans*, and four of *Staphylococcus aureus*. The authors conclude that this treatment should be of value in preventing relapses of rheumatic fever.

[The role of the 22 control children is obscure, because the result of throat swabs from these children is not given.]

R. S. Illingworth.


This work is reported from Columbia University and the Arthritis Clinic of the Presbyterian Hospital, New York.

Serum was obtained weekly from patients with rheumatic fever, 0.1 ml. of each specimen being mixed with an equal quantity of another sample from the same patient, incubated for 2 hours at 37° C., put in an ice-box overnight, and then centrifuged, agitated, and examined with a hand lens. Each sample was tested, with controls, against all the other samples from the same patient. The technique has been described in *J. exp. Med.*, 1939, 69, 143.

No correlation was found between the occurrence of precipitation and the occurrence of any clinical episodes of sore throat or rheumatic fever. Furthermore, when the test was positive, dilution with an equal volume of saline produced negative results; this tends to show that the sera did not contain true precipitins. Diluted positive sera did not fix complement. Carmine dyes and colloidion particles were used in an attempt to make the reaction more easily visible, but no agglutination occurred.

Extract of heart, lung, or placenta from rheumatic
SUBJECTS, 0.2 ml., was mixed with 0.2 ml. of serum taken from patients of the same blood group with active rheumatism. To this was added 0.2 ml. of diluted complement containing 4 haemolytic units. After 30 minutes' incubation 0.2 ml. of sensitized sheep erythrocytes was added. No evidence of complement fixation was found with dilutions of serum and tissue extract which were not anticomplementary alone.

To tubes containing 0.2 ml. of colloidal particles and dilutions of clear saline extracts of antigen (non-rheumatic heart), 0.5 ml. of dilutions of various antibodies was added. After 2 hours at room temperature the mixture was centrifuged, agitated, and examined. The method gave positive results with known antigen-antibody systems, but inconsistent qualitative relations were found when the same tests were repeated. There were no false-positive reactions. Further antigens were made up from various materials obtained at necropsy and prepared after storage with solid carbon dioxide by grinding with sand and extracting with cold saline to give a 20 per cent. mixture by weight. This was then centrifuged and mixed with sera of patients with active rheumatism or syphils and of the same blood group. The results were not specific. Normal sera rarely gave positive reactions with these antigens. Peter Harvey.


Rheumatic Heart Failure with Respiratory Failure. (1949.) Amer. J. Med., 6, 781.


Data on Rheumatic Fever and Rheumatic Heart Disease in Peru. (Datos sobre fiebre reumática y cardiópatía reumática en el Perú.) SUBIRIA CARRILLO, R. (1949). Gaz. méd. Lima, 4, 35.


**Chronic Articular Rheumatism** (Rheumatoid Arthritis)


The essential features of Felty's syndrome are chronic progressive symmetrical arthropathy, splenomegaly, and leucopenia with relative lymphocytosis and sometimes monocytosis. Additional features may include swelling of the lymph nodes, skin pigmentation, periods of pyrexia, hypochromic anaemia, enlargement of the liver, eosinophilia, and an achlorhydria that in some cases may be histamine-refractory. Many cases from the literature are discussed, and the authors add two of their own.

There are three theories concerning the pathogenesis of the syndrome. (1) The hypertrophied spleen inhibits maturation of the myeloid series of cells, and prevents their release into the blood stream. (2) The spleen destroys an excessive number of leucocytes, and this leads to an attempt by the marrow to respond with hyperplasia. (3) Both spleen and bone-marrow lesions are due to an infective agent, which also causes the joint lesions. The authors believe that there is a definite causal relation between the blood and marrow changes on the one hand and changes in splenic function on the other, because in some cases there is a certain correlation between changes in the size of the spleen and changes in the severity of the disease, and because in some cases splenectomy leads to a considerable leucocytic response. The syndrome is differentiated from Still's disease by the presence of leucopenia, the early appearance of lesions in cartilage and bone and, generally, the higher age incidence. Borderline cases, however, may occur. There is a certain resemblance to Banti's syndrome, so far as the changes in blood and spleen are concerned. Treatment is unsatisfactory. Some cases respond well to splenectomy by an increase in leucocyte count, occasionally with some improvement in the joint lesions and the general condition. Frequently, however, such improvement is only transitory. The less serious the changes in blood and marrow the more successful removal of the spleen is likely to be. Considerable narrow hypoplasia is a definite contraindication to the operation. R. Schneider.


The author discusses the fall in serum iron and rise in serum copper levels occurring in infections, considering these metals to be involved either in the production of antibodies, or as part of a non-specific and more primitive defence system, as the changes precede the formation of antitoxins. He regards his own observation of alterations in the serum iron level in patients with rheumatoid arthritis (as compared with normal fluctuations throughout the day found in controls) as indicative of an infective component in the aetiology of rheumatoid arthritis. As further evidence of infection he found the serum anti-streptolysin titre to be raised in 23 per cent. of his cases. More significant still appeared to be a positive finding in 65 per cent. of his cases on testing for agglutination for group A streptococci, the result being negative in all cases of long (10 to 20 years) duration. A case is described in which erythrocyte sedimentation rate, anti-streptolysin titre, and titre of agglutination of group A streptococci were observed throughout unsuccessful courses of treatment with gold and salicylates, and favourable treatment with streptomycin, and the use of these tests in prognosis and evaluation of treatment is recommended even if the role of streptococci in the aetiology and pathogenesis of rheumatoid arthritis remains obscure. D. Wolstenholme.


The author gives a long and detailed account of his personal experience of the treatment of cases of rheumatoid arthritis with gold salts. The cases were from both private and hospital practice. Many patients were not admitted to hospital and some were difficult to follow up. In the early cases a total of 1-2 g. of "myocrinus" in fifteen weekly injections was given. Later it was decided to halve the total dosage (0·6 g.) and to give 0·05 g. as the largest single injection. For the past 18 months very small doses of 7 to 17 mg. daily for ten to fifteen injections have been used, followed by a maintenance dose of 2 to 3 weeks for many months. Complications, of which an exhaustive list is given, occurred in many of his early cases, the commonest being stomatitis and dermatitis. With smaller doses there were comparatively few unfavourable reactions, and in a number of cases the condition was improved. Kathleen M. Lawther.


In an investigation of the acid-secreting function of the stomach in 200 cases of rheumatoid arthritis, by means

**ANNALS OF THE RHEUMATIC DISEASES**
ABSTRACTS


(Osteo-Arthritis)


Out of a series of 32 cases of sacro-iliac arthritis, thirteen patients were treated by partial resection and have been thoroughly studied. The aetiology was tuberculous in seven of the thirteen patients, of whom two died of post-operative sepsis (before antibiotics were available) and eleven were cured. Operation is indicated (1) when the sacro-iliac joint is the only, or the main, focus and abscesses reappear in spite of conservative treatment for 3 to 4 months; (2) when sinuses persist in spite of many months’ conservative treatment; and (3) when there is caries sica with persistent pain.

J. Agerholm-Christensen.


The average age of onset of the menopause in 99 women who developed idiopathic Heberden’s nodes was not found to differ from that of a control group. While in some individual patients there was a considerable interval between the menopause and the appearance of Heberden’s nodes, in the group as a whole the two events “seemed to be closely correlated in point of time”—where the menopause was early the onset of the nodes also tended to be early—the coefficient of correlation being +0·46 ±0·08. They therefore conclude, on statistical grounds, that 46 per cent. of the factors which determine the time of onset of the menopause are common to those determining the appearance of Heberden’s nodes. The authors review the literature of Heberden’s nodes in some detail. They point out some of the difficulties in determining the age at which the nodes first appear. It has been shown that there is a definite tendency for the condition to appear in families and it seems that the nodes develop in those individuals who are genetically susceptible to them. It is suggested that the factors which lead to the appearance of the nodes may be those which affect the peripheral circulation.

W. Tegner.


The authors describe in detail the technique and indications for the intra-articular injection of acid solutions which, they emphasize, should be used as a form of treatment only for post-traumatic arthritis and osteoarthritis. Complications are stated to be uncommon, and mainly due to faulty technique. The solution recommended is 0·2 per cent. lactic acid and 0·5 per cent. procaine in isotonic saline. The effect of the injection is to produce immediate relief of pain and relaxation of muscle spasm, thus increasing the range of movement at the joint. Two cases are described in detail, and the authors state that marked improvement resulted in about 75 per cent. of forty patients thus treated. [The joints affected and the length of observation are not stated.] Some cases (no details) were treated by injection of 1 per cent. procaine alone, and others by injection of a solution of monopotassium phosphate, but although some improvement was seen in these cases, it was concluded that the combination of procaine and lactic acid was more effective.

K. M. Lawther.


ABSTRACTS

Arthrosis of the Hip. (La coxarthrie ou coxarthrose.)

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(Spondylitis)

Pulmonary Disease Manifestations of Ankylosing

Ankylosing spondylitis or ankylosing spondylarthritis
tends to be associated with hepatic and renal inefficiency
and a make-up of personality sometimes loosely called
“neurotic.”

G. F. Walker.

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Ankylosing Spondylitis. Measurement of Hip and Spine
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Ankylosing Spondylitis. (Spondylarthrite ankylosante.)
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Course and Delimitation of Infective Spondylitis. (Verlauf
und Abgrenzung der Spondylitis infectiosa.) Tettge,

(English.)

Arthrosis of the Hip. (La coxarthrie ou coxarthrose.)

Ankylosing spondylitis or ankylosing spondylarthritis
affects not only the vertebral bodies and apophyseal
joints but tends invariably to limit freedom of movement
at the costo-vertebral articulations. By this process the
movements of the ribs are impeded and the thorax tends
to be held rigid in a position of maximum inspiration.
The important result of such rigidity of the ribs is lack of
expulsive power in coughing. Without power to cough
depends adequately a person is unable to expel mucus, bacteria,
and epithelial debris swept into the trachea by ciliary
action.

A point of clinical importance is that persons with
ankylosing spondylitis are more than usually prone to
pulmonary atelectasis in the presence of mild respiratory
tract infections. They are apt to suffer from deep-seated
pulmonary disease after upper respiratory tract infections
and they are liable to organic pulmonary disease after
anaesthesia.

Bronchiectasis, pulmonary fibrosis, and chronic
bronchitis must therefore all be looked upon as
accompaniments of ankylosing spondylitis. [There is a
well known clinical association between ankylosing
spondylitis and asthma. Also, ankylosing spondylitis


(Miscellaneous)


Undecylenic acid was used in the treatment of chronic psoriasis, the dose being increased over a period of at least 6 days until a standard daily dose of 19-8 g. was reached. This was given as fifteen "pearls", each of 0.44 g., orally three times a day. The side-effects, which were slight and transient, were mild gastro-intestinal upset, occasional nausea or vomiting, and "fishy-taste" eruptions, but these did not interfere with treatment. The stools became loose in most cases. Of the forty patients treated, eight had arthropathic psoriasis. "Unequivocal improvement" was noted in twelve patients, fifteen were "somewhat improved", in ten there was no change, and in three the condition was aggravated. Of the eight arthropathic patients, in seven the pain was relieved. No rationale for the treatment is suggested by the authors, who are continuing their researches on further controlled series. G. A. Hodgson.


The tendon lesions occurring in "rheumatic" conditions are briefly described, and the differential diagnosis is discussed. In rheumatoid arthritis these lesions are of two types. The first, a tendo-vaginitis, gives rise to cystic swellings of variable size attached to the tendons; these tend to come and go with exacerbations and remissions. The second is an inflammation of the tendon insertion, and gives rise to many of the periarticular symptoms.


The addition of aureomycin to the diet, subcutaneous administration, and gastric intubation of the antibiotic prevented and cured experimental polyarthritis of rats due to the L8 strain of pleuroneumonia-like organism. In vitro aureomycin prevented growth of this microorganism in broth. In preliminary clinical trials, several patients with chronic rheumatoid arthritis who responded unsatisfactorily to several therapeutic agents also failed to respond to aureomycin.—[Authors’ summary.]


The authors attempt to establish diagnostic criteria for "psychogenic rheumatism"—if this entity exists. Fifteen patients (fourteen women and one man) thought to be suffering from psychogenic rheumatism were subjected to psychiatric examination. A control group, consisting of patients of the same age and sex distribution suffering from painful somatic disorders of known causation (osteo-arthritis, brachial neuralgia, injury to a joint, cervical rib, periarthrits, intervertebral disk lesion, rheumatoid arthritis, and alveolar abscess), were investigated in the same way. Differences between the two groups were noted. Discomfort in the test group was clearly difficult to describe; descriptive terms used by patients in the control group were recognizable. Distribution of discomfort in the test group was usually extensive enough to merit the phrase "pain all over"—it was more or less localized in the control group. Discomfort was aggravated in the control group mainly by touch or movement; in the test group, by such factors as work, relaxation, mood, noise, heat, or cold.

In thirteen patients in the test group and in only two controls the onset was associated with emotional tension. In ten control patients, but in only one of the test group, no psychiatric abnormality was found. A summary of each case in the test group is given; each concludes with a tentative formulation of the pathogenesis of the rheumatic complaint. Some examples are: "somatic expression, perhaps in muscular tension, of strong moral resentment of father’s behaviour"; "somatic expression of self-punitive trend at her failure to bear children"; and so on.

The authors conclude that the condition seems to merit recognition as a clinical entity, and that it is aptly described by the term "psychogenic rheumatism".

K. Stone.


At Bellevue Hospital, New York, 28 patients with gonorrheal arthritis received 0.5 million to 7 million units of penicillin as the basic treatment over a period of 3 to 30 days. In each case a bacteriological cure was effected of the extra-articular focus of infection, such as the urethra or cervix, but the arthritis was not improved in five patients; it was, however, greatly improved in fifteen and cured in eight. Those cured had complete restoration of joint function; in those greatly improved, fever and inflammation quickly subsided and only slightly limited movement or tenderness remained; in the cases of failure there was residual deformity or no apparent improvement.

Because penicillin destroys gonococci so rapidly, prolonged immobilization should be replaced by increasing amounts of exercise and physical therapy to preserve joint function and to prevent disability. These results imply that penicillin administration supplemented by earlier physiotherapy and joint movement is at least as effective as, or better than, sulphanomide or fever therapy, and far superior to treatment given before the sulphonamide era.

T. Anwyl-Davies.
ABSTRACTS


Chronic pain in the shoulder may follow a single injury or repeated subclinical abduction strains. The three commonest lesions found are those of the supraspinatus tendon, those of the tendon of long head of biceps, and a subdeltoid bursitis. Initial treatment varies slightly, according to the lesion, but all three lesions if neglected give rise to a "frozen shoulder", the treatment of which consists of intensive physiotherapy, aided by procaine infiltration and blocking of the supraspacular nerve, or even the sternal ganglion.

The supraspinatus tendon is pressed between the acromion and the greater tuberosity during the middle range of abduction and this acromial friction may produce a tendinitis, a partial or total rupture of the tendon, or a reactionary ostitis of the acromion. Repeated procaine infiltration about the insertion of supraspinatus will relieve the tendinitis. Pain sensations from the shoulder may be arrested by procaine block of the supraspacular nerve at the supraspacular notch: a new approach is described by which the nerve is blocked at the spinoglenoid notch and the motor branch to supraspinatus spared. In cases of tendinitis resistant to treatment acromial resection is indicated.

The shoulder may also suffer friction in the bicipital groove, with consequent tenosynovitis, partial or total rupture, or habitual luxation. Local infiltration with procaine is again indicated, but for cases resisting treatment and for luxations fixation of the tendon in the groove may be required. The author believes that a chronic subdeltoid bursitis is always secondary to a tendinitis of the underlying supraspinatus. Six selected case reports are presented, illustrating these various treatments.

R. F. G. Sandon.


A form of polyarthritis, named by the authors "senile prostatic rheumatism", is described. It affects elderly men, and is accompanied by prostatic symptoms. The onset is usually acute, with pain and swelling of the hands and feet. A characteristic feature is oedema of the joints, soon followed by a fibrosis of the peri-articular tissues. The swollen fingers are held in semi-flexion, and movement is impossible. After weeks or months joints become less swollen, but remain stiff; there is no deformity of the joints, but the fingers are fixed in a semi-flexed position by fibrosis. The same process may involve feet, knees, and lumbar spine. Joint symptoms are accompanied by severe malaise. Radiologically, rapid decay of subarticular bone is visible, but there are no joint changes. The erythrocyte sedimentation rate is raised to from 40 to 80 mm. in one hour (Westergren).

The condition does not respond to gold therapy. Rapid improvement, however, usually follows the administration of stilboestrol. A daily dose of 5 mg. was given. Only two out of twelve cases did not respond.

When joint swelling had abated, physiotherapy was needed for the residual fibrosis. Four case histories are given.

K. Stone.


The authors have investigated the effects of different methods of applying heat to joints on the temperature within the joint. Simultaneous determinations of internal joint and skin temperature were made on 24 normal and arthritic subjects. Passive movement of the joint through its painless range raised the joint temperature slightly, the mean elevation in eight cases being 0-8° F. (0-4° C.). Active weight-bearing exercises produced a more marked effect.

After hydrotherapy in a Hubbard tank at a temperature of 101° F. (38-3° C.) there was little elevation in the joint temperature. A more marked effect was obtained by the application of radiant heat and the application of paraffin wax at a temperature of 130° F. (54-4° C.). Both methods raised the joint temperature about 3° F. (1·67° C.). Heat applied by conventional short-wave diathermy and by a microwave generator produced the most marked effect, raising the joint temperature 6 to 8° F. (3·3 to 4·4° C.).

The rate of cooling was more rapid in normal than in rheumatoid arthritic or osteo-arthritic joints and the authors suggest that retention of heat by the latter may be due in the first place to the excessive amount of fibrous and adipose tissue around the joint, and secondly to the diminution of its circulation. They point out that the methods of using heat in the treatment of arthritic conditions should be re-evaluated in relation to the change of temperature produced in the joint tissue and not simply to surface changes, as it is well known that pain which is relieved by the application of radiant heat is very often aggravated by the application of conversion types of heating, which would appear to have a greater effect on the intra-articular temperature.

M. H. L. Desmarais.


The intravenous injection of procaine is described as an adjuvant to other methods of treatment of chronic arthritis with the special object of alleviating pain and spasm. The results are considered sufficiently satisfactory to warrant further application and investigation of the method. In a series of 250 cases there was no fatality or morbidity, "although the intravenous injection of procaine was till recently regarded as an almost fatal accident". The aim of the method was to inject a maximum of 4 mg. procaine hydrochloride per kg. body weight, to be administered in 20 minutes. A 1 in 1,000 solution of procaine hydrochloride in isotonic saline was used, except in hypertensive patients, when 5 per cent. dextrose in water was substituted for the isotonic saline. For better control and ease of administration a rotameter, was used (Graubard and others, Anesthesiology, 1947, 8, 372). Infusions were given daily, weekly, or as governed by the degree of recurrence of pain. The
authors state that the treatment seems to have a cumulative effect, a longer period of improvement following each serial infusion. The authors' 10 patients, treated in the course of 3 years, received a total of 1,894 infusions, and the majority have been under observation for at least one year after the cessation of treatment. They are subdivided into three groups: rheumatoid arthritis, 54 patients given 526 infusions; arthritis due to direct trauma, 42 patients given 175 infusions; and osteo-arthritis, 154 patients given 1,193 infusions. The number of infusions per patient varied between 1 and 96. (Spondylitis ankylopoietica is included within the rheumatoid arthritis group.) The results (presumably in respect of pain) are classed as "good" in 199 cases, "fair" in thirty, and "poor" in 21; while in respect of mobility there was improvement in 211 cases.

The authors discuss the possible mode of action of procaine, which is largely a matter of controversy. The authors believe it to be due to the analgesic action of procaine on the "dysfunctioning capillary unit" of the affected joint and the irritated nerve endings therein, breaking the reflex arc pattern and thus permitting the return of normal circulation. Less satisfactory results have been reported to the authors by Whitaere, which they consider to be attributable to the increase of the patient's intake of ascorbic acid, which substance was apparently given together with the procaine in many of the authors' cases. In two of the cases reported the patient received 1 mg. of ascorbic acid for every 1 mg. of procaine given, that is, 280 and 220 mg. respectively of ascorbic acid per infusion. It was found that procaine, the ester of diethylaminoethanol and p-aminobenzoic acid was more effective than the diethylaminoethanol salt of p-aminobenzoic acid, which in turn was more effective than the substituted alcohol by itself.

[These results are somewhat difficult to assess in view of the unknown quantity of intravenous ascorbic acid, which the patients may have been given (see Lewin and Wassén, Lancet, 1949, 2, 993).] Harry Coke.


The reflex vasodilatation, as measured by skin temperatures, and the photoelectric plethysmograms of the fingers of sixteen normal controls and of eleven patients with chronic discoid lupus erythematosus and single cases of chronic disseminated, subacute, and acute lupus erythematosus have been studied under rigidly controlled conditions. It was found that the temperature of the lesions was higher than that of comparable areas of normal skin and the more active lesions tended to have higher temperatures. There was no apparent difference in reactive hyperaemia in the fingers of patients and the control group. The reflex vasodilatation of the fingers of the patients with chronic discoid lupus erythematosus produced by immersion of the legs in a bath of warm water was found to be slower than that of the controls. They also showed a decrease in the number of the prominent with chronic discoid lupus erythematosus showed abnormally long crest times and obliteration of the dicrotic notches. The patients with chronic disseminated, subacute, and acute lupus erythematosus had slower reflex vasodilatation and increased crest times and obliteration of the dicrotic notches in their photoelectric plethysmograms.

It is concluded that patients with chronic discoid lupus erythematosus have a defect in the circulation of the fingers. The possibility that this defect is due either to a change in the elasticity of the small arteries or an abnormal activity of the arteriovenous shunts has been discussed. It is suggested that chronic discoid lupus erythematosus may be a generalized vascular disease.—[Author's summary.]


A woman aged 36 years with acute disseminated lupus erythematosus of 9 months' duration associated with arthralgia, fever, and raised erythrocyte sedimentation rate was treated with 150 mg. adrenocorticotropic hormone (ACTH) daily for 5 days. There was almost complete clinical recovery but an immediate relapse following withdrawal of the drug. A second administration of the drug for 3 days again caused partial recovery but no further ACTH was available and the patient died. ACTH, 100 mg. daily for 5 days, produced dramatic improvement in a second case of acute febrile lupus erythematosus in a woman aged 30 years, but immediate relapse followed withdrawal of the drug.

The authors suggest that the treatment only masks peripheral manifestations of the disease and does not affect the underlying cause. They note the similarity between the effects of salicylates and adrenal hormone in this type of disease. John T. Ingram.


The treatment of 58 cases of miscellaneous "rheumatic" conditions with a slowly acting suspension of D-tubocurarine (3 per cent.) in wax and peanut oil (4-8 per cent.) is recorded. Good results are reported in the relief of muscle spasm and pain in non-adhesive periarticulars of the shoulder and low back pain due to acute strain and hypertrophic arthritis of the spine. The drug was ineffective in advanced rheumatoid arthritis, osteo-arthritis, fibromyositis, and "psychogenic" rheumatism. Among the toxic reactions accompanying its use were diplopia, vertigo, and severe muscle weakness, but these were relieved by giving neostigmine. Henry Cohen.


Impressed by the claims made by Szucs for the efficacy of calcium succinate and acetylsalicylic acid in the treatment of certain chronic rheumatic diseases the author investigated the effects of a combination of these drugs in 63 cases, 27 of rheumatoid arthritis, seventeen of osteo-arthritis, and nineteen of non-articular rheumatism. The improvement which was noted in rather more than half of the cases was chiefly subjective, and relapses occurred in half the cases shortly after treatment was discontinued. There were no controls nor was the effect of acetylsalicylic acid and succinate combined...

The effect of intravenous injection of procaine was tried, in a controlled study, on 33 patients suffering from a variety of painful disorders, 6 mg. per kg. being given in 0.1 per cent. solution in 20 to 30 minutes. Careful evaluation of pain before, during, and after the infusion was made.

In only one case (of low back pain) was major improvement attained. In four others improvement was greater, or more lasting, than could have been expected from other methods of analgesia. In the rest improvement was either minor and transient or did not occur. One patient died, presumably from procaine intoxication.

Ronald Woolmer.

ABSTRACTS


The difficulty of assessing the extent of a tear of the musculo-tendinous cuff of the shoulder-joint by clinical examination is well known; in this paper a practical test is presented for revealing those cases in which rupture is complete and in which, therefore, surgery might be indicated.

The test consists in infiltrating the area of the tear with a local analgesic; if the patient is then able to elevate the arm, the presumption is that the cuff is intact. If, however, despite anaesthesia the patient is still unable to initiate and sustain abduction, rupture of the cuff is to be presumed. In the six patients in whom the cuff was explored as a result of this test, tears were found in all cases.

Clinical investigation of 109 cases diagnosed as supraspinatus tears showed that in 87 per cent. there was complete recovery in an average of 5± weeks if the condition was originally regarded as "mild". In those cases with symptoms clinically assessed as "severe" recovery was complete in 50 per cent. in about 12 weeks.

John Charnley.


The pathology of the "frozen shoulder" is discussed, the author quoting authorities who state that the prognosis in this condition is excellent, though it may take from 6 months to 2 years for painless movement to be regained.

This is not the author's experience, for of 21 patients only six regained normal function after 3 years, while nine had both weakness and pain and six had either weakness or stiffness. Biopsy material was obtained from four patients and compared with similar specimens taken from the bursa, supraspinatus tendon, and biceps tendon removed from normal patients at necropsy.

The author is of the opinion that the initial lesion is a degenerative one in the supraspinatus tendon, and that the process does not start diffusely throughout the capsule and the whole of the tendinous cuff, as is perhaps generally imagined. The nature of the degeneration is unknown, but the author has seen necrotic areas in the tendon, with a surrounding inflammatory process as a secondary phenomenon.

John Charnley.


The principles underlying the operation of excision of the acromion for shoulder pain are described. The simple mechanical explanation is accepted that lesions of the supraspinatus tendon produce pain on abduction of the arm because these tissues are pressed between the acromion and the humerus in full abduction.

In the first nine cases in which the acromion was excised, five unsatisfactory results were obtained; this was attributed to the fact that only the bone distal to the acromio-clavicular joint was resected. The whole acromion should be resected through the acromio-clavicular joint, and the cut edge of the deltoid muscle should be sutured to the coraco-acromial ligament.

The author is an enthusiast for the operation as a result of personal experience his own acromion having been resected, and he reports results in 95 cases, in eighty of which the operation was completely successful. Apparently only four patients in the series gained no relief at all. At operation in 56 cases there was induration and injection of the tendon, with oedema of the synovial lining of the bursa. In ten cases no lesion of the supraspinatus tendon appeared to be present, but the walls of the bursa were red and thickened and the cavity contained free fluid and in a few instances, small loose bodies. In fifteen cases calcified deposits had been seen in radiographs and the tendon appeared rough,


This paper deals with those cases in which calcification is seen in radiographs of the supraspinatus tendon and in which there is characteristic sudden spontaneous pain of extreme severity. This violent pain continues for several days, and calcification is seen in the tendon at the first radiographic examination.

This interesting group constituted 1 per cent. of 300 cases of painful shoulder reviewed. Six cases are reported and the interesting observation made that complete recovery occurred spontaneously in 14 to 28 days, during which time absorption of the calcified deposit took place.

Recovery when rest and heat are used in these cases is as rapid as when analgesics are injected or attempts made to irrigate through two or more needles. The author believes that the violent onset of pain is due to extrusion of the calcified deposit from the tendon into the subdeltoid bursa, and suggests that the more acute the onset, the more rapid will be the spontaneous cure.

John Charnley.
thickened, and opaque. In fourteen cases tears of the supraspinatus tendon were found, but there was no retraction of the torn end.

Exact details of operative technique are given. Excision of the acromion is contra-indicated if there is doubt about the diagnosis or if there is true limitation of shoulder movement. John Charnley.


The author discusses the causes of chronic hydrops of the knee and reviews the results of 36 operations for partial synovectomy carried out on 34 patients. In fourteen cases the patient had had polyarthritis for an average of over 5 years, and in twenty, hydrops of unknown or uncertain origin for the same period. In one case in the former group patelllectomy was performed, and in about half the cases in the latter group chondrectomy was carried out at the same time as the synovectomy.

At follow-up examination 2 to 11 years later 21 out of 34 patients were free from exudate (six of the fourteen with polyarthritis and fifteen of the twenty with hydrops). In the cases with polyarthritis, however, the value of the operation is reduced by the considerable risk of reduced mobility of the joint. Careful selection of the cases for operation is important. J. Agerholm-Christensen.


This paper is an admirable, practical, and commonsense clinical study of 100 cases of shoulder disorders characterized by pain, limitation of movement, and normal radiographic appearances. Cases of calcification of the supraspinatus tendon have been excluded. All patients had been discharged from treatment for one to 3 years at the time of the review. The average age was 52, the sex-distribution approximately equal. A definite history of injury was present in 60 per cent.

Three clinical groups are recognized: (1) rupture of the supraspinatus tendon; (2) supraspinatus tendinitis; (3) capsulitis. Rupture of the supraspinatus was encountered in twelve cases. This condition is diagnosed when, after an injury, the patient is unable to elevate the arm, though the range of passive movement is full. The deltoid contracts strongly, but is unable to move the arm because the fixing action of the short muscles is lacking. It is impossible to determine clinically whether the rupture is complete or incomplete because the infraspinatus is a more powerful fixator of the humeral head than the supraspinatus, and its action is probably also inhibited.

Supraspinatus tendinitis was encountered 27 times. Here, after injury or even spontaneously, pain develops at the mid-range of elevation, though all passive shoulder movement is free. There is often an abnormal scapulo-humeral rhythm. The author considers that impingement of the humeral head on the acromion is not always the correct explanation because the syndrome in one case followed a suture of the supraspinatus where the whole acromion had been removed. He therefore inclines to the view that the pain is directly due to tension in the supraspinatus tendon.

Capsulitis, found in 61 cases, may occur spontaneously or after injury, and is characterized by pain associated with limitation of both active and passive movements. The author differentiates early and late stages; the early phase he calls "irritative capsulitis," full range of movement being present under anaesthesia, while in the later stage, "adhesive capsulitis," there is limitation of movement under anaesthesia.

The results in this series of 100 cases do not suggest that surgical treatment is advisable. Of twelve cases of rupture of the tendon five were treated conservatively and all patients returned to full work. In the remaining seven complete rupture was present, and complete acromionectomy was carried out, but only two of the results were regarded as good. The two good results were in cases in which the tendon was sutured longitudinally without attempt to re-attach to the tuberosity. Of the 27 patients with tendinitis thirteen recovered full function without treatment, or without anything more elaborate than rest in a sling. In the remaining fourteen the acromion was excised; in eight cases tears in the region of the supraspinatus were present; this illustrates the difficulty of differentiating clinically between tendinitis and rupture of the tendon. In two cases there was swelling of the tendon and splitting of the upper surface. The best results were secured when the tear was brought together longitudinally without tension: results were bad when an attempt was made to suture the tendon to the tuberosity.

In twenty of the 61 cases of capsulitis the lesion was diagnosed as "irritative" and the average duration of pain was 7 weeks. There was no evidence that elaborate splintage in abduction was better than a sling, and many patients could not tolerate an abduction frame because of pain. Full movement was restored within 3½ months. In only three cases did the condition progress to adhesive capsulitis and require manipulation.

All 41 cases of adhesive capsulitis were treated by manipulation under anaesthesia and splinting in abduction for 2 weeks, active movements being encouraged throughout. Full recovery was obtained from 2 weeks to 4 months after manipulation. In five cases manipulation was repeated twice, but in the remaining 36 only one manipulation was necessary.

The author considers that approximately 25 per cent. of cases of painful shoulder are probably due to rupture of the supraspinatus tendon. John Charnley.


The author is interested in the relation of radiological changes in the head of the humerus to lesions of the musculo-tendinous cuff. He believes that radiological changes are present before there is clinical evidence of rupture of the tendons.

Photographs are reproduced of necropsy material from a man who died of head injuries, and had no symptoms of shoulder dysfunction. Cystic degenerative changes in the head of the humerus were radiologically demonstrable. It is believed that this degenerative process is of primary importance in the aetiology of complete and incomplete tears of the musculo-tendinous cuff. In 145 cases of shoulder pain following injury the most significant finding was that every patient with
radiological evidence of degeneration in the humerus reported residual disability 6 to 12 months after injury; by contrast, in no case without these changes were there any residual signs or symptoms. John Charnley.


[Results in Rh. Arthritis and Fibrositis showed that the Treatment was of no value.—S.G.]


Sciatica


The author tries to show that sciatica is not due to root compression alone, since compression can occur without pain. He believes that a non-specific infection occurs in the roots, and quotes the histological findings of others in support of his thesis. The local anatomical arrangement—deep root pockets in the lumbo-sacral segments and connexions between the meningeal spaces and radicular lymph channels—favour the localization of an infection at the level of the L5 and S1 roots. Moreover, the erythrocyte sedimentation rate is often raised and in some of his cases there was a history of preceding acute respiratory infection.

In three cases root section was performed because of intractable pain, and study of biopsy specimens revealed chronic non-specific neuritis with round-cell infiltration, especially in pericapillary areas. Case histories are given. Disk protrusion was not found in any. He considers that compression, usually from a disk, leads to nerve irritation, this being aggravated in the lumbo-sacral area by movement of bone over a relatively fixed nerve, and that infection subsequently localizes there with resultant sciatica. Sciatica is uncommon in the old because the joints are rigid, and uncommon in the young because disk protrusion is rare. Perhaps therefore a stabilizing procedure should be performed if laminectomy is undertaken.

The pain of sciatica is, he considers, at least partly sympathetic in origin; lumbar block may relieve the pain, coldness, and hyperalgesia arise from vasoconstriction, and an intragluteal histamine injection gives a weak response on the affected side. Pain on sneezing or coughing may be due to sudden movement at the lumbar joints; the author has never been able to cause pain by jugular compression. (Naffziger's sign is not mentioned.)

[This is a long and largely theoretical paper. A long index to the literature is given but few non-continental authors are quoted.]

D. P. Jones.


The incidence, frequency, and relation of attacks of cramp in patients suffering from sciatica caused by prolapsed intervertebral disk were investigated in 204 cases. All the patients had been operated upon and in 142 of them the operation had included the division of one or more posterior roots. In sixteen patients (8 per cent.) cramp occurred before the operation and in six it persisted afterwards. In 52 patients (26 per cent.) cramp first came on after operation. The calf muscles were the commonest site and in most cases the attacks were nocturnal. Post-operative cramps were frequent immediately after the operation and disappeared gradually within 5 years. Sex, age, the presence of arthritic spinal changes, and severity of sciatic pain appeared to play no part in the aetiology. The degree of weakness and wasting of muscles was not significantly different from that seen in patients without cramp. Neither the incidence nor the site of cramp bore any definite relation to the level of the prolapsed disk, though there was some indication that a large lateral prolapse was more likely to cause cramp. The presence of cramp appeared to have no prognostic significance for the therapeutic result of the operation.

On the other hand, a division of one or more sensory roots had been performed in 43 (83 per cent.) of the patients with post-operative cramp and in 99 (65 per cent.) only of those who did not develop cramp. [The difference is statistically significant. \( \chi^2 = 5.6, P = 0.02 \).] There was a slight tendency for the thigh muscles to be more affected by cramp when the 4th lumbar root was divided, and for the foot to be more involved after-division of the 5th lumbar and 1st sciatic roots. Post-operative cramp seems more likely to occur the longer the duration of symptoms before the operation. It is considered probable that damage to the sensory roots is causally related to the incidence of post-operative cramp.

F. K. Taylor.


In a series of 151 cases of sciatica in which laminectomy was performed for a ruptured intervertebral disk, there were 34 instances in which the findings were doubtful,
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Of these, 32 cases are discussed in some detail and in 18 the underlying pathology is considered. It is suggested that eight were due to a bulging disk, four were due to bony hypertrophy, one was due to spondylolisthesis and that one was due to dural deformity. In the remaining fourteen cases the findings were negative but, in spite of this, laminectomy was sufficient to give satisfactory results in eight instances. In the analysis of these 34 cases the authors have laid down a code of rules for the handling of cases of low backache and sciatica.

G. F. Rowbotham.


The lumbar spine was examined radiologically and anatomically post mortem in 100 cases, and 15,160 patients with backache were studied, during the years 1936-46; 9,419 of the latter were also radiographed. It was found that regressive changes in the intervertebral disks increase with age, and that definite degeneration must be presumed when there is rupture of the annulus. In principle, the disk degeneration is an osteoarthritis. When radiographs show instability—which may be one of the first signs—narrowed interspace, sclerosis, and osteophytes, the degenerative changes in the disk are marked. Normal radiographic appearance does not mean that the disk is intact. Instability was the only radiographic sign in 15 per cent. of patients with disk degeneration. It was seen in 70 per cent. of cases of degeneration of the 4th lumbar disk, which is the disk most frequently affected. The 4th disk was affected in 47·6 per cent. of all cases of degeneration, and the 4th or 5th disk in 75·2 per cent.

J. Agerholm-Christensen.


Gout


Case histories are used to illustrate the clinical variations of gout. The following features are thereby stressed:

1. The severity can vary from mild to severe and crippling, and the age of onset from youth to old age.
2. The disease may be associated with kidney lesions that lead to uraemia, or that conversely renal disease may lead to metabolic gout and eventually to a degree of gouty arthritis.
3. The passage of urate stones or gravel may precede or be associated with the disease, but that gout is not an inevitable consequence of urate stones.
4. Trauma may precipitate the onset of an attack, and obscure the correct diagnosis.
5. Rheumatoid Arthritis may occur in association with gout, and require separate treatment.

David P. Nicholson.


Neither the traditional association of gout with "liverishness" nor the scientific suggestion that gouty hyperuricaemia results from a deficiency of uricolytic enzyme in the human liver will bear scrutiny if the latter is undertaken with proper scepticism. From the data herein presented, including a great array of tests of liver function in patients showing various forms of gout, and from a critical review of the literature it is clear that, except in the presence of an independent complicating morbidity process, liver function is normal in gout. Gout is not, as a rule, associated with functional hepatic impairment. Disease of the liver is neither a cause nor a result of gout.

G. F. Walker.


Whereas in the general population the incidence of a blood uric acid content higher than 6·5 mg. per 100 ml. was, in those of normal kidney function, approximately 1 in 26, practically every patient with gout showed a hyperuricaemia. In the relatives of gouty patients the incidence of hyperuricaemia was 18 per cent. among eleven mothers, 17 per cent. among 24 brothers, 21 per cent. among 24 sisters, and 15 per cent. among 33 sons, though not a single daughter among 45 tested had hyperuricaemia. In the male this hyperuricaemia was found to be independent of age; in the female it appeared after the menopause.

On the assumption that gout and hyperuricaemia are the expression of the same genotype, both in the same family and in different families, it resembles in some cases an autosomal recessive, in others an autosomal dominant. The authors assert, however, that this is satisfactorily explained if the gene involved is an autosomal dominant which lacks penetration in both sexes, but with a much lower penetrance in female than male. A tentative estimate of the penetrance, which is in good agreement with a tentative estimate of gene frequencies in the general population, is about 84 per cent. in the heterozygous male, and about 12 per cent. or less in the female.

Henry Cohen.


The image contains a page from the journal *Annals of the Rheumatic Diseases* with the following text excerpt:

**Non-Articular Rheumatism**


The author briefly outlines the historical background of the clinical entity of “fibrositis” emphasizing the paucity of pathological evidence. He then presents a classification based on the structure of the nodules found. A series of young soldiers suffering from fibrositis was investigated and pain charts were constructed based on the sites of nodules and trigger points. The back of every patient who died in hospital was dissected, special reference being made to the areas shown on the pain charts. As a result of this, in many instances herniations of oedematous fat through defects in the deep fascia were found, of three different types: (a) pedunculated, (b) non-pedunculated, (c) foraminal. The author quotes 22 cases in which removal of these fatty herniations resulted in relief of symptoms.

The distribution of localized collections of fat in the body is described together with the common sites of fatty herniation and it is suggested that oedema or herniation may produce areas of fat under tension which are in fact the painful nodules of fibrositis. An experiment is quoted in which relief of pain was achieved in thirteen of 22 patients with fibrositis, by inducing a state of clinical dehydration, thus reducing the tension in these fatty herniae. Endocrine imbalance leading to fluid retention is considered an important aetiologic factor with exposure to cold as the precipitating agent.

The author differentiates two syndromes due to abnormalities of fatty tissue: (a) fibrositis, occurring in different normally found fat pads; (b) panniculitis occurring in abnormal deposits of fatty tissue. He considers that Dercum’s disease is but a variant of these conditions.

Dietetic treatment associated with diuretics and dehydration is considered helpful and local massage and injections may cause relief of pain by disruption of the nodules. Surgical treatment is limited to the removal of larger fatty collections, but is rarely indicated.

*R. H. J. Fanthorpe.*


In extirpated lumbar fatty hernias, pathological changes can be found corresponding to definite clinical pictures which give to this condition an individuality distinguishing it from other types of lumbar fibrositis. Sometimes the patient has symptoms and signs of a lumbar fibrositis, and occasionally the history is solely one of fibrositis. More commonly there is a lumbago with multiple symptoms, depending on the tissues affected by the inflammatory process caused by the presence of the hernia.

Different variations and combinations of signs and symptoms in lumbar hernias are described, and the authors emphasize that, when a lumbo-sacral fibrositis exists, careful search must be made for other possible causes—exogenous and endogenous intoxications (especially from the gut), metabolic disturbances, septic foci, and endocrine disorders.

Histological examination of excised lesions reveals congestion and intense oedema in cases of speedy onset. In more advanced cases, necrotic lesions occur, with large lipophagic granules, and surrounded by an area of defensive tissue reaction, often with encapsulation and deposition of calcium salts. These findings are considered as pictures of the successive changes due to strangulation of the hernial pedicle.

Conservative treatment does not get rid of the hernias themselves, and the authors favour surgical removal, the technique for which they give. *Rénê Ménendez.*


**Endocrinology**


Articular lesions were produced in rats by daily subcutaneous injections of 2 to 4 mg. desoxycorticosterone (deoxycortone). The lesions appeared on the 10th to 20th day of administration before any other signs of disease became apparent and they resembled closely articular lesions in experimental or human acute or subacute rheumatism. Later vascular lesions of the periarthritis nodosa type, Aschoff bodies, sclerotic changes in the kidneys, and minute haemorrhages in the brain appeared. Although vascular and myocardial damage appeared in all treated animals, articular lesions were present in only 40 to 60 per cent. of the rats and their appearance was favoured by high salt intake, unilateral nephrectomy, thyroidectomy, or ovariectomy, and by cold. An injection of a streptococcal culture on the 14th day of treatment increased the incidence of arthritis. Similar changes can be produced by the administration of adrenal corticotrophic hormone but only if the adrenal cortex is intact. The possibility that rheumatic polyarthritus is due to an overactivity of the adrenal cortex secondary to bodily stress caused by various agents known to be in relation to the genesis of polyarthritis is discussed.

*Jan Brod.*


This is an account of the treatment with ACTH (adrenocorticotropic hormone) of one patient suffering
ABSTRACTS

from gout and three suffering from rheumatoid arthritis.

The first patient, who suffered from tophaceous gout, was considered to have a mild exacerbation of gouty arthritis in the right foot and right knee. He was given one injection of 25 mg. ACTH and within 24 hours was free from pain. He continued to take the salicylate he had been having previously; there was a period of complete quiescence after the single injection lasting for 7 days, after which there was a severe exacerbation of the symptoms.

The case history of one of the three patients with rheumatoid arthritis is given. The patient was a man aged 70 who had apparently had rheumatoid arthritis for 25 years. "He had moderate swelling and tenderness of the affected joints and slight limitation of motion in the shoulder joints." He was given 15 mg. ACTH intramuscularly every 6 hours for 5 days. There was rapid loss of pain and stiffness, and he was able to shave himself for the first time in 18 months. There was a great sense of well-being. When the injections were stopped the condition relapsed but not completely. The other two patients responded similarly.

The authors conclude that while ACTH is not a cure for gout or rheumatoid arthritis the objective results of treatment with it are superior to those seen with any other form of therapy.

W. Tegner.


Desoxycorticosterone acetate (DOCA) and anterior pituitary preparation (APP) were tested in unilaterally nephrectomized female rats fed a high protein and a high sodium diet. DOCA (2-5 mg. a day) elicited hypertension in all animals; APP had this effect in only a relatively small proportion of animals tested. Combined treatment with DOCA and APP had no more effect on blood pressure than DOCA alone; rather, the animals rapidly sickened and died. DOCA caused severe diuresis, while control and APP-treated groups showed only a slight increase in urine formation at the beginning of the experiment. In rats treated with crude APP there was an association between hypertension and increased adrenal weights. But these large adrenals are often haemorrhagic or necrotic. The relationship of adrenal weight to blood pressure disappears when animals are treated with a partially purified APP extract. The hypothesis that APP hypertension in rats depends on hypersecretion of DOCA-like compounds thus appears unlikely.—[Authors' summary.]


In wounds produced experimentally in rabbits treated with cortisone there is a striking reduction in the formation of new connective tissue: new blood vessels were few or entirely absent. After 8 days' treatment there were compact nests of fibroblasts surrounding the previously existing blood vessels. G. M. Findlay.


The permeability of the synovial membrane of the rabbit to fluids is increased by hyaluronidase and desoxy-corticosterone (deoxycortone) acetate (DOCA) and decreased by cortisone. 21-Acetoxyprogrenolone is as active as cortisone in decreasing permeability: it also antagonizes the effect of DOCA and hyaluronidase on the synovial membrane. Seven ambulatory patients with active rheumatoid arthritis received intramuscular injections of 100 mg. 21-acetoxyprogrenolone on the first day, 200 mg. on the second day, and 300 mg. on the third day for a total period of 14 days. In all cases there was a reduction in swelling, lessening of pain, and increased motility in the affected joints. G. M. Findlay.


Working at the Northwestern University Medical School, Chicago, the authors have studied the effect on the eosinophil count of injection of pituitary adreno-corticotropic hormone (ACTH) and of certain selected steroids, related in chemical structure to cortisone. The subjects were three patients with eosinophilia, in whom, for the previous 6 months, the eosinophil count had never been less than 2,000 per c.mm. The patients fasted for 12 hours before the injection, and eosinophil counts were carried out in the morning before, and 2, 4, and 6 hours after, the injection of the substance under test intramuscularly into the buttocks. The different substances tested were given in succession at 3-day intervals to each patient, beginning and ending with ACTH (25 mg.). In all three patients, ACTH alone and the substances tested reduced the eosinophil count significantly. Therapeutic trials of the seven steroids tested on patients with rheumatoid arthritis failed to show any ameliorating effect comparable to that shown by ACTH.

Walter H. H. Merivale.


Large doses of progesterone were administered to five patients with rheumatoid arthritis. No evidence of therapeutic benefit was obtained. No fall in the number of circulating eosinophils was noted after the injection of 100 mg. progesterone. It is suggested that the remissions of rheumatoid arthritis which occur during pregnancy are not due to progesterone but may be attributable to increased production of other steroids by the adrenal cortex.—[Authors' summary.]


In nine cases of articular rheumatism of 2 weeks' to 15 years' duration immediate relief from pain, with consequent increase in mobility, followed upon (a) intramuscular injection of 5 mg. desoxycorticosterone acetate in arachis oil and (b) intravenous injection a few minutes later of 10 ml. of a 10 per cent. solution of ascorbic acid (1 g). Pain was relieved within half-an-hour, the relief
Pituitary Adrenocorticotrophic mg. doses. During the treatment, swelling, and being cases was found more convenient to give the dose daily for muscularly doses in arthritis. The average length of treatment was one month.

Pregnenolone caused improvement in 76-6 per cent. of cases from the 10th to 15th day of treatment. Improvement consisted of diminution of pain, analgesics being unnecessary in most cases, diminution in articular swelling, and increase in joint mobility. Testosterone, on the other hand, not only failed to improve the condition of patients, but in some cases caused increase in pain.

S. S. B. Gilder.


In 1946 the adrenocorticotropic hormone (ACTH) was isolated from other hormones in the pituitary gland, its function is to stimulate the production of those steroids (from the adrenal cortex) which have oxygen linked to carbon in the 11-position (group 2 hormones or "sugar hormones", such as cortisone). It has a molecular weight of 20,000, an isoelectric point of 4.65 to 4.8, is soluble in water, and is thermostable. Thorn and his colleagues have studied the effects of a single dose of 25 mg. ACTH. The most constant findings were a diminution in the number of circulating eosinophils and an increase in the proportion of uric acid to creatinine excreted in the urine. Where there is adrenal insufficiency these findings are absent because the cortex fails to respond to stimulation by ACTH. Thorn has suggested the use of the latter property to measure adrenal function, and the application of this test in cases of the anterior pituitary syndrome would be of interest. The authors tried it in seven normal subjects (all medical men), six cases of Addison's disease, thirteen cases of rheumatoid arthritis, and a mixed collection of other conditions. In normal subjects the reduction in number of circulating eosinophils was between 80 and 100 per cent. (sternal puncture in three cases showed little variation in the marrow) and in cases of rheumatoid arthritis the fall was almost as dramatic; in cases of Addison's disease the decrease was but moderate. In normal subjects, again, the quantity of uric acid excreted tended to be increased and that of creatinine diminished so that the uric acid/creatinine ratio rose considerably (mean figure of 120 per cent.); in the cases of Addison's disease there was a slight increase in the ratio (average of 16 per cent.), while in those of rheumatoid arthritis there was generally no variation at all. In the latter the excretion of both constituents was low, but in some control cases the ratio remained unaffected because excretion of both constituents had increased. The significance of the observations made is fully discussed.

Clinically, a single injection of 25 or 50 mg. ACTH sufficed to cause marked and sustained improvement in some cases of rheumatoid arthritis. It is significant that in two cases in which no benefit was derived from ACTH there was also a reduction in eosinophil count; this suggests that the adrenals must be capable of reacting to the stimulus. In two severe cases of the disease, of longstanding, 25 mg. ACTH was given daily for about one week and a smaller maintenance dose thereafter; the response was spectacular. [The small discrepancy between the figures given in the summary and those in the text does not detract from the value of the paper.]

D. Preiskel.


On the basis of previous experiments indicating that desoxycorticosterone (deoxycortone) acetate (DCA) and impure lyophilized anterior pituitary preparations (LAP) may occasionally produce joint lesions in rats resembling "rheumatic arthritis", the author came to the conclusion that DCA in large doses created a "partial hypocorticoidism" and seemed to show effects opposed to those of glucocorticoids in shock, in the alarm reaction, and in hypertension. The increased glucocorticoid production under stress (in the "general adaptation syndrome") may be unable to keep pace with the mineral-corticoid elaboration and this may result in "diseases of adaptation" (rheumatism, collagen disease, gout, nephroclerosis).

A method of consistently producing arthritis, or perhaps more accurately, a chronic cellulitis of the limb, in adult male Wistar albino or peibald rats has therefore been elaborated: it consists simply of injecting 0.1 ml. of 4 per cent. or 1 per cent. formaldehyde into the hand-paw pad. If 2-5 mg. adrenocorticotropic hormone (ACTH) is given subcutaneously 25 minutes before the weaker solution of formalin the resultant inflammatory action is inhibited almost completely. With prolonged pre-treatment and the stronger formalin solution, although the immediate reaction was the same in ACTH-treated and control groups, the former group showed rapid subsidence of oedema and inflammation. Lyophilized anterior pituitary powder (40 mg. injected subcutaneously in 10 per cent. aqueous alcoholic solution) increased adrenal weight to the same extent as did ACTH but slightly increased the inflammatory reaction rather than diminished it. A similar difference was seen in the action on the regional lymph nodes, which shrunk...
in ACTH-treated but enlarged in LAP-treated rats. The former also showed most take-up of ink particles after phagocytosis.

In unilaterally nephrectomized rats drinking 1 per cent. saline, it was found that 5 mg. DCA in 0·1 ml. corn oil subcutaneously twice daily for 14 days aggravated the inflammatory response to formalin injection. In adrenalectomized rats drinking 1 per cent. saline, cortisone (5 mg. in two doses subcutaneously daily) decreased the response to formalin. DCA seemed to make no difference, either with or without cortisone.

Finally, rats fasted for 48 hours and subjected to various "alarming" procedures (freezing, forced exercise, spinal transection) and repeated 10 per cent. formaldehyde injections showed little or no inflammatory oedema; this was not ascribed merely to decreased vitality. In discussion of these results, the author suggests that gluco-corticoid inhibition of the inflammatory response is due to direct action on the tissues, possibly of a anti-hyauronidase or anti-histamine nature. He finds it difficult to explain the apparent antagonism between DCA and cortisone, mentioning substrate competition as a hypothetical possibility.

In his recorded experiments, which are not individually detailed, DCA did not act "antagonistically" when given with cortisone. It seems possible that DCA merely acted (in conjunction with nephrectomy and 1 per cent. saline imbibition) by retaining salt and water; inflammatory reaction may well be increased in size under such circumstances. E. G. L. Bywaters.


A review is given of the rapid development of knowledge of the clinical effects of Kendall's compound E (cortisone), and of pituitary adrenocorticotrophic hormone, since Hench's report, in early 1949, of the beneficial effects of cortisone in rheumatoid arthritis. Extension of these therapeutic methods is hindered at present by the difficulty and expense of preparation of the active principles. It is suggested that the implantation of fresh pig pituitary tissue by the author's technique may afford a useful alternative. This has been carried out on 62 occasions in 23 cases of polyarthritis, and it is claimed that some degree of clinical relief resulted in all except four cases, the relief, where it occurred, being rapid and of short duration. The laboratory findings were similar to those reported after administration of cortisone, that is, leucocytosis with diminished numbers of circulating eosinophils and lymphocytes, reduction in the erythrocyte sedimentation rate, and increase in the urinary excretion of urates and ketosteroids. In general, improvement was limited to 6 to 8 days, but renewal of the implant regularly brought further relief.

From one to four glands were used in each case, and were either implanted subcutaneously in the thigh under local analgesia, or minced finely and injected intramuscularly with penicillin. The activity of the glands was preserved by removing them from the freshly slaughtered animal directly into liquid air, and thawing only immediately before use. **G. C. Kennedy.**


Testosterone propionate, oestradiol benzoate, and certain of their derivatives have been used in large dosage in the treatment of ninety patients with rheumatoid arthritis. In addition to these, four patients with tophaceous gout, two with rheumatic fever, and two with painful shoulders received similar treatment. The authors of this paper consider that the results obtained in 81 of the ninety cases of rheumatoid arthritis were sufficiently striking to warrant publication. Improvement in respect of pain, oedema, weight, appetite, morale, and blood count and erythrocyte sedimentation rate was greater than they had experienced with any other type of therapy. They consider this improvement to be due to the non-specific metabolic activity of the steroid substances rather than to any specific anti-rheumatic property. It is also pointed out that these steroids are potentially dangerous when administered over a long period of time, and that caution should therefore be observed in such therapy. No response was obtained in four cases, and the other five patients are reported to have responded erratically. It is suggested that the value of testosterone itself may lie in the possibility that it is changed in the body to another steroid form.

This report is of considerable interest at this stage, but would be of much greater value if metabolic studies had been carried out pari passu with the clinical observations recorded. It also appears that some of the patients included under the heading of rheumatoid arthritis were in fact cases of ankylosing spondylitis—a distinction which is often ignored in American literature but which seems important to workers in Great Britain.) **W. S. C. Copeman.**


The authors report the treatment at the Presbyterian Hospital, New York, of rheumatoid arthritis in eight patients (sexes equally divided and ages ranging from 18 to 62) by the intramuscular injection of pituitary adrenocorticotrophic hormone (ACTH) at 6-hourly intervals, the average daily dose being 40 mg. Stiffness was relieved in 12 to 24 hours and clinical improvement rapidly followed. When treatment was discontinued all but one of the patients relapsed completely (again in 12 to 24 hours), but after a period of 4 to 10 days there was a return of the sense of well-being and some of the objective improvement originally noted was maintained. The patient who did not relapse passed from a state of euphoria into one of mania which was terminated, after 11 days, by electric convulsion. Two of the patients had subcutaneous nodules and these appeared to become much smaller; flexion contractures were improved; and there was a definite increase in the size of the heart in two of the cases. Excretion of sodium was decreased and that of potassium slightly increased (the gain in body weight was between 1 and 4 kg.); there was an increase in uric acid excretion and a temporarily increased creatinuria. The erythrocyte sedimentation rate (Westergren) returned to normal within a week and was followed.
by a rise within 48 hours of stopping the injections. The serum agglutinin titre against group-A haemolytic streptococci and sensitized sheep erythrocytes were not significantly affected, and serum cholesterol figures could not be satisfactorily interpreted. Sugar tolerance tests were not carried out, but in two of the patients the fasting blood sugar level rose when the daily dosage of ACTH was increased; increased excretion of glucuronic and gentisic acids, usually observed after ingestion of salicylates, did not occur.

The development in some cases of some of the features of Cushing's syndrome (as has been reported in patients treated with ACTH by others), and the fact that wounds would not heal, owing to absence of granulation tissue, during the period of treatment suggested the presence of hyperadrenalism, and post-mortem examination in one case showed the adrenals to be three times the normal size. The authors suggest that excessive amounts of adrenal steroid suppress "the activity of mesenchymal tissue" and ascribe the beneficial effects of ACTH to the production of hyperadrenalism. The results of these studies confirm the work of Hench and others (Proc. Mayo Clin., 1949, 24, 181).

The authors selected six patients with moderately severe rheumatoid arthritis, and gave them a low-sodium diet and 10 mg. desoxycorticosterone acetate (desoxycortone acetate) intramuscularly and 1 g. ascorbic acid intravenously every day, without relief of symptoms. The ascorbic acid was then discontinued, but the injections of desoxycorticosterone acetate and the diet were still used. Five days later, half of the patients were given adrenocorticotrophic hormone (ACTH) in divided doses without their knowledge. The other three were given distilled water under the same conditions. The three who received ACTH claimed prompt relief within 8 hours, and this continued steadily during the 3 days in which the injections continued. The condition relapsed promptly, however, when the injections were stopped.


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In this report the authors describe the treatment of 23 patients suffering from rheumatoid arthritis with deoxycortone acetate and ascorbic acid by the method described by Lewin and Wassén (Lancet, 1949, 2, 993). They point out that in rheumatoid arthritis there are great variations in the course of the disease quite apart from any effects of therapy. But they state that in their previous experience they have never seen sudden improvement comparable with that seen in six of their patients within 10 minutes to 2 hours of treatment by this new method. Of the other patients treated, fifteen were temporarily improved, with lessening of pain and spasm, increase of joint movement, and a subjective feeling of well-being, and in two patients the treatment failed.

[No laboratory data are given in this report. In view of the contradictory reports which are being published in the medical literature, much more detailed work will be necessary before the value of this form of therapy can be accurately assessed.]

W. Tegner.


At the Rheumatological Clinic in Lund various hormones and combinations of hormones have been tested for their effect upon rheumatoid arthritis and Still's disease. Adrenocorticotrophic hormone (ACTH) yielded favourable results in all of three cases. Pituitary implantation was attempted in seventeen cases in which illness had lasted for from 4 months to 4 years. The general impression of this treatment is favourable, particularly for patients under 40 years; six out of nine patients observed for 9 months have been discharged free from symptoms and with a normal erythrocyte sedimentation rate. The increase in 17-ketosteroid excretion following the implantation was very short-lived in every case. Adrenaline was administered in a small number of cases; the results were not impressive, although there was some diminution of joint stiffness. Deoxycortone acetate and ascorbic acid were administered in four cases in the dosage advised by Lewin and Wassén. There was no reaction in three and some improvement in the fourth. Progesterone was administered to four female patients in their fifties, with marked improvement in one; the dosage was about 100 mg. daily. Finally, testosterone in doses of 100 mg. 1 to 3 times daily was administered to ten men and ten women. There was subjective and objective improvement in every case and a considerable increase in the excretion of 17-ketosteroids.

B. Nordin.


A 62-year-old woman with a 6-months' history of rheumatoid arthritis was treated with adrenocorticotropic hormone (ACTH). The blood picture underwent the following changes. Haemoglobin value and erythrocyte count rose slightly, but fell at once after treatment. Serum iron level rose sharply during treatment, but fell thereafter to its original level. The white cell count rose from 6,000 to 12,000 per c.mm., and then fell; the mononuclear count remained unchanged. The eosinophil count was reduced from 125 to nil during the first and from 272 to nil during the second course of treatment. Marrow puncture showed an improvement in the haemato poetic picture, which became temporarily almost normal.

B. Nordin.
ABSTRACTS


In this paper the authors describe the effects of intramuscular injections of pituitary adrenocorticotrophic hormone (ACTH) in four patients suffering from different diseases.

ACTH was given in 15 mg. doses 4-hourly to a man with rheumatoid arthritis. The usual objective and subjective improvement began within 24 hours of the initial injection. During the four days of treatment the blood pressure rose slightly and he gained 11 lbs. (5 kg.) in weight, due to water retention as evidenced by the development of pitting oedema at the ankles. Oedema disappeared and the weight returned to its previous level within a week of stopping treatment. There was no improvement in the marked anaemia (erythrocytes 2,200,000 per c.mm.; haemoglobin 7·1 g. per 100 ml.). Symptoms began to return 12 days after stopping treatment, and relapse to the condition before treatment was complete within 8 weeks. The patient was then given intramuscular injections of seven different steroids each for 4 days at a daily dose of 200 or 300 mg. (except in the case of deoxycortone acetate, for which the total dose was 20 mg.). The substances administered were: pregnene-(4)-triol (17a, 20g, 21)-one (3)-diacetate; pregnane-3, 12, 20-trione; 17-methyl-5-androstendiol-3 (B), 17(a); 17-a-hydroxyprogesterone; 17-a-hydroxy-11-deoxycorticosterone-21-acetate; deoxycortone (deoxycorticosterone) acetate; ergostany1 acetate. No significant effects were observed with any of these substances. The patient now received a further course of ACTH and again showed the characteristic improvement and rapid relapse on cessation of treatment. It is reported that the above findings were typical of those observed in four other patients with rheumatoid arthritis similarly treated.

A single dose of 30 mg. ACTH produced symptomatic improvement within 30 minutes in a patient with atypical mild gout (blood uric acid level 6·7 mg. per 100 ml. or more). Within 12 hours relief was complete and at the time of reporting, 4 months later, there had been no recurrence. The only significant laboratory finding was a profound and sustained fall in blood uric acid level: 4·2 mg. per 100 ml. after two days; 1·7 mg. per 100 ml. after 4 days; and 3·9 mg. per 100 ml. after 2 months. In three other patients relief from symptoms of acute gout is stated to have been obtained when ACTH injections were started early enough.

The third case was one of psoriasis with arthritis manifestations; this woman received eighteen doses each of 15 mg. of ACTH at 6-hourly intervals. Within 70 hours of the start of treatment some amelioration in the skin lesions was noted: 24 hours later slight improvement in the joint condition began. The patient experienced marked elation. A week after she stopped treatment the skin condition began to deteriorate and a week later the arthritic symptoms began to return.

The fourth case was that of a woman complaining of attacks of asthma, hay-fever, urticaria, and pain in the wrists, hands, knees, and ankles. She had eosinophilia (1,000 to 3,000 eosinophils per c.mm. blood) and produced thick spumon containing many eosinophils. She received 10 mg. ACTH twice daily for 4 days. Within 2 days of starting treatment all symptoms had disappeared, the eosinophil count having fallen to normal within a few hours of the first injection. Ten days after stopping treatment the joint symptoms began to return. The eosinophilia returned 3 days after the last injection. [The title of this paper is quite misleading.]

G. I. M. Swyer.


The adrenal cortical hormone, cortisone acetate ("compound E") acetate; 17-hydroxy-11-dehydrocorticosterone acetate) was administered for short or relatively short periods to eight patients with rheumatoid arthritis. Definite, but temporary, improvement in the clinical and certain laboratory features of the disease was observed in each case.

Five of the eight patients had severe rheumatoid arthritis and were given large doses of cortisone acetate for short periods (total of 1 g. in divided doses over 8 days). The immediate results were decidedly pronounced improvement in three, pronounced improvement in one, and moderate improvement in one case. Prompt or fairly prompt relapse of the disease, with return of clinical manifestations approximately to their original severity, occurred after withdrawal of the endocrine preparation in four of the five cases. In the fifth case, 2 months after discontinuance of the use of cortisone, approximately 75 per cent. of the initial improvement was retained.

Three additional patients with less severe rheumatoid arthritis (two with moderate and one with mild disease) were given smaller doses of the drug for longer periods. With daily doses of 50 mg. the symptoms and signs were adequately, but not completely, controlled. Doses of 50 mg. of cortisone acetate given every other day were not as effective in controlling the clinical manifestations.

Because of the small number of cases reported and the brief periods of administration of cortisone, definite conclusions cannot be drawn. However, the results in eight cases indicate that this adenal cortical preparation, when given in large or relatively large doses, will rapidly suppress the clinical manifestations of rheumatoid arthritis. The results reported herein confirm the observations made originally and described recently by Hench, Kendall, Sloumb, and Polley.

W. S. C. Copeman.


Clinical notes are provided of two cases of rheumatoid arthritis treated with pituitary adrenocorticotrophic hormone (ACTH). In the first case the initial dosage was 25 mg. 6-hourly (100 mg. in 24 hours) for 2 weeks; then 50 mg. daily in three 8-hourly doses for 25 days; then 30 mg. daily in two 12-hourly doses for some 4 months. The second patient received 20 mg. 6-hourly (80 mg. in 24 hours) for 12 days; then 20 mg. 8-hourly (60 mg. in 24 hours) for 24 days; and finally 40 mg. daily in two 12-hourly doses for some 3 months. No untoward symptoms occurred in either case. Both patients improved dramatically, one within 72 hours, the other from the first day of treatment. In both cases relapse occurred when administration was discontinued for 3 days.

Kenneth Stone.

The nature of the effects exerted by the various adrenal cortical hormones are first described in three general groups: (1) Electrolyte regulation, involving urinary potassium, chloride, and sodium excretion, interstitial fluid control, and sweat composition. The most potent of the adrenal steroids in this respect is 11-desoxycorticosterone (deoxycorticosterone). (2) Regulation of intermediate metabolism, including effects on carbohydrate, protein, and fat metabolism, on uric acid excretion, and on the numbers of circulating lymphocytes and eosinophil granulocytes, which are reduced by adrenal activity. Examples of the “S” hormones responsible for these effects are the 11-oxyosteroids (Kendall’s compounds A and B) and the much more active 11:17-oxyosteroids (compounds E and F). (3) The adrenal androgens or “N” hormones, such as adrenosterone, resemble testosterone in structure and effect. They are excreted as 17-ketosteroids, the estimation of which in the urine serves as a measure of their secretion.

Only synthetic deoxycorticosterone acetate and whole adrenal extracts are at present available commercially as sources of the hormones. However, purified adrenocorticotropic hormone from the pituitary (ACTH) has become available in adequate quantities for investigation and has been shown on injection (10 mg. 6-hourly) to produce an increase in all three aspects of adrenal activity as listed above, while its prolonged administration gives rise to a clinical picture suggestive of a mild Cushing’s syndrome. Patients without intact adrenal glands, as in Addison’s disease, will not respond in this way. After the discovery by Hench and others (Proc. Mayo Clin., 1949, 24, 181) of the therapeutic effect of cortisone in rheumatoid arthritis, ten patients with rheumatoid arthritis were treated with ACTH (10 mg. 6-hourly). Clinical improvement was observed in 12 to 24 hours in nine of them and their erythrocyte sedimentation rate reached a normal level in about one week. On withdrawal of the hormone, symptoms returned in 1 to 24 hours. The return of symptoms, however, could be minimized by gradual withdrawal. Six-hourly injections of adrenalin produced slight improvement in some patients and the authors suggest its use to buffer the sudden withdrawal of ACTH. Very slight improvement only was obtained with injections of 0.1 ml. lipoadrenal cortex intramuscularly every 3 to 4 hours for 1 or 3 days in five patients with rheumatoid arthritis. In three cases of rheumatic fever treated with ACTH for 8 to 14 days a striking improvement was obtained. In one case, arthritis, pericarditis, and gallop rhythm disappeared in 48 hours. Although salt and water retention might be expected, the improvement in heart efficiency led to a diuresis rather than retention. In three cases of disseminated lupus erythematosus, ACTH administration led to a rapid disappearance of rash, fever, and splenomegaly, with fall of erythrocyte sedimentation rate to normal in one week, but no lasting cure resulted: two subsequent courses of ACTH had beneficial effects lasting up to 6 weeks. In a case of gout treated with ACTH, the urinary uric-acid concentration increased and that in the serum decreased; this was accompanied by increased mobility of the joints, diminished pain, and softening of tophi. A mild attack occurred 2 days after withdrawal, as had been reported in other cases.

In discussing the therapeutic effect of cortisone in rheumatic diseases, the authors suggest that, since ten times as much cortisone is required as is needed for a patient totally deficient in adrenal cortex, its action is pharmacological rather than physiological. No undesirable effects have been noted as yet, although the possible danger of persistent cortical hyperplasia is envisaged. [There are many interesting suggestions in this article which it has not been possible to mention.]

E. G. L. Bywaters.


Working at the New York Hospital, Kingsbridge Hospital, and Cornell University, the authors have studied the effects of the administration of pituitary adrenocorticotropic hormone (ACTH) to five patients moderately or severely ill with myasthenia gravis. The patients were all women aged 24 to 45, all under treatment with neostigmine bromide, taken at frequent intervals throughout the day, and three of them with ephedrine as well. For the purpose of the experiment the patients were allowed to continue this treatment and were warned not to expect any improvement from the injections of ACTH. After a week’s observation in hospital each patient received 20 mg. ACTH intramuscularly every 6 hours for 5 days. Tests were continued during, and for 3 months after the administration of the hormone, ten healthy women, aged 27 to 44, acting as controls. Electromyograms and myograms (by means of the ergograph) were taken daily at the same time each day, 3 hours after, taking neostigmine bromide before and during the hormone administration, and from 6 to 15 hours after neostigmine when the hormone administration had been completed, the frequency being reduced to twice a week after the first 4 days. Acetylcholine synthesis in the presence of serum was studied before the injection of hormone, on the third day after the last injection, and twice a week thereafter. Malaise, headache, fatiguability, diarrhoea, and excessive menstrual bleeding were experienced during ACTH administration and until the second day after the end of the course, after which patients felt increasingly well and voluntarily reduced their intake of neostigmine and other drugs. Facial muscle strength improved and general myasthenia, fatiguability, ptosis, and difficulty in swallowing diminished and the patients could hold heavy objects in their hands for some time. Appetite increased. The remission was incomplete, but the improvement had been maintained at the time of writing for 3 months in all cases. Electromyograms on the four severely ill patients before ACTH therapy showed a 35 per cent. decrease in action potential with 10 pulses per second and more than 55 per cent. decrease with 30 pulses per second; the one mildly ill patient gave the same reactions as healthy controls. After ACTH therapy the action potential in patients was maintained in the same way as in the controls. On the ergogram, the patients showed, before treatment, a variable impairment of their capacity for muscular work compared.

A woman of 53 years with a 14 years’ history of rheumatoid arthritis was treated with pituitary adrenocorticotrophic hormone (ACTH) for 15 days. The clinical effects were very similar to those reported by other authors, one feature being the disappearance of a large infiltrated area of fibrous tissue in the region of the left trochanter. Extensive biochemical and haematological investigations were carried out and the findings agreed with those of other authors. The following changes in steroid excretion were noted: excretion of 17-ketosteroids, corticoids, and glucocorticoids all rapidly increased shortly after the start of treatment. After 2 days there was a fall followed by a further rise to an even higher level. The excretion curves of all three steroids showed a remarkable resemblance to each other. Glycosuria was also noted. A few days after discontinuation of the treatment, symptoms and signs of the disease (including the infiltrated area over the trochanter) reappeared and laboratory findings returned to their previous levels. The patient was then treated with testosterone propionate for 14 days; this was followed by an increased urinary output of 17-ketosteroids, but no other clinical or pathological changes.

H. A. Burt.


The author attaches considerable importance to the role of the anterior pituitary in the treatment of “ankylosing” rheumatism and in support quotes the clinical improvement due, probably, to the gonadotropic factor in cases of rheumatoid arthritis during pregnancy. He has tried the effect of insulin in some cases of rheumatoid arthritis, but the results were poor. Six cases of chronic rheumatism (both osteo-arthritis and rheumatoid types) are described, in all of which a favourable response was obtained to the administration of anterior pituitary extract. The tendency to ankylosis was arrested and freer joint movement ensued. Severe focal sepsis interfered with the beneficial effects of the hormone. The extract of “total” gland was more effective than pure gonadotrophins and the author mentions the possibility of suprarenal stimulation with reference to recent American work on cortisone. He considers that the question of dosage merits close attention.

P. B. Woolley.


**General Pathology**


In order to provide an explanation of the tendency of severe typical rheumatoid arthritis to depress the serum albumin-globulin ratio, sera selected for their low ratios on the basis of chemical fractionation were subjected to more sensitive procedures. Electrophoretic analysis of samples from four patients confirmed previous observations of increases in the α (inflammatory response) and γ (antibody response) components, chiefly the latter. In addition three of the four showed a T component, not previously reported in rheumatoid arthritis serum. Less conspicuous in normal sera by the technic used herein, this fraction, like the γ component, is attributable to immunization. Examination of samples from ten patients by an immunologic method, utilizing rabbit anti-human γ globulin serum, showed greatly increased γ globulin values, which averaged more than twice the normal content of this component.

In a discussion of the "hyper-immunity" of severe rheumatoid arthritis it is suggested (a) that the responsible antigen is not necessarily of infectious origin but could be derived from the patient's own tissues, (b) that the antibodies serve no evident useful purpose, and (c) that for the sake of excessive antibody production the patient is apparently sacrificing his plasma albumin, his haemoglobin and his general tissue nutrition.

These data are interpreted as indicating that the hyperglobulinemia of active rheumatoid (atrophic) arthritis is the result of the combined effects of inflammation, tissue destruction and immunization, the last being the major contributor in all but the early stages of the disease.—[Author's summary.]


An account is given of the histological findings in synovial biopsy specimens taken from twelve patients with rheumatic arthritis. The authors consider the procedure to be especially helpful in those cases where other investigations have proved to be inconclusive, but it is contraindicated in cases of caseous tuberculous joint lesions or cold abscesses. René Méndez.


A modification is described of the haemagglutination test for rheumatoid arthritis (Rose and others, *Proc. Soc. exp. Biol.*, N.Y., 1948, 68, 1), involving the agglutination of sheep erythrocytes by the patient's serum. The original test was diagnostic if the titre at which the erythrocytes were agglutinated was sixteen times less than the titre at which erythrocytes sensitized with sheep-cell haemolysin from rabbit's serum were agglutinated. The modification involves the preliminary absorption of the normal agglutinin responsible for the agglutination of the unsensitized erythrocytes by the addition of inactivated serum of one-quarter volume of packed sheep erythrocytes. After standing for 40 minutes at room temperature with gentle shaking, the mixture is centrifuged and the absorption repeated once more. Serum may be stored at —20° C. for at least 5 months without loss of potency. The only additional absorption necessary is of the heterophile antibody in infectious mononucleosis, when one quarter volume of the packed sediment of a 20 per cent. boiled ox erythrocyte suspension is used. The technique is described in full [for the details, the original must be consulted].

The original Rose test, the modified test, and a streptococcal agglutination test (as performed by Lipman at the Presbyterian Hospital) were carried out in 39 cases of rheumatoid arthritis with x-ray changes (eight with spondylitis as well), fifteen cases of spondylitis alone, thirteen cases of early rheumatoid arthritis without x-ray change, fifteen cases of inactive rheumatoid arthritis (seven with spondylitis), nine cases of psoriatic arthritis, thirty cases of various other arthropathies, and in 28 control cases of non-arthritic disease and nine cases of infective hepatitis. In all except four of the cases of active rheumatoid arthritis the modified test gave a positive result, as against 61 per cent. positive results with the original Rose test and 58 per cent. with the streptococcal agglutination test. The modified test was negative in pure spondylitis, in inactive rheumatoid arthritis, in psoriatic arthritis, and in the controls with the exception of those with infective hepatitis, of whom two out of nine gave a positive titre (that is, a titre of 1 in 28 or higher, with complete agglutination in the first two tubes). In the four cases of active rheumatoid arthritis in which the result of the modified test was negative the Rose and streptococcal agglutination tests were also negative. In the thirteen cases of probable early rheumatoid arthritis without radiological change all three tests were negative.

The authors found no relation between the test results and the clinical severity of the disease. The results suggested that the factor concerned is an antibody and is different serologically both from the natural amoebocyte of human serum and from the heterophile antibody of glandular fever. E. G. L. Bywaters.
ABSTRACTS


Collins discussed cytological examination of synovial fluid and biopsy examination in the investigation of cases of the rheumatic diseases. Synovial fluid should be collected in three containers—the first for bacteriological examination, the second (oxalated) for cytological examination, and the third for study of clot formation. A high cell count (for example, 20,000 per c.mm.) differentiates rheumatoid arthritis from osteoarthritis (for example, 2,000 cells per c.mm.). Blood pigments are characteristic of traumatic effusions; mucin content is not of much significance.

Biopsy examination of the joint yields valuable evidence and the author believes that a positive diagnosis of rheumatoid arthritis can always be made if the following five features are present: (1) hyperplasia of synovial membrane and villi; (2) hyperplasia of lining cells; (3) massive lymphocyte or plasma cell infiltration with focal collections; (4) inflammatory hyperaemia and oedema; (5) absence of other specific histological features. Tendon sheath lesions in rheumatoid arthritis, tuberculosis, and synovioma also present characteristic histological appearances, as do subcutaneous nodules in various conditions. Finally, marrow biopsy may give valuable help in the diagnosis of myeloma and carcinoma.

Gibson compared the results of determination of plasma viscosity (relative to water) in the rheumatic diseases with results of various other empirical blood tests, such as the erythrocyte sedimentation rate and the plasma gel test. He used the technique of Woodmansey and Wilson (Ann. rheum. Dis., 1948, 7, 235), all tests being made in the same viscometer at 20°C on oxalated plasma. The normal range is from 150 to 180 (compared with water, 100).

Of 365 observations on 286 consecutive patients with rheumatoid arthritis 41 were within the normal range, compared with 38 out of forty in healthy persons. The erythrocyte sedimentation rate (E.S.R.) in the same cases (measured by the Spa Hospitals method) was within the normal range in 34 cases compared with 39 out of forty controls. The maxima of the distribution curves in controls and patients respectively were close together in the viscosity tests and widely separated in the sedimentation-rate tests, thus indicating that on this criterion the E.S.R. was the more informative. The correlation between viscosity and corrected E.S.R. was no better than that between viscosity and uncorrected rate. In thirteen cases viscosity was abnormal and E.S.R. normal, in twenty cases the reverse was true. In 21 cases with normal results in both tests there were typical clinical signs of active rheumatoid arthritis. It is concluded that E.S.R. and plasma viscosity show two different aspects of plasma abnormality, the former influenced mainly by fibrinogen, the latter mainly by globulin; there may be a time lag in the development of the latter abnormality, both in rheumatoid arthritis and in other diseases. Correlations with plasma gel formation and haematocrit readings were also found, but not with results of colloidal-gold, thymol-turbidity, or flocculation tests in ninety cases.

In ankylosing spondylitis only three out of 34 cases showed values within the normal range, but with a high E.S.R.; the reverse was seen in one instance only. The colloidal gold test gave weakly positive or negative results. In 24 out of 42 cases of osteo-arthritis the E.S.R. was raised, and in 22 out of 42 viscosity was raised. In cases of fibrositis viscosity was slightly raised in one, and the E.S.R. in four out of 32 cases. There was no increase in viscosity in primary and haemorrhagic anaemia. It is concluded that plasma viscosity determinations are important as aids, supplementing but not replacing determinations of the E.S.R.

In discussion Coke reported measurements of serum viscosity by a Whittington instrument in 400 cases of "chronic rheumatic disease". There was a significant correlation between serum viscosity and E.S.R. measured by the Wintrobe method, but a less significant correlation when the E.S.R. was corrected for anaemia.

Harkness mentioned the chaos bound to result from using multiple methods of measuring plasma viscosity and offered to calibrate any new viscometer by his own. Dawson reported that the plasma viscosity was less liable to unaccountable fluctuation than was the E.S.R.

E. G. L. Bywaters.


Pleuro-pneumonia-like organisms were isolated from the cervical or prostatic secretions of eight out of 25 patients suffering from a variety of rheumatic diseases. The cultures became negative after aureomycin therapy, but were unaffected by gold therapy. Aureomycin therapy produced subjective improvement of arthritic symptoms in six out of eight patients with demonstrable urinary infection due to pleuro-pneumonia-like organisms and in thirteen out of seventeen patients without this infection.

Martin Hynes.


Plasma viscosity was measured by a viscometer accurate to about one part in 500, only about 0.7 ml. of plasma being required for each test (Harkness and others, Acta tuberc. scand., 1945, 19, 153). Either sodium citrate or potassium oxalate could be used as the anticoagulant; with the former the range of normality was both absolutely and relatively narrower than with the latter, but there was the disadvantage that the proportion of citrate solution to plasma depended on the volume of erythrocytes present, since a given volume of blood was added to a fixed volume of citrate solution. It was therefore necessary to make an accurate haematocrit estimation followed by an empirical correction to the observed plasma viscosity. On the basis of the relation of citrated plasma viscosity to the maximum citrated erythrocyte sedimentation rate, the viscosity range was divided into eleven zones.

Tests on 289 patients with pulmonary tuberculosis showed that plasma viscosity increased with the spread of disease. In 42 tests on 32 patients with clinical and radiological evidence of pleural effusion, 76 per cent. of
the results lay in zones six to eight. This suggests that zones six to eight form a region in which it is highly probable that figures from cases of exudative disease will lie. If a pleural effusion was aspirated while the viscosity was in zone seven the effusion re-formed at once.

In cases of rheumatic disease more than 700 tests were performed. In every case in which the plasma viscosity was raised to an abnormal level (above 1·950) an underlying organic cause was found. In rheumatic fever the viscosity increased as the disease progressed and decreased during recovery. In rheumatoid arthritis the increase in viscosity was roughly in proportion to the severity of the pathological processes and to the systemic reaction. In cases of non-articular rheumatism with no systemic reaction, the viscosity values remained within normal limits.

The plasma viscosity test is non-specific. It appears to be of value in following the course of various rheumatic diseases as well as of pulmonary tuberculosis. Values depend almost entirely on changes in the plasma protein, particularly the fibrinogen and globulin fractions, since ultrafiltration experiments have shown that the viscosity of the ultrafiltrate is practically constant. R. B. Lucas.


Plasma obtained from the venous blood of patients with acute disseminated lupus erythematosus was incubated with bone marrow from patients with other diseases. Typical L.E. cells (Hargraves and others, Proc. Mayo Clin., 1948, 23, 25), and also nucleolysis and agglutination, were observed in concentrated preparations. It is maintained that these observations support the hypothesis that Libman-Sacks disease (acute disseminated lupus erythematosus) is a result of hypersensitivity. The L.E.-cell phenomenon is evidently immunological in nature and further investigation is required to elucidate the mechanism involved.

R. J. Ludford.

OBITUARY

LESLIE SCOTT LATHAM

Dr. L. S. Latham, President of the Royal Australasian College of Physicians, died on January 21, 1950, at the age of 71.

Dr. Latham deserved well of rheumatology, since it was under his presidency (and largely at his personal instigation) that a committee was appointed by his college to consider the inauguration of an Australian Rheumatism Council. This body was formed last year with Dr. S. A. Smith, an ex-president of the Royal College, as chairman. Their first act was to seek affiliation with the Empire Rheumatism Council, in England, and H.R.H. the Duke of Gloucester consented to accept the position of Patron of the Australian Rheumatism Council in addition to that of the Empire Rheumatism Council. Dr. Latham was consulting physician to St Vincent’s Hospital, Melbourne, and Examiner in Medicine to the University of Melbourne, of which he was deputy Chancellor from 1947 to 1949.