ABSTRACTS

Acute Rheumatism

Ultraviolet Blood Irradiation Therapy (Knott Technique) in Rheumatic Fever in Children. 


The authors give a detailed account of the results of ultraviolet light irradiation of blood in the treatment of 22 consecutive hospital cases of acute rheumatic fever with severe carditis, and of the results of this method in preventing recurrences in 107 cases of rheumatic fever over periods of 2 to 4 years.

The method consists of withdrawing 1-5 ml. blood per lb. (454 g.) body weight, citrating it, irradiating it with ultraviolet light, and returning it to the patient. This is done in one operation by means of a Knott "haemo-irradiator." Among the many advantages claimed for the technique are simplicity and complete absence of harmful effects.

The results of the series are thought to indicate that this form of therapy can be relied upon consistently to terminate an attack of rheumatic fever in children and to exert a prophylactic effect against further heart damage and against recurrences for at least 2 to 4 years.

Kathleen M. Lawther.

Antirheumatic Activity of Ascorbic Acid in Large Doses. 

Preliminary Observations on Seven Patients with Rheumatic Fever. 


In this paper certain observations are presented which appear to suggest that ascorbic acid, when administered in daily doses of 4 g. by mouth, possessed an antirheumatic activity in seven cases of rheumatic fever in adolescents treated by the authors.

They suggest that the beneficial effects recorded may have been related to increased activity of the adrenal cortex [although no evidence is given for this hypothesis]. There was a follow-up period of from 12 days to 2 months in three of these cases in which therapy had been discontinued. The other four cases were still receiving treatment at the time of publication of this paper.

W. S. C. Copeman.

Oral Penicillin in the Prophylaxis of Streptococcal Infection and Rheumatic Relapse. 


A series of 155 children between the ages of 5 and 13, convalescing from rheumatic fever, were given prophylactic doses of penicillin (100,000 units of calcium penicillin per 5 cent. glucose) by mouth three-quarters of an hour before breakfast at the Children's Heart Home, Lancing; 145 children of similar age groups, also convalescent, were not given penicillin and acted as controls. Weekly nose and throat swabs were cultured and erythrocyte sedimentation rates and anti-streptolysin O-titres were estimated monthly.

The duration of the streptococcal carrier state in the two groups was in the ratio of 4 : 1 in favour of the group given penicillin. There was one case of tonsillitis in the penicillin group and seven cases in the control group; in six of the latter the anti-streptolysin titre rose and in five the sedimentation rate was raised. There were no relapses of rheumatic infection in the penicillin group but four relapses occurred in the control group.

The author concludes that oral administration of penicillin has a definite beneficial effect as a prophylactic against streptococcal infection and relapses of rheumatism in children convalescent from rheumatism.

R. J. H. Fanthorpe.


The authors compare the results achieved with penicillin in 798 cases of streptococcal throat infection with those obtained in 804 cases of a similar infection without specific treatment. It was found that only two of the treated patients, compared with seventeen in the untreated group, developed rheumatic fever. Criteria for the diagnosis of rheumatic fever are given. The percentage of throat cultures free from beta-haemolytic streptococci was higher in the treated group than in the untreated. It was also found that penicillin therapy inhibited development of antistreptolysin O.

It is concluded that these figures are statistically significant, indicating as they do that rheumatic fever can be prevented by the administration of penicillin in streptococcal infections.

Kathleen M. Lawther.

Electrolyte Partition in Patients with Edema of Various Origins. Qualitative and Quantitative Definition of Cations and Anions in Cardiac Decompensation. 


Over a period of three to four weeks, the intake and urinary output of water and electrolytes in two young patients with congestive heart failure following rheumatic carditis were studied daily. One patient maintained a normal renal filtration rate and plasma flow, and in the other a 50 per cent. reduction in both was present. There was an absolute reduction in the excretion of sodium, such excessive reabsorption being considered to be due to extrarenal factors. Excretion of other electrolytes showed no significant change.

A study was also made of the effect of various diuretics. Of the mineral diuretics ammonium chloride, potassium
ANNALS OF THE RHEUMATIC DISEASES

chloride, and potassium acetate were found to act mainly on water excretion and only slightly on sodium and chloride ions. The effectiveness of these drugs reached a peak after three days and declined steadily thereafter. Mercurial diuretics resulted in a fluid output approximately double that in the control period and the increase in sodium excretion was even more marked.

J. Maclean Smith.

Effect of ACTH and Cortisone on Rheumatic Fever.


A report is presented on the effect of pituitary adreno-corticotropic hormone (ACTH) in three cases of rheumatic fever, one of which had previously been treated with cortisone. A girl of 15 with severe rheumatic fever of 3 weeks' duration when first seen, had a large pericardial effusion, showed marked orthopnea and cyanosis, and was extremely debilitated. A dramatic clinical response followed administration of ACTH in four to six daily intramuscular injections, a total of 400 mg. in 12 days. On the morning following the first injection the temperature returned to normal and the pulse rate fell from 140 to 85. Within 16 days the pericardial effusion had practically resolved. She developed furuncles in the axillae and the temperature rose on cessation of ACTH administration. A few days' treatment with penicillin soon cleared this condition.

A woman of 28, had rheumatic fever of 1 year's standing, with a slight response to salicylates and the subsequent development of pericarditis with effusion. When first seen she was debilitated, anaemic, and perspiring, her temperature was 40° C. (104° F.) and her pulse rate 100 per minute. Most joints were swollen and painful and there was an incipient decubitus ulcer on the back. She received 300 mg. ACTH in 10 days. Within 24 hours of the first injection the temperature became subnormal and remained so. The erythrocyte sedimentation rate fell and the erythrocyte count rose slightly. During treatment the decubitus ulcer became worse and the sites of previous venipunctures became infected; rapid healing, however, followed discontinuation of the treatment. The cardiac size and the pulmonary congestion were unaffected. On cessation of treatment the general condition worsened owing, apparently, to a streptococcal urinary infection which responded to treatment with dihydrostreptomycin, after which the patient gradually recovered over a period of 2 months.

A boy of 16 with illness of only 5 days' duration had high fever, painful but not swollen joints, and cardiac enlargement with a friction rub. He received 1,000 mg. cortisone in the course of 11 days, six injections being given daily. The temperature remained high, and he perspired profusely, was cyanotic, and required continuous oxygen. Articular and precordial pain remained severe and radiographs showed persistent enlargement of the cardiac shadow. Five days after cessation of cortisone, administration of ACTH was begun, 250 mg. being administered over 6 days. Moderate general improvement resulted. After discontinuation of ACTH the temperature again fluctuated and the general condition worsened. Penicillin and salicylates were given and gradual recovery followed.

[In view of the known increased susceptibility to infection and inhibition of granulation-tissue formation during treatment with ACTH and cortisone, illustrated by the fact that each of these three patients required subsequent therapy with antibiotics, it would seem that the concomitant administration of penicillin and, perhaps, sulphonamides, would be a wise precaution in severely debilitated patients.]

G. I. M. Snyer.


This paper is supplementary to a previous paper by these authors (J. exp. Med., 1949, 89, 687), which described the production in rabbits of a state similar to that of rheumatic fever in man by a series of multiple successive skin infections with group A streptococci of several serological types. It consists of a generously and well-illustrated comparison of material from the hearts of seven such rabbits which died or were killed within a period of 8 to 15 days after the last infection, and from the hearts in twelve cases of rheumatic fever in humans. No bacteria were cultured from the sections nor were any streptococci seen. No comparable lesions were found in normal control rabbits or in those dying or killed after one intracutaneous or intravenous inoculation of living or dead streptococci. Twenty photomicrographs illustrate the lesions in rabbits and are compared with those of nineteen carefully picked human lesions. The endocardial lesions are similar to the early palisading valvulitis in man, but the verrucae found in the human disease at a later stage are not seen.

The myocardial lesion " approximates almost, if not absolutely, that of rheumatic fever in man ", and so do the changes in the vessels. No periarteritis-like lesions are seen. After a review of published work on serum carditis with its accompanying periarteritis-like lesions, the authors conclude that the rabbit streptococcal lesions and those of rheumatic fever in man resemble each other closely, but are different in several respects from those of serum carditis in man and in animals.

[For the first time, something approaching rheumatic fever clinically and histologically has been produced in animals; that it should have been produced by this method is every strong evidence for Swift's hypothesis of the nature of rheumatic fever.] E. G. L. Bywaters.


The Q-T interval of 143 rheumatic children between the ages of 7 and 14 was measured; 102 with quiescent rheumatic heart disease had Q-T intervals similar to those of normal children, and 29 with fatal pancarditis had Q-T intervals within the normal range, but their average Q-T was slightly longer than that of normal controls.

In a group of patients with active rheumatic fever,
changes in the Q-T interval occurred parallel with changes in the clinical condition in about 66 to 75 per cent. of the cases, but the opposite was also noted in a significant proportion.

Duration of the Q-T interval may be determined in the study of rheumatic patients as a part of an over-all estimate of activity of the disease. Its usefulness is minimized by technical difficulties in measurement and by the infrequency with which it is abnormal.—[Authors' summary.]


The case histories of ten patients with acute rheumatic fever treated with adrenocorticotropic hormone (ACTH) are summarized. Nine had signs of valvular involvement, eight had fever, seven had joint involvement, four had pericarditis, four had congestive heart failure, three had subcutaneous nodules, and one had chorea. The erythrocyte sedimentation rate was raised in nine. Treatment lasted for between 10 days and 14 weeks, generally between 5 and 7 weeks. The initial daily dose varied between 30 mg. and 50 mg. and was given in four equal intramuscular injections. The dose was reduced progressively to as little as 10 mg. daily in some cases. The response to treatment was very variable. Fever and joint symptoms and signs usually subsided within 24 hours and at the most within 3 to 4 days, pericardial friction sounds in from one to 14 days, rheumatic nodules in 45 to 50 days, congestive heart failure in 14 to 56 days. The sedimentation rate fell to normal in from 6 to 87 days. The patient with chorea had treatment for 10 days only. There was striking improvement during treatment and his symptoms disappeared in 30 days. Several patients with marked tachycardia showed pronounced slowing of the heart rate soon after treatment began and in three the auscultatory signs of heart disease disappeared. One of these had had aortic diastolic and mitral mid-diastolic murmurs of moderate intensity, and two others had mitral systolic and mid-diastolic murmurs. The action of ACTH on congestive heart failure is twofold. It causes a retention of water which exaggerates the failure, and later it improves myocardial function which reduces the failure. The water retention can be counteracted by reducing the salt intake and by the administration of mercurial diuretics.

The premature reduction or cessation of treatment caused a return of symptoms and signs in several patients. A rise in the sedimentation rate was the most constant feature and a return of fever next. Pain and swelling reappeared in the joints of one patient and signs of pericarditis in another. The symptoms subsided promptly with resumption of treatment or increase in the dosage, but in several instances the sedimentation rate fell and fever subsided in a few days without more treatment.

Most patients given ACTH showed a rapid improvement in appetite and a gain in weight. Acne developed in several. Several patients had moderate anemia which disappeared with ACTH treatment. Elevation of the blood sugar level, glycosuria, and hypertension did not occur in any. One patient had severe abdominal cramp believed to be due to contaminating posterior pituitary extract in the ACTH. Later she developed severe mental depression, which gradually disappeared after treatment was stopped.

The result of treatment is regarded as favourable in all but one patient. This was a 7-year-old girl who was extremely ill with subcutaneous nodules, severe valvular damage, cardiac enlargement, and congestive failure. Her general health remained poor, her pallor persisted, her enlarged liver failed to shrink completely, and she later developed new subcutaneous nodules, showing that the rheumatic fever was still active. A. C. Crooke.


Although subcutaneous nodules were recognized and described as an important manifestation of acute rheumatic fever by Barlow and Warner in their classical account of this disease in 1881, the mechanism whereby these nodules are produced in the body is still poorly understood.

Ducket Jones and others (J. clin. Invest., 1937, 16, 125, 129) reported that they had been able to produce such nodules artificially on the elbows of patients by injecting some of the patient’s own blood subcutaneously over the olecranon process. They considered that the frequency with which such nodules could be produced and the size of the induced lesions were related roughly to the degree of activity of the rheumatic process. The clinical characteristics and the histological appearances of the induced lesions appeared to be identical with those of the naturally occurring nodules. In view of the observed facts that, microscopically, the structure of the subcutaneous nodule of rheumatic fever is similar to the structure of the myocardial lesions in this disease, and that most patients who develop nodules also develop cardiac disease, it appeared logical to conclude that the mechanism of the production of nodules is similar to that of the production of rheumatic heart disease. The possibility, therefore, of producing such nodules artificially seemed to offer a method of studying one of the basic processes of rheumatic fever.

In the present report the authors confirm and extend their previous observations. They conclude that the development of nodules in rheumatic fever results from injury to the subcutaneous fibrous tissue, the reactivity of which is altered by the rheumatic process, and that their previous hypothesis of a nodule-stimulating process present in the blood of active rheumatic patients is untenable. Nodules were also induced in some rheumatic patients by the subcutaneous injection of hyaluronidase. This observation, together with the reports of other workers that trypsin is also an effective nodule-inducing agent, suggests that enzymes may play a part in nodule formation, although their action may be non-specific, injury to the subcutaneous fibrous tissue being still the essential factor.

W. S. C. Copeman.


The author describes the painful pseudorheumatic and rheumatic manifestations encountered in normal and
sick children. The first group consisted of 1,000 normal school children, and the author studied their pains and the possible relation between these pains and infectious foci, climate, and mechanical factors. The second group was made up of children treated in private practice and in the National Institute of Cardiology, Mexico, who were similarly studied.

Of the apparently normal children 32.2 per cent. were suffering from pains of various types; these children were divided into four main groups. In the first were those with lower-limb pains (24.2 per cent.), which were probably due to lack of adaptation to environment, as would appear from their close relation to weather changes and the absence of any evidence that they were related to focal or general infections, or other aetiological factors. In the second group were the children who had true arthralgias (4 per cent.), which were probably due to such factors as infection, rheumatic fever, and mechanical causes. Children who had pains due to mechanical factors such as various defects of bone, muscle, and tendon were placed in the third group, and in the fourth group those with rheumatic fever. The various types of pain were studied in detail, and their aetiology determined not only by clinical manifestations, but also by the use of special examinations to detect any focal infection in the tonsils, teeth, or nasopharynx.

René Méndez.


The author estimates that in some 50 per cent. of cases of rheumatic fever there is no carditis; this view is supported by his clinical impressions. He reviews a series of cases of rheumatic fever from Taplow, 72 per cent. of which were complicated by carditis, because of selection. The chief signs of carditis were: (1) Mitral systolic murmur, usually early in onset, long, loud and blowing. The late mitral systolic murmur would appear to be particularly related to organic mitral incompetence, of which the author recognizes two types, the first type being associated with left ventricular enlargement and the second with aneurysmal dilatation of the left auricle. (2) Carey Coombs murmur, a soft low-pitched short mitral diastolic murmur. This is best heard with a bell stethoscope with the patient lying on the left side and is thought to be due to turbulence set up by the thickened mitral leaflets. This murmur was heard in 58 of 75 cases at Taplow. (3) Aortic diastolic murmur, soft, high-pitched, and short, heard best with a Bowles type stethoscope and present in 34 of 75 cases. (4) Cardiac enlargement. Radiology was considered disappointing in demonstrating cardiac enlargement. (5) Pericarditis. The presence of friction, pain, or an effusion provided good evidence of carditis. The electrocardiogram was disappointing since only 25 per cent. of tracings were regarded as typical, a marked contrast with cases of tuberculous pericarditis. Various methods of diagnosis of pericardial effusion are discussed; the alteration of Q-Tc and the position of a catheter in the right auricle are considered the most helpful signs. (6) Heart failure. The development of cardiac failure is considered to be grave, the majority of patients dying in a matter of weeks. Digitalis in high dosage was the most valuable drug. (7) Electrocardiographic changes.

The P-R interval was prolonged in 10 per cent. Prolongation of Q-Tc was considered to be a more valuable index of carditis. R. H. J. Fanthorpe.


The author considers that the extra costs involved in treating children with rheumatic fever in hospital are justified, provided that the facilities available include satisfactory arrangements for the child's psychological and educational development, necessitated by a stay in hospital of from 6 to 12 months.

The differential diagnosis in children and adults is discussed. Penicillin in large doses is advocated when the possibility of osteomyelitis is entertained. The occasional occurrence of clubbing and petechiae in rheumatic fever is mentioned. Rest in bed, flat, is advocated since the total cardiac work is reduced by this measure. Such rest should be continued until, in most cases, the erythrocyte sedimentation rate (uncorrected Westergren) returns to normal levels. The author quotes the occasional exception of the adolescent girl with a persistently raised sedimentation rate. The return of the Q-Tc to normal is also considered useful. Salicylates are not thought to be a "cure" for rheumatic fever but their use is advocated for the relief of pain and fever, the latter tending to reduce the work done by the heart. The occasional toxic effects are not considered sufficient to restrict their use. The employment of adrenocorticosteroid and cortisone is discussed but no definite conclusions are set out.

The author advocates efficient after-care of these patients, with the co-operation of the general practitioner and the school medical officer along the lines of the old L.C.C. scheme. R. H. J. Fanthorpe.


ABSTRACTS


Chorea Minor, Review of 175 Cases with Reference to Etiology, Treatment and Sequelae. SCHWARTZMAN, J. (1950). Rheumatism, 6, 89.


Chronic Articular Rheumatism (Rheumatoid Arthritis)


This report is based on a statistical analysis of the records of certain clinical observations on rheumatoid arthritis made by a number of clinicians throughout the country under the direction of the Scientific Advisory Committee of the Empire Rheumatism Council. Exhaustive interrogation and examination of 532 patients were carried out and for each patient a normal person or one suffering from a condition not related to rheumatoid arthritis, comparable in age, sex and civil state, was similarly investigated.

The clinical pattern of rheumatoid arthritis as described in standard textbooks is largely confirmed, but in a surprising number of instances the results bring no support to a widely accepted belief that certain antecedents are aetologically important. Among other unexpected findings are: that the risk of developing the disease increases progressively for males and single females with each 10-year age group from 15 to 24 to 45 to 54; that a history of events likely to produce psychological disturbance was obtained as frequently in the control as in the patient group; that there is no evidence that pregnancy or parturition, the disturbance of the menopause, home conditions, occupation and conditions of work, or any particular body type, is aetologically important. A statistically significant difference was found between the incidence of arthritis in the relatives of patients and those of controls, suggesting that a familial factor may be concerned. Figures are given indicating that peripheral vascular abnormalities are not only associated with rheumatoid arthritis, but frequently antedate its onset, suggesting the presence of some pre-existing constitutional abnormality which may be of aetiological significance. It was found that whereas 40 to 50 per cent. of patients denied that climate had any effect on their symptoms, the remainder were affected by climatic changes, most being adversely affected by cold, damp conditions.

It is suggested that further study of the familial factor, of the influence of climatic conditions, of abnormalities of the peripheral circulation, and of the effect of pregnancy and the menopause is especially desirable.

NOTE

This Report is being published in full as a supplement to this Journal.


A short general account is given of the recent work on the treatment of rheumatoid arthritis with cortisone and pituitary adrenocorticophrin. Of twelve cases of rheumatoid arthritis treated by the writer with a total adrenal extract, satisfactory results were obtained in two only and in five the treatment was a complete failure. Subjective and objective improvement in varying degree was observed in the remainder. This improvement persisted for 3 months after cessation of treatment in one case, in which the erythrocyte sedimentation rate was also reduced. Exacerbations of symptoms occurred in one case. Of three cases treated with deoxycortone one was completely unaffected, while the condition of the other two deteriorated.


The therapeutic results to be obtained in rheumatoid arthritis with cortisone and pituitary adrenocorticotropic hormone (ACTH) have naturally suggested the possibility that other steroid substances might yield similar results. Theoretically, Δ⁵-pregnenolone might prove to be effective in view of the probability that it is a precursor of more active steroid hormones, of its effect in decreasing
fatigue, of its reported sparing action on the suprarenal cortex, and of its lack of toxicity. It is also said to be equally effective when given by mouth as by the parenteral route.

The authors have treated thirty patients with rheumatoid arthritis of varying degrees of severity with pregnenolone or pregnenolone acetate by mouth in doses averaging 500 mg. daily for periods of about 6 weeks. They report that fifteen of the patients experienced striking relief, eleven showed a mild degree of improvement, and the condition of four patients remained unaltered. In sixteen patients in whom treatment was discontinued, improvement was maintained at the end of 6 weeks’ observation. No toxic effects of any sort were noted in this series. W. S. C. Copeman.


An attempt was made to evaluate the usefulness of certain steroids in the treatment of active rheumatoid arthritis. Comparable groups of cases were treated with large doses of methyl testosterone, testosterone propionate, ethyln oestradiol, progesterone, deoxycorticosterone acetate, and choric gonadotrophin, and with the same steroids combined with ascorbic acid given intravenously or intramuscularly.

The clinical results are described, and in view of the reported improvement in some of the patients the authors consider that further investigation is advisable. At the same time, however, they advise caution in the use of deoxycorticosterone and ascorbic acid. D. P. Nicholson.


Post-mortem studies over the past 5 years have revealed an incidence of rheumatic heart disease in patients dying of rheumatoid arthritis considerably higher than that in the general population. This fact is at variance with clinical findings in patients suffering from rheumatoid arthritis.

The authors carefully examined 114 patients with rheumatoid arthritis and 33 with rheumatoid spondylitis for cardiac abnormalities at the Army Rheumatism Centre, Hot Springs, Arkansas; 100 members of the staff were examined as controls. The examination was specifically directed to a discovery of minor cardiac abnormalities, and two different observers examined each patient independently. The methods used included auscultatory, radiological, and electrocardiographic ones, all the findings being carefully correlated.

The investigation revealed that the incidence of rheumatic heart disease, judged on clinical evidence, was similar in the arthritic and control groups.

R. H. J. Fanthorpe.


Sera from 224 patients with rheumatoid arthritis, 44 with other rheumatic disorders, and 102 controls were tested by agglutination, the antigen being a group-A type-1 streptococcus. More than half of the sera from rheumatic patients gave positive agglutination reactions, but only 2 per cent. of the controls. E. Neumark.


A beneficial response of rheumatoid arthritis, especially of recent origin, to the administration of copper salts is reported. Copper salts were found to be less toxic than gold salts. Copper salts may be given with safety to patients who cannot tolerate gold. Copper salts appear to be an adjuvant to, rather than a substitute for, gold salts.—[Authors’ summary.]


An investigation is described in which seventeen patients suffering from rheumatoid arthritis were given deoxycorticosterone acetate and ascorbic acid, according to the method of Lewin and Wässen (Lancet, 1949, 2, 903). Three patients noticed some subjective improvement, which was not confirmed objectively. Two of these patients were subsequently given saline injections with a similar result. In view of the normal day-to-day variations in the course of the disease, great care must be taken in assessing the results of treatment, and the authors are of the opinion that this latest method is of little or no value. D. P. Nicholson.


About thirty cases of rheumatoid arthritis complicated by amyloid disease have been reported in the literature and the author describes two further cases. The first patient, a woman of 23, had suffered from chronic rheumatoid deformity of the limbs for 44 years when she was found to have hepatomegaly and splenomegaly, and liver biopsy showed the presence of amyloid disease. Her plasma protein concentration was 7·5 g per 100 ml. and the thymol-turbidity test was negative; there was marked proteinuria. With treatment the joints improved, but the liver and spleen remained unchanged. The second patient was a man of 65 who had had rheumatoid changes for 4 years and was admitted because of haematemesis. He died of uremia, and necropsy revealed hepatomegaly due to amyloid disease, although the spleen showed no such change. The kidneys were sclerotic, probably following amyloid infiltration.

In “rheumatoid amyloidosis” the kidneys are first affected, then the liver and spleen, death occurring from uraemia in many cases. The author describes the theories of causation, mentioning vaccine therapy as a possibility. The amyloidosis is of the secondary type, the protein being deposited in connective tissue. Albuminuria in a case of rheumatoid arthritis should raise a suspicion of amyloid change. Oedema is not always present. The Congo red test is only of value in secondary amyloidosis. If the primary cause can be removed then the prognosis is reasonably good. Paul B. Woolley.

In this investigation by a team from the Mayo Clinic an attempt was made to demonstrate an effect upon the peripheral circulation, body temperature, and heart rate of contrast baths. The empirical use of hydrotherapy throughout the centuries for improvement of peripheral circulation in cases of rheumatoid arthritis, in which disorders of the circulation are common, had stimulated this investigation.

A review of previous publications is included. Observations were made of the blood flow by means of the venous-occlusion plethysmograph with a compensating spirometer recorder. In the upper limb the plethysmograph included hand, forearm, and elbow up to two inches (5 cm.) above the olecranon; in the lower limb the apparatus extended up to one inch below the tibial tuberosity. Sixty observations were made upon 51 patients with rheumatoid arthritis divided into three groups, and the results are set out in full in various tables.

The authors summarize their findings thus: "Patients of Group 1 were given contrast baths to the forearms including the hands; Group 2 to the legs including the feet, and Group 3 to both forearms and legs simultaneously. Contrast baths were given at temperatures of 110° and 60° F. (43.3° and 15.6° C.) beginning with an initial period of ten minutes' immersion in the hot water, alternating in the cold and hot water every one and four minutes respectively and ending with the hot water, making altogether a total of thirty minutes. This procedure produced a maximal average increase in peripheral blood flow of 95 per cent. in the upper extremities when these alone were treated, 62 per cent. in the lower extremities when these alone were treated, and 100 and 70 per cent. respectively, in the forearms and legs when all four extremities were treated simultaneously. Forty-five minutes after the contrast bath to four extremities simultaneously there was still an average increase in blood flow of 63 per cent. in the forearms and 55 per cent. in the legs. An average increase of 0.3° to 0.5° C. in oral temperature was observed as a result of contrast baths to the extremities." The heart rate increased in most cases; in Group 1 by an average of 10 beats per minute, in Group 2 by 9 beats per minute, and in Group 3 by 15 beats per minute. *Harry Coke.*


**Views on Felty's Syndrome.** (Betrachtungen zum Felty Syndrom.) Petry, H. (1950). *Z. Rheumaforsch.*, 9, 73.


**Studies on the Pathogenesis of Rheumatoid Arthritis.** II. The Differential Response of the Glucose Tolerance in Patients with Rheumatoid Arthritis Contingent on the Previously Induced Production of Adenosine Triphosphate.

**III. Clinical Observations During and After a Course of Insulin and Simultaneous Administration of Glucose and Glucose Metabolites to Patients with Rheumatoid Arthritis.** Haydu, G. G. (1950). *Rheumatism*, 6, 57 and 133.


[A brief preliminary note on successful treatment of two cases with nitrogen mustard.]

**ABSTRACTS**

423
treatment of osteo-arthritis, supported by a clinical review of the results of the operation. The authors point out that the force acting on the head of the femur during weight-bearing is very considerably greater than the total body-weight and quote Inman as showing that this force, in the normal subject, is at least twice as great as the body weight, the hip joint acting as the fulcrum of a lever whereby the glutei oppose the force of gravity. They describe a simple model in which a pelvis is balanced on a stationary femur and weights and pulleys are used to apply forces equivalent to the pull of the glutei and the body weight. The effects of these forces on the hip joint are recorded as changes in hydrostatic pressure by means of a capsule inserted into the hip joint. When the femur is adducted the vertical axis of the centre of gravity of the body passes farther away from that of the hip joint than when the leg is in the normal position, and similarly that with the leg in the abducted position the axis of the centre of gravity passes closer to the hip joint. The adducted position requires greater weights on the gluteal side of the hip joint to balance the pelvis than does the abducted position. In a patient weighing 150 lb. (68 kg.) the force acting on the joint in the adducted position will be approximately 450 lb. (204 kg.). After displacement osteotomy has been performed, so that the distal shaft of the femur bears against the pelvis, it may be shown with the model that the joint is by-passed and bears very little of the body weight.

The end-results in 75 cases of osteo-arthritis of the hip treated by displacement osteotomy are reviewed. Pain was relieved in 81 per cent.; the average shortening was 1 inch (2.5 cm.). The degree of movement after this operation was unpredictable, but in all successful cases there was limitation of addition (in 95 per cent. of these a solid check to addition was encountered at about the neutral position). The flexion range varied considerably, being between 10° and 60° in 47 per cent. of the successful cases and less than 10° in 30 per cent., while in 23 per cent. there was practically full range of flexion. In twelve patients with persistent pain there was absence of a block to adduction. The authors therefore regard this block as the criterion of a successful mechanical result and this is in conformity with their mechanical analysis. They believe that in those cases in which pain is relieved, but with no block to adduction, the result will not be permanently successful; an analysis of twenty cases in which displacement was inadequate showed a return of symptoms in an increasing number during a period of 4 years after operation.

[One of the most striking features of this paper is the demonstration of the return of joint space in some of the cases where body weight has been successfully transferred from the hip joint to the pelvis. Those interested should read the article in the original as it contains many important technical details of this apparently simple operation.]

John Charnley.


In fifteen cases of osteo-arthritis the proximal interphalangeal joints were examined at necropsy and radiological and histological studies made. The production

These three papers by the openers of a discussion on arthrodesis of the hip in coxalgia were read at the first Spanish Orthopaedic Congress at Bilbao in July, 1949. They are of interest in that they show the growing acceptance of Brittain's ischio-femoral arthrodesis for the treatment of active tuberculosis of the hip in adolescents and adults at the leading Spanish centres. Some [apparently rather involved] modifications and technical aids are described in Santurio's contribution. The number of patients treated by each surgeon is still small.

[In the discussion some older and more conservative methods were praised by a few speakers, but the general impression is that Brittain's arthrodesis is becoming the method of choice in one more country, and one which for long has been so largely dependent on Latin and German influences in surgery.] L. Michaelis.


(Spondylitis)


(Miscellaneous)

This paper deals with the treatment of fibrous and bony ankylosis of the temporo-mandibular joint. The author believes that condylectomy is as effective as arthroplasty. Asymmetry in unilateral cases is regarded as due rather to loss of the stimulus of function than to damage to condylar growth centres, and restoration of muscle function after freeing the mandible allows it to " catch up with its allotted span of growth ".

The author's operation consists of excision of the articular portions of the bones followed by skeletal traction, and is planned to minimize risk of damage to the facial nerve. The incision starts above the helix and curves downwards to end just anterior to the tragus. After reflection of the temporal fascia and muscle subperosteally, the joint is exposed from above by resection of the root of the zygoma and articular tubercle. The condyle and coronoid are then exposed subperio steally from above and removed by a combination of Burr and rongeur. [The stages of the operation are well illustrated.] Skeletal traction to keep the raw bone ends apart is applied through a Kirschner wire in the chin. The advantage of this over a wedge between the teeth is that it is a dynamic force: it stretches the contracted tissues and allows the muscles to work against tension and regain their strength. For children, a head-and-torso plaster jacket must be used to safeguard the cervical spine.

The author describes three cases. Illustrations show the extent of opening of the mouth at 4, 6, and 8 months after operation. [The problem of post-operative anterior open-bite is not discussed.] Timely application of skeletal traction to the angle of the mandible is suggested for treatment of fracture dislocation of the condyle.

V. E. Ireland.


Bone involvement of the cervical spine in brucellosis is considered to be extremely rare; only twelve cases have been recorded in the literature, yet, in a period of some two years, the authors collected sixteen cases. [Their references are mainly to French literature.] In brucellosis the cervical spine is examined radiologically only when severe or persistent signs and symptoms have drawn attention to that region. If, on the appearance of even the mildest and most transient symptoms, radiographs were taken of the neck a surprisingly high incidence of bony lesions would be found. Clinically, pain is present in an upper limb, or limbs, and often there is torticollis. The commonest lesion is a narrowing of the interspace between C5 and C6 with, or without, marginal lipping; fusion of two adjoining vertebrae may occur. The cerebrospinal fluid (C.S.F.) may show slight changes and lipiodol " block " may take place at the site of the lesion. In all sixteen cases there were positive agglutination reactions against Brucella melitensis and the organism was recovered from six of them.
The authors assume that the C.S.F. changes occasionally found as well as the lipiodol block must be due to brucellar arachnoiditis or meningitis. Nearly all the patients were middle-aged and, in a high proportion of them, the only radiological evidence was the narrowed intervertebral space referred to above. [Prolapse of the nucleus pulposus may cause all the signs and symptoms described, yet this condition, significantly enough, is not even mentioned in the differential diagnosis.] D. Preiskel.


After discussing the difficulty of assessing results of treatment in so variable a disease as brucellosis and the failure in turn of its treatment with every new antibiotic, the author describes nineteen cases of infection due to *Brucella melitensis*, proved by blood culture, treated at the Med. Clin. in Rome. The results were described when the patient was discharged from hospital. The results were shown by a sustained fall in temperature beginning between the second and eleventh days. A single course of aureomycin was given to seven patients and a combined course of aureomycin and dihydrostreptomycin, to one. These were all free from symptoms 6 months later. A further seven were treated by the combined scheme after an initial course of aureomycin, and these are also regarded as "cured", though the length of follow-up is not given.

Any favourable interpretation of results must take into account the short period of follow-up; relapses occurred in six out of the nineteen cases at intervals up to 6 months after treatment. There is little doubt, however, that the initial response to these drugs may be dramatic, as in the rapid recovery of a man of 64 who was comatose when treatment began.

A. Paton.


The authors point out that the lesion which they describe as pigmented villonodular synovitis masquerades in the literature under various names. Clinically the lesion causes a definite syndrome which includes swelling of a single joint, frequently the knee, of insidious onset and intractable course. There may be palpable nodules in the synovia and the joint fluid is hyperchromatic. The radiograph is negative.

The diagnosis is made histologically. There are synovial-lined villi with a vascular stroma. Within the stroma are collections of small lymphocytes, plasma cells, and monocytes but foreign-body giant cells are absent. The authors feel that this picture suggests an inflammatory rather than a neoplastic aetiology. The response to radiotherapy is slow but definite; a synovectomy may, however, be indicated. The case histories of five patients are detailed together with the histological findings.

Ronald Furlong.


The article presents an objective analysis of a group of 117 cases in which arthrodesis of the hip joint was carried out and the patient followed up at least one year later. No case of tuberculosis was included, and if bony fusion had not occurred by the end of 2 years the operation was considered to have failed. The cases are grouped under the following headings: (1) Poliomyelitis with dislocation; nine cases. Average age 22.5 years. Operation was performed for instability and pain. Seven patients discarded the use of crutches after operation. (2) Congenital dislocation of the hip: (a) Under 21. Eleven cases. Operation performed for limp, pain, fatigue, and deformity. (b) Over 35. Nine cases. Operation performed for pain and deformity. Results were better in the younger group [because, as Smith-Petersen pointed out in the discussion afterwards, the older group included five bilateral cases, in which arthrodesis is rarely indicated]. (3) Suppurative arthritis; nineteen cases. Average age 16 years. Operation performed for pain and restriction of activity. (4) Osteoarthritis; 69 cases. Average age 45 years. Operation performed chiefly for pain.

The operative procedures included the trochanteric graft (Hibbs type of fusion), the iliac graft, the intra-articular fusion (Watson-Jones type with Smith-Petersen nail), the intra-articular Smith-Petersen nail and graft, and intra-articular and square nails. The most satisfactory results appeared to be obtained with: (a) intra-articular fusion, plus a bone graft, plus Smith-Petersen nail; and (b) intra-articular fusion plus the insertion of three vitallium nails. In the whole series, failure of fusion in the required time occurred in 23 per cent of cases, and there was 3.4 per cent mortality. For fixation after operation, the average position was flexion 35°, abduction 10°, and external rotation 15°, but the most satisfactory positions for normal gait were those in which there was no shortening, but very slight adduction. Not all cases of pseudarthrosis were incapacitated and in some cases bony fusion occurred after as long as 24 months.

Nine charts are presented demonstrating severity of limp and maximum walking ability before and after operation, pre-operative hip pain and percentage failure in relation to pathological condition, percentage failure in relation to age and to type of operation, location of pseudarthrosis in cases where bone grafts were used, and incidence of knee and back pain before and after operation.

W. E. Tucker.


A method of fusion of the vertebral bodies of the lumbar spine in non-infective lesions by an extraperitoneal approach is described. The approach is to the left side of the bodies by an incision lateral to the lumbosacral muscle mass, the colon and kidney being pushed forward. A gutter is cut on the lateral aspect of the vertebral bodies and intervertebral spaces, and an osteoperiosteal graft from the iliac crest or tibia inserted. After 2 weeks recumbency, a spinal jacket is worn for a further 6 to 8 weeks.

J. S. Maxwell.


The aetiology of disseminated lupus erythematosus is discussed with particular reference to hypersensitivity of the tissues to infection, photosensitivity, and the
The Treatment of arthropathy, Hypertrophic Pulmonary are Study cases complicated 47 to months ratio lasting remissions but has been and leucopenia the changes membranes, on extent, Mortality Hargreaves and others in about 50 Albuminuria persistent. symptoms, of these substances. Robert de Barity and others have reached aetiology the other workers have reached

Pulmonary Hypertrophic Osteo-Arthropathy and Deformities of the Extremities Due to Intrathoracic Disease. Anatomical, Clinical, and Evolutional Aspects with Reference to 25 Cases. (L'Osto-arthropathie hypertrophiant pneumique et les dysacromielies d'origine thoracique. Aspects anatomo-cliniques et evolutifs (a propos de 25 cas.) A Study of the Interelevation and Pathogenesis of Clubbing of the Fingers and Pulmonary Hypertrophic Osteo-Arthropathy. (Essai sur les rapports et la pathogenie de l'hippocratisme digital et de l'osto-arthropathie hypertrophiante pneumique.) The Treatment of Deformities of the Extremities due to Intrathoracic Disease. (Le traitement des dysacromielies d'origine thoracique.) Bariety, M., and Coury, C. (1950). Sem. Hop. Paris, 26, 1681, 1709, 1719. These three papers together form a careful and well-documented study of hypertrophic pulmonary osteoarthropathy, based on a survey of the literature and on researches on a number of personal cases, which includes 25 fully-developed examples of the syndrome. Considerable attention is paid to the question of the relation between clubbing of the fingers and the complete syndrome. The authors conclude that the two conditions are identical, the latter being merely a more advanced stage than the former, as all stages in between can be recognized if searched for carefully. [This view of the clinical identity of finger-clubbing and hypertrophic pulmonary osteo-arthropathy is generally accepted in Britain, but is still a source of considerable dispute in France.] The clinical, radiological, biochemical, and pathological changes associated with the disorder are discussed in great detail. Certain points seem to stand out. One is that the fully-developed syndrome is seldom found except in association with tumours of the lung, though clubbing is associated with a much wider range of causes. Another is the not infrequent association of the characteristic limb changes with "acromegaloid" changes in the face and skull. Another point the authors lay stress on, because it has not received much notice in the past, is the frequency of neuropathic changes in the affected limbs—warmth of the skin, venous dilatation, alterations of sweating, paraesthesiae, hyperaesthesia, and altered pigmentation.

From these and other observations the authors suggest that hypertrophic pulmonary osteo-arthropathy is due to interference with the autonomic nervous system. They further suggest that the frequency of its association with lung tumours, particularly those arising near the hilum of the lung, can perhaps be explained by the rich network of autonomic nerves in that situation. The many points against this theory are frankly discussed and, in order to deal with some of them the authors further postulate that another factor, namely, a constitutional tendency towards hyperpituitarism, is concerned. In other words, the syndrome in its mildest form (clubbing) may develop whenever there is considerable interference with the autonomic nerves, but it is only likely to become severe when there is a constitutional tendency towards acromegaly.

Finally, treatment is discussed. The authors emphasize that only cure of the causative pulmonary (or other) lesion will lead to complete disappearance of the osteo-arthropathy. They have found, however, that in one or two inoperable cases relief of the osteo-arthropathy followed the administration of synthetic oestrogens. They suggest that this line of treatment is worth further study.

This is an excellent and thoughtful series of papers on a perennially baffling disorder. The authors' views on aetiology are interesting, though their hypothesis of an "acromegalic tendency" is open to attack from many points. But, as regards the "neuropathic" theory of causation, they might have made the point that other workers have reached similar conclusions about the aetiology of the peripheral neuritis sometimes seen in association with lung cancer. See, for example, Wyburn-Mason (Lancet, 1948, 1, 203.) John Forbes.

Treatment of Arthritis with "Anathion", Libenson, L., and Wittenborn, W. F. J. (1950). J. med. Soc N.J., 47, 105. The authors recall that one of them had used tetra-thiodiglycolic acid in the treatment of patients suffering
from rheumatoid arthritis, osteo-arthritis, and fibrositis in 1936. They now claim that the sodium salt of thiodiglycollic acid, "anathion", is equally effective and does not cause pain at the site of injection. They claim that their method of treatment is based on the mode of action of gold salts, which they suggest cause a continuous destruction of sulphhydril compounds in the tissues and the production of hydrogen sulphide or oxidized forms of glutathione. Sodium thiodiglycollate produces both hydrogen sulphide and oxidized glutathione in the tissues, but does not cause the toxic effects of the continuous destruction of sulphhydril compounds as does gold.

They describe a series of 34 patients suffering from rheumatoid arthritis, osteo-arthritis, and fibrositis treated with intravenous injections of anathion. Up to 60 injections were given on alternate days; the detailed case histories are given of four patients who suffered from rheumatoid arthritis and responded very favourably to treatment. The authors consider that their results show that sodium thiodiglycollate is highly effective in the treatment of rheumatic diseases. W. Tegner.


Brachial neuralgia—pain radiating down the arm—may be due to root irritation from a prolapsed intervertebral disk; the commonest cause, however, of root irritation is, according to the author, osteo-arthritis of the neurocentral joint. Of 66 selected cases of brachial neuralgia 24 were difficult to classify and were discarded; in the remaining 42 it appeared that there was irritation of nerve roots, and in 24 of these cases a single nerve root was involved (C6 and C7 being commonest). The 42 cases were classified as follows: (1) 24 of osteo-arthritis; (2) six of prolapsed disk; (3) twelve of "root irritation" (costo-clavicular syndrome and so on).

The author describes three illustrative cases. Diagrams show the relation of the neurocentral joint to the intervertebral foramen, and it is postulated that osteophytes formed in this joint are certain to narrow this foramen. The joint can be seen on antero-posterior and oblique radiographs. When a disk is damaged the neurocentral joint is subject to excessive strain and osteo-arthritic degeneration takes place in it, with subsequent narrowing of the intervertebral foramen. Radiographs usually show loss of the normal curve and narrowing of the disk space.

The author states that the three common causes of brachial neuralgia are osteo-arthritis of the spine (neurocentral joint), prolapsed intervertebral disk, and the "drooping shoulder" syndrome. The differential diagnosis is discussed.

In medical treatment, rest if required, possibly with immobilization. Injections of procaine sometimes give good results. Operation may be difficult and may entail damage to the cord. When there is no relief from medical treatment operation has to be seriously considered.

Paul B. Woolley.


Milkmans described under the title of "multiple spontaneous idiopathic symmetric fractures" a disease of the bones which was characterized by atypical pains in the lumbar region, spontaneous fractures with absence of callus formation, and some degree of general osteoporosis. In the radiograph symmetrical zones of decalcified bone are visible. The syndrome was found to be slowly progressive and failed to respond to any treatment. After reviewing the literature about Milkmans syndrome the author concludes, as did Herold and Guillain, that the existence of this disease is not proved. It resembles other diseases of bones such as renal rickets, osteogenesis imperfecta tarda, and osteomalacia, and is not a separate entity. This syndrome is found in different diseases of bones either due to the absence from the diet of vitamin D or to anatomical defects. The author describes a case in a 3-months'-old female baby who was admitted to hospital with whooping-cough and florid rickets. Symmetrical fractures of the 8th rib were seen in the radiograph; post-mortem examination showed that symmetrical fractures of the 5th to the 8th ribs had been taken place. The reason for the occurrence of fractures is twofold—generalized disease of the skeleton and body flexion due to the weight and muscular traction.

Franz Heimann.


A procedure is presented by which a hand seriously deformed and extremely painful due to rheumatoid arthritis was satisfactorily reconstructed. A deformed functionally impaired thumb was reconstructed by complete dissection and shortening of the proximal phalanx. Fusion of the metacarpophalangeal joint was obtained and the distal phalanx could be repositioned into its normal position. Useful active function could be maintained in this interphalangeal joint. The patient has been followed for 14 months.

A case is reported in which proximal shifting of the metacarpal heads was performed on the second and third metacarpal bones of the right hand. Functional and cosmetic improvement was obtained and maintained for a period of 14 months. The merits of the two procedures—one which removed the metacarpal heads and the other which shifted the cartilaginous cups—are weighed and discussed.—[Author's summary.]


Of eighteen cases of solitary loose bodies in the elbow, all in males, sixteen were on the right side; this suggests a traumatic origin for the complaint. In eight cases a history of injury was obtained which was of sufficient importance to be significant.

The clinical signs were pain and loss of function, and only in three cases was effusion or actual blocked movement the first sign. Limitation of active and passive movement was the most usual feature. The diagnosis is entirely radiological and two types are apparent: (1) sepal deformity with a loose body of increased density occupying the olecranon fossa; (2) loose body in the olecranon fossa without septal deformity.

Multiple chondromatosis and arthritis deformans are
ABSTRACTS

429

easily excluded. Olecranon sesamoids consist of one or two small nodules situated in profile over the olecranon and well behind the septum. Osteochondritis dissecans is only seen in epiphyseal areas covered by cartilage, on the condyle, the trochlea, the head of the radius, or sigmoid notch. This condition is rarer than sepal loose bodies.

The occurrence of septal loose bodies is easy to recognize by arthroscopy, but explanation of their occurrence is difficult. They may be due to a damage to the synovial membrane. If their origin is attributed to detachment of bone flakes it is difficult to explain the occasional operative finding that the body is extra-synovial. Section of loose bodies shows a central necrotic fragment, and in a few cases evidence of some necrosis of the surface of the humerus in the vicinity of the olecranon fossa has been demonstrated. The general impression given is one of aseptic necrosis of bone in the olecranon fossa, secondary to constant impingement of the olecranon. The fragment, once separated, takes on a thin cartilaginous coat by metaplasia and is moulded to the shape of the olecranon fossa. This theory differs little from that of the formation of loose bodies from synovial damage, but probably offers the most likely explanation.

[In this excellent paper the significant details of the gross and microscopical pathology of the condition are discussed, and the author places in correct proportion the views on its aetiology which have remained confused since the article of Morton and Chrysler (J. Bone Jt Surg., 1945, 27, 12) under the unfortunate title 'Osteochondritis dissecans of the supratrochlear septum'. It is made quite clear that in this region the anatomical conditions which form the basis of osteochondritis dissecans do not exist and that it represents a separate entity. The processes of solitary loose-body formation in any joint are still indefinite and no claim is made that the formation of loose bodies in the elbow-joint differs in any way from that in other joints; the increased frequency in the elbow is due to the anatomical peculiarity of the joint and can be most probably explained by micro-traumatic aseptic necrosis of the septum.]

J. G. Bonnin.


American authors, following Jaffe's description in 1935, consider osteoid osteoma to be a bone tumour, because of the absence of histological evidence of infection. Brailsford and others considered it to be a subperiostial abscess of infective origin. Saegesser of Geneva is of the opinion that it is micro-traumatic in origin and analogous with fatigue fractures.

Macroscopically there is a marked thickening of the cortical bone extending over a variable length along the diaphysis. The bone and the periosteum show no distinctive reaction. The histological appearances described vary with the opinions expressed by the authors. Jaffe finds dense bone surrounding a small central nidus which is never larger than a pea and contains vascular osteogenic connective tissue with trabeculae of new bone. Brailsford describes the culture of staphylococci from such cases and Saegesser has found small avascular necrotic fragments.

Clinically there is an insidious onset with localized pain, slight tumefaction, and absence of general signs. Radiologically there is a dense deposit of cortical bone in the metaphyseal region of the long bone surrounding a small clear zone, the central nidus. In a few cases slight narrowing of the medullary cavity occurs. The differential diagnosis includes chronic sclerosing osteomyelitis (distinguished by the febrile onset and frequent history of trauma), syphilitic osteo-periostitis, diaphyseal tuberculosis, malignant bone tumour, and infantile cortical hyperostosis. This last condition occurs only in infants, is multiple, and is accompanied by fever, irritability, anaemia, and a raised erythrocyte sedimentation rate.

None of the theories so far put forward explains the condition satisfactorily. It is considered that it is more likely to be a non-infective process; the only satisfactory treatment is by excision of the lesion.

[This paper is a useful summary of the views on osteoid osteoma, but the author does not produce any new evidence which might shed light on the aetiology.]

J. G. Bonnin.


This report from the Mayo Clinic describes an unusual group of cases related to Libman-Sacks disease in which the clinical and pathological findings were so similar as to constitute a recognizable syndrome. The patients, three male and four female, were aged 17 to 41 years. The first occurrence was a transient migratory arthritis of small and medium-sized joints which left no residua. The first evidence of renal involvement was albuminuria with casts, erythrocytes, and leucocytes in the urinary deposit. This was followed by nephrotic oedema with marked albuminuria, low serum albumin levels, and increased plasma cholesterol and total lipid values. Blood pressures of 125/75 to 180/105 mm. Hg were recorded. A mitral diastolic murmur with a recurrent pericardial friction rub was heard in one case, and apical systolic murmurs were heard in five others. Retinal changes were seen in three cases. One woman had erythematous macules on her face, trunk, and thighs, another had macules on her arms and trunk, and a third urticarial lesions on her feet and ankles. Ptosis of the eyelids occurred in one case. Most patients were pyrexial and anaemic, and had markedly increased erythrocyte sedimentation rates. Blood cultures were negative. After a period of massive oedema varying from 2 weeks to 10 months urinary output fell and rapidly increased nitrogen retention was followed by death in uraemia. Necropsy was allowed in four cases, of which three showed evidence of subacute and one of chronic glomerulonephritis. The kidneys were large and pale. The basic lesion was proliferation of the endothelial cells of the capillary loops causing obstruction; crescent formation and wire-loop changes were also found in some cases. The heart was always enlarged; myocarditis, valvulitis, pericarditis, and arteritis was usually present. The similarity of these findings to those in glomerulonephritis, rheumatic fever, and periarteritis nodosa, which are regarded by some workers as hyperergic diseases, leads the authors to suggest that the hyperergic state may be an important factor in the Libman-Sacks syndrome.

I. Ansell.

A review of the literature on Behcet’s disease, Reiter’s disease, Stevens-Johnson disease and ectodermosis erosiva pluriorificialis is presented, together with eleven case reports.


ABSTRACTS


Sciatica


Contralateral recurrence of a distal hernia at the same interspace occurring in four cases out of a series of 300 is reported. In three of these the recurrence was verified by operation, and one additional case is described in which contralateral symptoms due to a herniated disk were relieved by operation on the normal side.

The operative findings showed that the contralateral recurrence might be due to: (1) Incomplete removal of all the herniated material at the first operation, further trauma producing the typical symptoms and lesion. (2) Failure to carry out bilateral exploration at the first operation, the contralateral protrusion dating from the original injury. (3) A mid-line protrusion producing bilateral symptoms.

The author (wisely) advocates complete laminectomy in all cases in which bilateral symptoms are present, and a transdural removal of the herniated disk in cases of midline protrusion. It is to be noted that in some of these cases the clinical picture resembles that of a spinal neoplasm.

W. A. Law.


Non-Articular Rheumatism


Several investigators, principally Copeman and his associates, have shown the importance of fat tissue in the subfascial spaces as factors in painful syndromes generally diagnosed as fibrosis. From a review of the literature and observations on ten patients it is evident that abnormalities of subfascial fat tissue do constitute an important factor in the development of painful disabilities of the back. The principal factors responsible for chemical manifestations are oedema and herniation of fat tissues. A knowledge of the principles and the mechanism of referred pain is essential for the evaluation of the clinical picture. [Author's summary.]


The Development of Calcification of the Supraspinatus Tendon in Periarthritis of the Shoulder. (Evolution des calcifications du tendon sus-épineux dans les peri-


The Role of Mechanical Factors in the Production of Rheumatic Muscular Pain. (Die Bedeutung des mecha-

nischen Faktors für die Entstehung des muskel-

Endocrinology


The authors of this long and important paper are the members of the team who described the original successful results of the use of cortisone and pituitary adreno-
corticotropic hormone (ACTH) in the treatment of rheumatoid arthritis (Proc. Mayo Clin., 1949, 24, 181). In this article they describe further experience with these hormones, emphasizing, as they did in their previous communications, that these are to be regarded as studies in clinical physiology rather than in practical therapeutics.

They start with a useful summary of their experimental work and lines of thought leading up to their first successful use of cortisone in 1948. Since then they have given cortisone to 21 patients with rheumatoid arthritis, and ACTH in six similar cases; all these cases are reported in detail. Eight patients with acute rheumatic fever and six with severe lupus erythematosus were also treated, together with a few patients suffering with other disease processes. In the rheumatoid series, twelve of the 21 patients reacted in a “very marked” manner to cortisone; in eight the effect was “marked”, and in one only “moderate”. The drug was administered in some cases daily for periods up to 187 days in doses averaging 100 mg. daily. The clinical improvement followed the characteristic pattern previously described, while the effect of both hormones on the erythrocyte sedimentation rate was generally rapid. The haemoglobin level and erythrocyte count increased, while the blood protein patterns tended to become more nearly normal. A variety of metabolic and other biochemical effects were studied and in general bore a quantitative relation to the dosage of cortisone and ACTH and the duration of treatment. There seemed to be an initial retention and subsequent liberation of salt and water, together with a reduction in the serum potassium level. A negative nitrogen balance was sometimes provoked and when this was marked it appeared to be correlated with certain symptomatic side-effects. It is interesting to note that no impairment of carbohydrate tolerance was observed amongst the 23 patients given cortisone or ACTH.
Articular biopsies were performed in several cases and revealed a marked reduction of synovial inflammation after treatment with these hormones. On withdrawal, symptoms and signs of arthritic activity returned quickly in most cases, but in a few a state of remission appeared to have been induced which lasted in two cases for 10 and 12 months respectively. The various side-effects met with are exhaustively studied, but the authors' general conclusion is that these have been, to date, transient and reversible. The acute manifestations of rheumatic fever were generally abolished promptly by cortisone or ACTH. No evidence of the development of new cardiac lesions or increase in those previously present was observed within the following 8 to 10 months. It will, however, require more prolonged observation before the role of these hormones in the prevention and control of rheumatic carditis can definitely be evaluated.

The authors conclude that the action of cortisone appears to be "group-specific" rather than disease-specific or non-specific, and outline their studies of its action in several non-rheumatic conditions. They suggest that cortisone may constitute one of the body's chief defences against the action of stress agents on certain tissues.

[This paper may be said to summarize our knowledge of the effect of these hormones to date, and it should be read in full by all who have an interest in this rapidly developing field of knowledge.] W. S. C. Copeman.


This is a study of the effect of adrenaline (epinephrine), pregnenolone, and testosterone propionate in cases of rheumatoid arthritis, including rheumatic spondylitis.

Other workers have shown that the administration of adrenaline stimulates the pituitary-adrenal system in man. The action of cortisone and adrenocorticotropic hormone (ACTH) on rheumatoid arthritis encourages the hope that adrenaline may also be effective. Previous work has suggested also, though with less reason, that pregnenolone and testosterone may be of value. It has been claimed that pregnenolone brings about a reduction in 17-ketosteroid excretion, and clinical improvement, in rheumatoid spondylitis; a small proportion of patients with rheumatoid arthritis have also improved. It is claimed, with this treatment. It has been reported also that in 65 per cent. of patients with rheumatoid arthritis there is decided improvement within 24 hours when 100 to 300 mg. testosterone propionate is given intramuscularly daily.

The fall in number of circulating eosinophils is regarded as the most sensitive indicator of adrenal cortical activation. Blood for the count was obtained at 8.30 a.m. and this was followed immediately by injection subcutaneously of 1-5 mg. of adrenaline; a second count was made 4 hours later. Each of ten healthy controls responded by a fall in eosinophils of 40 per cent. or more; this figure was selected as a significant fall. Of sixteen patients given two or more such tests, in seven there was a consistently significant fall, in three a consistently insignificant response, and in six inconsistent responses.

Twelve patients were treated by subcutaneous injection of 0.5 mg. adrenaline in saline 6-hourly for 6 to 65 days. The results were uniformly negative.

Nineteen patients were given 100 to 300 mg. pregnenolone, usually daily but in some cases two or three times weekly, over a period of 7 to 51 days. No subjective or objective improvement was noted in any case, with the exception of one in which the general condition was thought to be somewhat improved.

Eleven patients with rheumatoid arthritis and two with gout were given 100 or 200 mg. testosterone intramuscularly, either daily or two or three times weekly. Apart from subjective improvement in three patients, there were no true remissions. In the two cases of gout the condition was made worse. Several patients experienced malaise; two women noted deepening of the voice and increase in hair on the upper lip. Kenneth Stone.


Two cases of rheumatoid arthritis were treated with relatively small doses of adrenocorticotrophin (ACTH). The first case was in a woman with a long history of arthritis. She was given 37.5 mg. ACTH daily in three divided doses for 4 days. This was followed by intravenous use of insulin, 1 unit per 10 kg. body weight being given three times a day for 30 days. Clinical remission occurred on the second day of ACTH therapy and was maintained in significant degree during the insulin therapy which, it was believed, would ensure a continued stimulation of the cortex. Eosinophil counts, which fell to zero under ACTH therapy, rose to above initial values during the first week of insulin treatment. Erythrocyte sedimentation rate, which had fallen a little under ACTH therapy, continued to fall for the first fortnight of insulin therapy. First signs of relapse were on the 19th day of insulin administration when the erythrocyte sedimentation rate had again risen. By the 23rd day optimism and euphoria had gone, pain in the knees returned, and relapse was quite evident.

The second case was in a woman of 43, severely disabled with rheumatic deformity and who also had extensive psoriasis. Initial erythrocyte sedimentation rate was 115 mm. Acetylsalicylic acid produced little benefit. After administration of 12.5 mg. ACTH four times daily for 2 days a great clinical improvement occurred, evident from the first evening, but the sedimentation rate only fell to 86 and the eosinophil count did not fall greatly. Insulin therapy, as in the first case, was then started and continued for a month. Joint pains did not recur for 3 weeks. Charts illustrating joint mobility changes are given. Psoriasis was much improved. Clinical improvement continued under the insulin treatment. The authors believe that insulin therapy prolonged the remission more than could be accounted for by mere chance. C. L. Cope.


A specific cytological change is described in the anterior lobe of the pituitary gland in rheumatoid arthritis. The cytoplasm of the affected cells is partly
filled with gamma granules and partly with simple protein granules; this is demonstrated by a special staining technique described previously by the author. He regards the cells as identical with those described by Crooke and Russell as “abnormal transitional basophil cells” found in large numbers in Addison’s disease and he contrasts them with the hyaline basophil cells described by Crooke in Cushing’s syndrome. He found the change only rarely and in isolated cells in a series of over 200 control pituitary glands, and he considers that it is secondary to adrenal dysfunction in both rheumatoid arthritis and Addison’s disease. A. C. Crooke.


Ten cases of active rheumatoid arthritis with an erythrocyte sedimentation rate above 25 mm. (Westergren) and with radiological signs of bone and joint destruction were chosen for careful study. The severity of each case was assessed by measurements of grip, of angles of flexion and extension of affected joints, of pain on pressure, and by joint function and movement tests, together with the patient’s statement of symptoms.

Three experiments were performed: (1) Three patients were admitted to hospital for a week or more for investigation and to become familiar with the procedure. They were then given an injection at the same time each day and measurements made ½ hour and ½ hour before and ½ hour after each injection. The injections given were of saline intravenously, procaine intravenously, and deoxycortone intramuscularly with ascorbic acid intravenously. (2) Three cases of rheumatoid arthritis in children were similarly studied, injections of saline and of deoxycortone acetate and ascorbic acid being given. (3) Three cases of rheumatoid arthritis were observed after saline injections had been administered for 7 days and deoxycortone and ascorbic acid thrice daily for 3 days. In addition case I which had responded dramatically to adrenocorticotrophin was treated with deoxycortone and ascorbic acid for 3 days and saline injections for a further 3 days.

The results of the investigation were studied statistically and it is concluded that deoxycortone and ascorbic acid have no immediate appreciable effect on rheumatoid arthritis. *Kathleen M. Lawther.*


This study was undertaken on the hypothesis that rise in blood level of naturally produced progesterone might be the factor responsible for the remission of symptoms in patients with rheumatoid arthritis in pregnancy, hepatitis, and jaundice.

The authors treated fourteen patients suffering from rheumatoid arthritis with progesterone and anhydroxyprogesterone for periods of 12 to 40 days. They made careful metabolic and other studies. Although definite clinical remission occurred in 1 patient on two separate occasions with each drug, there was no fall in the erythrocyte sedimentation rate or significant increase in the movement of the affected joints. Some moderate improvement was also noted in three of the other patients, but a comparable remission followed the use of an inert substance in each case. Three other cases seemed to be slightly subjectively improved, but no significant objective reaction could be detected. In one case only did the erythrocyte sedimentation rate fall towards a normal level.

The laboratory studies in this series were exhaustive and evidently carefully carried out. No relation could be shown between changes of this sort and clinical improvement.

The authors conclude that treatment with progesterone does not appear to be of any value in rheumatoid arthritis, in spite of reports from other centres to the contrary. *W. S. C. Copeman.*


Stimulation of the adrenal cortex by adrenocorticotropic hormone (ACTH), adrenaline, or stress is known to cause a reduction in the concentration of cholesterol in the cortex. No corresponding alteration in the cholesterol level is said to occur in other tissues and it is thought that the cholesterol in the cortex is the precursor of the cortical steroids. The authors have observed, however, that prolonged stimulation of the cortex with ACTH in man causes a fall in the serum cholesterol level. They measured the free and the ester cholesterol levels once or thrice daily, and the daily output of 17-ketosteroids and 11-oxysteroids in three normal men, two men with Addison’s disease, a woman who had apparently been cured of Cushing’s syndrome by bilateral subtotal adrenalectomy, and a woman with active Cushing’s syndrome. All the subjects were maintained on a constant diet and after a preliminary control period were given ACTH daily for 6 days. The dose varied between 26 and 100 mg. per day. In the normal subjects and in the patient with active Cushing’s syndrome there was no significant change in the serum cholesterol level during the first day of treatment, but subsequently there was a great fall in the level of ester cholesterol and a slight but definite fall in the level of free cholesterol. This change was most pronounced in the patient with Cushing’s syndrome. The patient with subtotal adrenalectomy showed the same change to a slight degree, but the two patients with Addison’s disease showed no significant change. The treatment of normal subjects with cortisone has no effect on their serum cholesterol levels. It is concluded that after the adrenal cortical cholesterol has been exhausted in the synthesis of cortical steroids the serum ester cholesterol is drawn upon for steroid synthesis. *A. C. Crooke.*


Thirteen paraplegic patients with osteoporosis of the affected limbs excreted an average of 0·63 mg. 11-oxycorticosteroids daily, which is a significantly high figure compared with 0·28 mg. in thirteen normal controls. In fourteen patients with rheumatoid arthritis, the mean level of excretion was 0·36 mg. Twelve of this group had
ANNALS OF THE RHEUMATIC DISEASES

osteoarthritis, but the excretion of 11-oxytococorticosteroids was not regarded as significantly elevated.

It is concluded that osteoporosis in cases of rheumatoid arthritis is not related to steroid hormone metabolism and that osteoporosis in cases of paraplegia may also be unrelated since it is localized, but the authors suggest that the disuse of the paraplegic limbs makes them more susceptible to steroid hormone influences.

A. C. Crooke.


The effect on body water and electrolyte distribution and renal function in normal dogs of the administration of deoxycorticosterone (deoxycorticosterone) acetate (DCA), 30 to 40 mg per day, and adrenal cortical extract (not containing DCA) was determined; the effects of giving these substances to adrenalectomized dogs in varying degrees of adrenal insufficiency were also studied. Extracellular space was measured as the volume of distribution of insulin (this method being found more reliable than the estimation of thiocyanate space); total body water was determined by the spade of distribution of heavy water (D2O), and renal function by insulin clearance, p-a-monohippuric acid clearance and maximal tubular excretory capacity for p-a-monohippurate (Tm\textsubscript{EH}p).

In normal dogs administration of DCA caused a decrease in intracellular volume with a corresponding increase in the extracellular space, apparent on the second day and maximal on the 11th day with a similar increase in the filtration rate, but Tm\textsubscript{EH}p was appreciably reduced. Serum potassium level showed a fall of 40 to 50 per cent., serum sodium level, unaltered. Total body sodium, measured in one dog, showed a 30 per cent. increase and total potassium a decrease of 12 per cent. Administration of adrenal cortical extract increased intracellular volume and total body water, with little change in the extracellular space or renal function; plasma sodium and potassium levels were unchanged.

Two adrenalectomized dogs maintained with 10 to 15 mg. DCA daily were treated with DCA as above, and similar changes were observed. Determinations made after withdrawal of DCA revealed a progressive increase in intracellular water and a similar decline in extracellular volume and progressive reduction in renal function.

Plasma volume showed no marked changes in these experiments and is not considered a reliable index of body water changes.

F. W. Chatoway.


A woman aged 34 years was seen in September, 1949, suffering from an iritis of 10 days' standing in her left eye. She gave a history of previous attacks of iritis 4 and 2 years previously, and of rheumatic fever in childhood. The condition resolved under the usual treatment; her physical condition was normal except for changes in various joints, classified as arthritic. A month later severe iritis developed in the right eye and she was admitted to hospital on November 23, 1949, with pain and redness of the right eye, tenderness, pain and limitation of movement of the left shoulder, swelling and pain of both knees with fluid in the left prepatellar bursa, and fever. In addition there was a soft apical systolic murmur. The diagnosis on admission was of rheumatic endocarditis and an early acute rheumatoid arthritis. During the first few days in hospital a severe episcleritis developed in the right eye.

Treatment with pituitary adrenocorticotropic hormone (ACTH) was started on December 12, 1949, and continued until December 31, 1949. Within 36 hours of the commencement of treatment by ACTH the episcleritis had practically disappeared, and within 1 week the iritis had subsided. The patient's general condition improved and 3 weeks after cessation of treatment the eyes were quiet.

A. G. Leigh.


This paper consists of a brief report, chiefly in diagrammatic form, of the more interesting laboratory findings during the administration of pituitary adrenocorticotropic hormone to two women, aged 53 and 72 years respectively, suffering from rheumatoid arthritis. It was found that to obtain a full clinical effect it was necessary to depress the number of circulating eosinophils below 50 per ml., for which purpose a daily dose of 25 mg. or more of ACTH had to be administered. This resulted in an increase in the total leucocyte count, fasting blood sugar level, urinary 17-ketosteroid excretion, and blood pressure. The anaemia showed a small improvement, the electrophoretic pattern of the plasma (previously typical of active rheumatoid arthritis with hypo-albuminaemia and increased total protein, a and g globulin, and fibrinogen content) returned to normal, and the erythrocyte sedimentation rate and antistaphylolysin and streptococcus-agglutination titres (all previously raised) fell. The histaminolytic action and level of non-specific hyaluronidase inhibitor in the blood were reduced and the hexosamine content of the serum also fell during treatment. All these changes were reversed after cessation of treatment.

Certain clinical observations are also commented upon; thus the weight of the patients was found initially to rise sharply by about 2 kg. (thought to be due to contamination of the ACTH preparation with anti-diuretic hormone of the posterior lobe of the pituitary gland), only to fall between the seventh and tenth days of treatment and to rise again thereafter. An abrupt fall in weight followed the cessation of the treatment. One of the patients had two attacks of gall-stone colic during the period of treatment, as a possible explanation of which the suggestion is made that ACTH causes an increase in muscle tone in the bile ducts as well as in the arteries (as indicated by hypertension).

G. I. M. Swyer.


This is an addendum to a previous report (Abstracts of World Medicine, 1950, 8, 297). Clinical and laboratory responses were evaluated in comparable groups of patients with active rheumatoid arthritis to treatment by various steroid hormones with and without ascorbic
acid. The possibility was considered that the enzyme systems of the body might be able to convert other members of the cyclo-penteno-phenanthrene ring system into 11-oxosteroids.

This report deals with the clinical results of treatment with progesterone, "because in the previous report, this steroid has given as good results as any of those tried". Progesterone was given in doses of 100 mg. twice weekly together with: (a) ascorbic acid in doses of 1 g. intravenously; (b) riboflavin in doses of 30 mg. intramuscularly ("because this substance is widespread in the body tissues and is an important co-enzyme with many dehydrogenases"); (c) saline. Results showed no significant difference as between groups (a) and (b). In further groups investigated no difference was found between results of two injections of progesterone and riboflavin, and two of deoxycortone and riboflavin. A further series received: (a) saline; (b) 5 mg. deoxycortone and 1 g. ascorbic acid; (c) 5 mg. deoxycortone and three injections of 1 g. ascorbic acid at 4-hourly intervals; (d) 25 mg. deoxycortone and three injections of ascorbic acid as in (c). In a final series similar to the last, riboflavin was substituted for ascorbic acid. There were again no significant results. 

Harry Coke.


A severe and typical case of rheumatoid arthritis received three forms of therapy with adequate control periods. The object was to compare the response to adrenocorticotrophin (ACTH) with those obtained with adrenaline, and with deoxycorticosterone and ascorbic acid. ACTH was administered by four injections of 25 mg. per day for 9 days, with control periods of 8 days before and after, when normal saline was substituted. Clinical assessment was made by measurements with goniometer and spring-dynamometer, by the screwplate test, and by noting changes in hand volume and number of analgesic tablets required. A response occurred which was not so well demonstrated by the clinical tests applied as a result of the over-all improvement warranted, and which was better demonstrated by cinematographic records. Classical objective laboratory findings were recorded. Complete clinical relapse occurred one month after the cessation of treatment.

In a second period 0.5 mg. of adrenaline in oil at 6-hourly intervals for 14 days was given, with control periods of 7 days on saline. A third period was devoted to treatment with 5 mg. deoxycorticosterone acetate and 1 g. ascorbic acid intramuscularly simultaneously three times a day for 4 days. Adrenaline caused no subjective or objective clinical improvement. There was a slight fall in erythrocyte sedimentation rate from 75 mm. to 50 mm. in 7 days. Eosinophil count fell 50 per cent. during the first 24 hours, but rose afterwards to levels above the control period [no 4-hour eosinophil counts were made here; cf. Adams, Proc. First Clin. ACTH. Conf., 1950, Philadelphia, p. 81]. Fasting blood sugar levels rose during administration, without glycosuria. There was some rise in blood pressure, no change in excretion of urinary 17-ketosteroids, but some rise in 11-oxosteroids towards the end of adrenaline administration. During administration of deoxycortone and ascorbic acid no clinical changes were observed. Eosinophil counts fluctuated. The sedimentation rate rose from 46 mm. to 90 mm. during the test period. No records are given of urinary steroid excretion.

The authors conclude that there was some stimulation of the adrenal cortex by adrenaline, which was much less marked than the stimulation by ACTH. 

Harry Coke.


The patients in the series described included 32 suffering from rheumatoid arthritis and two from ankylosing spondylitis; there were equal numbers of men and women. Testosterone (100 mg. daily for 30 days in one case and 200 to 300 mg. daily for 10 days in another) improved the general condition and increased the appetite, causing a gain in weight of 10 kg. in one of the two cases thus treated. It had no effect on pain or on the joint condition, and the erythrocyte sedimentation rate (E.S.R.) and a number of circulating eosinophils were unaffected. Progesterone (200 mg. daily for 10 to 30 days, in combination with 1 to 3 mg. ascorbic acid given intravenously in two cases) had no clinical effect on four male patients. The body temperature rose slightly, as did the E.S.R. and eosinophil count. Uric acid excretion increased and the histaminolytic activity of the blood decreased. In these respects, therefore, progesterone had effects opposite to those of cortisone (Compound E). The patients showed an increase in libido and in hair growth during treatment. Pregnenolone [anhydrohydroxyprogesterone] (100 mg. daily for 7 days) was administered in one case and exacerbated the joint symptoms. Pregnenolone (200 mg. daily for 5 days) was also given in one case only, and had a good analgesic effect. Combinations of testosterone, progesterone, and deoxycortone acetate, and of testosterone, progesterone, oestradiol, monobenzzoate, and deoxycortone acetate were tried in two cases without success.

A combination of deoxycortone acetate (5 to 100 mg.) and ascorbic acid (1 to 3 mg.) was tried in seventeen cases, in only three of which there was relief of pain and improved power of movement. Adrenaline (0.3 mg. subcutaneously four times daily for 5 to 12 days) was given to three patients without effect. Hexoestrol (15 mg. daily) was given to one male patient and resulted in exacerbation of joint symptoms, rise in temperature, and increase in uric-acid excretion. In two male patients with ankylosing spondylitis, the subcutaneous implantation of small pieces of placenta was followed by definite improvement in the general condition together with a transitory rise in the 17-ketosteroid excretion in one case, but had no effect in the other. 

G. I. M. Swyer.


The authors describe a modification of Thorn's method of testing the pituitary-adrenal response to intravenous
infusion of adrenaline (Thorn and others, J. clin. Endocrinol., 1948, 8, 589), by the use of the monosemicarbazone, an oxidation product of adrenaline, termed adrenochrome. They claim that their technique is simpler, 0·5 mg. of this substance in 10 ml. pyrogen-free normal saline can be given by syringe injection over a period of 2 to 3 minutes without causing a rise in blood pressure or any untoward symptoms.

They carried out 58 experiments on forty patients with various pathological conditions and compared the response to adrenaline infusion (37 cases), adrenochrome infusion (three cases), intravenous injection of adrenochrome (twelve cases), and intramuscular injection of 25 mg. adrenocorticotrophin (ACTH) (one case). They claim that the results with adrenochrome are in agreement with those obtained with adrenaline.

Analysing the 58 experiments as a whole, they classify the response as: (1) positive (fall in both the eosinophil and lymphocyte counts in the circulating blood) in nineteen cases; (2) doubtful (fall in eosinophil count without alteration in lymphocyte count or vice versa) in ten cases; (3) dissociated (fall in eosinophil count with rise in lymphocyte count, or less commonly the reverse) in nineteen cases; (4) negative. Fluctuations in eosinophil and lymphocyte counts were not considered significant unless they were in excess of 10 per cent. of the initial level.

They stress the value of these tests not only in the diagnosis of adrenal insufficiency but also in assessing the non-specific defence reaction to infections, surgical operations, and the like, and claim that the response may have prognostic importance in such conditions; they mention a case of advanced pulmonary tuberculosis and one of severe chronic bronchitis and emphysema in which the response to Thorn’s test was negative a few days before death, though the suprarenals were found to be normal at necropsy. They also mention a case of severe rheumatic pericarditis and a case of paratyphoid fever in which a negative response was followed by a positive response; both patients recovered.

[This paper is not clearly set out and the tables do not give adequate confirmation of the claims made, nor do they show a fall in eosinophil count in excess of 50 per cent.]

Robert de Mowbray.

Occurrence of Peritonitis during ACTH Administration.


The authors report two cases in which peritonitis developed during administration of adrenocorticotropic hormone (ACTH) and in which the diagnosis was made difficult by the masking of certain cardinal signs.


In seventeen subjects without adrenal disease intravenous injection of insulin in a dose of 1 unit per 10 kg. body weight caused a reduction in blood sugar level varying from 27 to 88 per cent. This fall was accompanied by a reduction in circulating eosinophils, which was equally variable but averaged 68 per cent. of the initial figure. There was no correlation between the magnitude of the fall in eosinophil count and that in blood sugar level. If glucose was given with the insulin to prevent the fall in blood sugar level, no fall in eosinophil count occurred, showing that the effect was due to the hypoglycaemia. In three cases of Addison’s disease and in one of hypopituitarism, insulin hypoglycaemia caused no corresponding fall in eosinophil count. It is suggested that the test may be of value in the diagnosis of adrenal insufficiency.

[The work confirms, but was done in ignorance of, similar findings in the U.S.A.]

C. L. Cope.


General Pathology


Apart from the close association between the rheumatic diseases and bacterial allergy, it has occasionally been suggested that they have a close connection with the allergic diseases proper, such as asthma. In fact, if asthma is present in a patient suffering from rheumatoid arthritis or rheumatic fever, the diseases tend to alternate in that the onset of asthma is often preceded by a remission of the arthritis, or vice versa.

The whole subject is reviewed, and from a study of cases seen at the III Medical Clinic of the University of Helsinki between the years 1934-48, certain conclusions are drawn: (1) Rheumatoid arthritis and rheumatic fever have no greater tendency to occur in association with asthma than might be expected from the general incidence of these diseases. (2) The variations seen in the eosinophil count in the rheumatic diseases are typical of any general infection, and the high counts typical of the allergic diseases proper are not found in rheumatism.

(3) The administration of the anti-histamine drugs tends to aggravate rather than to relieve the symptoms of rheumatoid arthritis. (4) When asthma occurs together with rheumatoid arthritis or rheumatic fever, there tends to be a close relationship in time between a remission of the arthritis and the onset of asthma. Similarly, the onset of an acute recurrence of rheumatic fever is often associated with a remission of previous asthmatic symptoms.

The allergic diseases proper may be considered as being essentially vagotonic in nature, whereas the rheumatic diseases display many features indicative of sympathicotonia. The onset of either group of diseases with the attendant autonomic state, is, therefore, more or less incompatible with the presence of the other. A distinction must be drawn between bacterial allergy, important in the pathogenesis of rheumatism, and true allergy or atopy, which appears to have no fundamental connexion with rheumatism. On the other hand, anaphylaxis may give rise to rheumatic-like conditions, and here the mode of onset may be through the "general adaptation syndrome" of Selye, the reaction of the organisms to an unusually strong stimulus, such as that of anaphylaxis, possibly leading to the development of rheumatism.

D. P. Nicholson


C-protein is a substance present in the serum of persons suffering from pneumococcal pneumonia, acute rheumatic fever, staphylococcal osteomyelitis, and bacterial endocarditis. It gives a precipitation reaction with the somatic C polysaccharide of the pneumococcus; it is antigenic, and antisera may be produced against it by injection of purified C-protein into animals. The presence of C-protein may be shown by either precipitation tests with pneumococcus C polysaccharide, or precipitation with its specific antiserum, which gives no reaction with normal serum proteins. Cases are described which suggest that the presence of C-protein in the sera of cases of proved rheumatic fever is a useful indication of the degree of activity of the disease process, and may help in the differential diagnosis of complications. In general the concentration of C-proteins runs parallel with the erythrocyte sedimentation rate, but there are exceptions in both directions.

C-protein was paradoxically absent in several cases of Sydenham's chorea.

C. L. Oakley


Sera from patients suffering from acute rheumatic fever or from streptococcal infections were collected during 1947, 1948, and 1949, and titrated for streptococcal anti-hyaluronidase and for antistreptolysin O. In general the antistreptolysin O and anti-hyaluronidase titres of the sera of patients recovering from rheumatic fever were higher than those in patients recovering from scarlet fever: there was some variation in the magnitude of these differences from year to year.

Sera taken from scarlet fever patients at the onset of
ANNALS OF THE RHEUMATIC DISEASES

symptoms and 3 weeks later showed that patients vary considerably in their response to the two antigens; the increase in titres showed no correlation with one another; on the whole the response to streptococcal hyaluronidase was poorer. Many patients convalescent from scarlet fever had very low antihyaluronidase titres in their serum, whereas sera from rheumatic fever patients had relatively higher values.

The defects of the antihyaluronidase test as a diagnostic procedure are pointed out. C. L. Oakley.


A number of animal experiments are described which demonstrate that exposure to stress leads to a fall in the eosinophil leucocyte count and that this is caused by an increase in the secretion of pituitary adrenocorticotropic and so of 11-oxy steroids from the adrenal cortex. One means by which the stress stimulus is conveyed to the hypophysis is by the secretion of adrenaline and the injection of adrenaline will produce a fall in the eosinophil count similar to that provoked by stress, provided that the pituitary and adrenal cortex are intact.

This result of adrenaline injection may be used as a clinical test of the efficiency of the pituitary-adrenocortical system in man. When 0.2 mg. adrenaline in 200 ml. physiological saline is infused intravenously over a period of one hour a biphasic response occurs, the eosinophil count rising during the first hour and subsequently falling below its original level, the maximum reduction being found at the fourth hour. The average reduction in eosinophil count at the 4th hour is by 7 per cent. of the pre-injection figure in cases of Addison's disease, by 18 per cent. in cases of panhypopituitarism, and by 60 per cent. in normal persons. Similar results, with somewhat greater variance, are obtained when the adrenaline is given subcutaneously in a dose of 0.3 mg.

Peter C. Williams.


The differential sheep-cell agglutination test for rheumatoid arthritis was first described by Rose and others (1948), although, as the authors point out, Waaler (1939) had previously demonstrated the presence, in sera from 51 per cent. of cases of rheumatoid arthritis, of a relatively thermostable activator of sheep-cell agglutinins, which was unrelated to blood-group or heterophil antibody.

By Rose’s technique, the authors examined 17 sera from healthy persons, 73 from patients with non-arithmetic conditions (including bacterial infections, virus pneumonia, colitis, infective hepatitis, allergic diseases, glomerulonephritis, infectious mononucleosis, thryotoxicosis, osteomyelitis, neoplasms, and uterine and intestinal bleeding), 83 from cases of degenerative joint disease, 27 from those with miscellaneous diseases of the locomotor system, and 26 from cases of rheumatoid arthritis including spondylitis (three cases) and Still’s disease (two cases).

The only positive results (titre of 1 in 16 or over) were in thirteen of the 21 cases of peripheral rheumatoid arthritis, one case of degenerative joint disease, and in one case out of three of scleroderma. The cases of Still’s disease and spondylitis ankylopoietica without peripheral joint involvement gave negative results, as did also three cases of inactive rheumatoid arthritis, and five cases of active rheumatoid arthritis. "Those patients having the disease for three years or more would be more likely to exhibit a positive" reaction. “As a test for the early diagnosis of rheumatoid arthritis, its usefulness would appear to be of limited value.” E. G. L. Bywaters.

The Significance of the Skin Reaction to Histamine in Rheumatism Associated with Focal Infection. (Die Bedeutung der Histamin-Haut-Reaktion bei Rheumatismen im Hinblick auf die Fokaltoxikose.) Muller, P. (1949). Z. Rheumaforsch., 8, 332.


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